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EDITORIAL

PLAGIARISM FREE ACADEMIC ENVIRONMENT

Anwar Ali Siddiqui[1], Shamim Mushtaq[2]
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Plagiarism is found to be the most common form of misconduct among researchers across the globe. It is particularly affecting the biomedical sciences communities engaged in writing and reporting research. Unfortunately many young writers are not aware of the various types of plagiarism they might unintentionally indulge in [1]. Even in some cases, the writers do not consider plagiarism as a serious issue. Plagiarism can range from simple dishonesty in reporting parts of other's work without proper attribution to a more serious issue such as duplicate publication. With the emergence of new technologies and search engines it has become easier to copy and paste from innumerable sources and yet not citing the exact source. As one can accumulate information in a fraction of time, but quite often the creative skills and ability to write one's own original thoughts do not match the required level of output. Irrespective of position and ranks, this situation is in existence at all levels of education and research, In the current situation of knowledge explosion, we are also witnessing an increasing trend in the duplication, falsification and unverifiable data presentation in student reports, theses and even journal articles written by researchers. It is very important for the younger generation of medical students to follow ethical guidelines while writing any scientific publications[2]. Senior researchers and experienced writer are duty bound to explain basic reasons why plagiarism warrants a punitive action.

Most of the guidelines adopted by academic institutions tactlessly focus on the immoral aspect hence presenting it just as a grave sin, which needs to be punished. While the other accompanying drawback is that how plagiarism weakens one's own ability to refine skills of writing to document original thoughts and outcomes in research is grossly impaired[3]. It is therefore important that while creating awareness about plagiarism as a punishable offence, it is equally important to explain to the students and young scholars that how damaging it could be for their own career. Stressing to avoid plagiarism should not just be taken as a way to protect one's writing from being labeled as a forgery, but it would show that by appropriately citing references and paraphrasing the text one can demonstrate how well read the author is and how strong are the conceptual depths. The other positive aspect in citing references is that it provides the readers guidance from where further information can be obtained.

From the available literature and reports on addressing the menace of plagiarism as a form of academic and research misconduct it becomes the responsibility of the institutions of higher learning to create more awareness about misconduct in research in general and about plagiarism in particular. However, institutions and publishers in developing countries must jointly work to nurture a culture of plagiarism free academic environment.

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ORIGINAL ARTICLE

THE EFFICACY OF DOXYLAMINE SUCCINATE AND PYRIDOXINE COMBINATION IN NAUSEA AND VOMITING OF PREGNANCY

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ABSTRACT

Background: Nausea vomiting of pregnancy (NVP) is a common problem .A severe form called hyperemesis gravidarum occurs in 0.3–2.3% of pregnancies, which can adversely affect the lifestyle. This study is conducted to improve the confidence of obstetricians for treatment of nausea and vomiting of pregnancy.

Objective: To determine the efficacy of doxylamine succinate with pyridoxine combination in nausea & vomiting of early pregnancy.

Methods: Study conducted at Dr. Ziauddin University and Hospitals Karachi, from 25-02-2011 to 25-07-2011. Study design was case series, during the period of study total number of OPD patients in gynaecology and obstetrics department Ziauddin hospital were 821, out of them 190 patients of 20 years to 39 years of age with 9+ 2 weeks gestation were enrolled and sample was taken by Consecutive sampling.

Results: 182 (95.8%) patients reported improvement in symptoms i.e. positive efficacy, 7 patients (3.7%) reported no difference in nausea vomiting & only 1 patient i.e. 0.5% reported aggravation of her symptoms. Total PAQUE score before treatment was as high as 12.3526 with standard deviation of 2.12739, which reduced to 5.7211 with standard deviation 2.0908 after treatment of nausea vomiting with doxylamin succinate + pyridoxine combination. P value calculated for total PAQUE score before and after treatment is 0.000

Conclusion: This study concluded that for nausea and vomiting of pregnancy, doxylamine succinate is effective when given for moderate to severe symptoms. So it should be considered as 1st line of treatment for nausea and vomiting of pregnancy.

KEY WORDS: Doxylamine succinate and pyridoxine combination, nausea vomiting of pregnancy, efficacy.

INTRODUCTION

About 70-80% of women experience nausea and vomiting of pregnancy(NVP) during their 1st trimester.[1-3] In general, nausea vomiting of pregnancy appear between the fourth and sixth week of pregnancy, with a peak observed between week 8 and 12[4,5] and symptoms disappear by the 20th week in most women.[4] A more severe form of NVP, called hyperemesis gravidarum ,occurs in 0.3–2.3% of pregnancies[7].

Most women who suffer from nausea & vomiting will see their condition interfere with usual daily activities. Literature survey revealed that nausea vomiting of pregnancy have a significant impact on family life as well as the ability to perform usual daily & social activities, stress level, and intent to have other children.[8-10]

Treatment for nausea and vomiting of pregnancy ,needs life style and dietary modification encouragement. [11] According to American collage of Obstetrician and Gynecologists guidance on treatment of morning sickness, pyridoxine (vitamin B6) and doxylamine is safe and effective and should be considered as first line treatment. [12]

A large meta-analysis which involved several case-control and cohort studies of over 170,000 exposures found that the doxylamine-pyridoxine combination was safe; no potential adverse effects on the fetus were observed.[13]

Majority of obstetricians avoid prescribing medical treatment for nausea and vomiting of pregnancy. Our study has provided scientific data which will help to improve the confidence of obstetricians and thereby improve health and quality of life which is affected by nausea & vomiting during pregnancy.

METHODOLOGY

The study was conducted at Dr. Ziauddin University and hospital Karachi from 25-02-2011 to 25-07-2011 in outpatient department of gynecology and obstetrics during this period total OPD patients were 821, study design was case series, Sample size was 190 pregnant women (actual sample size 159 with 20% extra due to non compliance) patients of 20 years to 39 years of age with 9+ 2 weeks gestational amenorrhea with moderate to severe nausea vomiting of pregnancy were selected and given treatment (Doxylamine succinate + pyridoxine). Sampling technique used was Consecutive sampling.
Data collection procedure: After approval from ethical committee of Dr Ziauddin Hospital, all eligible women fulfilling the inclusion criteria were counseled and given detailed information about the protocol also informed consent was taken.

The severity of nausea and vomiting was measured by the motherisk-PUQE (pregnancy-unique quantification of emesis and nausea). [114] The system scores nausea, vomiting and retching separately, as reported by women in last 12 hours (Table 2)

Tablet Envepe (doxylamine succinate 10mg + pyridoxine 10mg) was prescribed according to severity of symptoms (for moderate symptoms three tablets per day i.e.1+0+2, for severe symptoms 4 tablets in a day i.e. 1+1+2) after 1 week of start of treatment patients were called on phone for any change in their symptoms according to PUQE scoring system ,changes recorded on Performa.

Data analysis procedure: Data analyzed by using SPSS version 10.0. A descriptive analysis of continuous and categorical variables was performed, data on continuous variables (age, hours of nausea, number of vomiting) presented as mean + SD, data on categorical variables (mild, moderate or severe grade of nausea vomiting) presented as percentages. The primary outcome of interest is change in PUQE score .i.e. from severe and moderate grade to mild grade of nausea vomiting or no nausea vomiting.

RESULTS

In our study patients belong to 20-39 years of age, among them 91 patients (47.9%) presented with moderate nausea vomiting and 99 pregnant women (52.1%) were having severe nausea vomiting shown in table 2. This was controlled very effectively i.e. after treatment 166 (87.4%) women were having mild or no nausea vomiting tabulated in table 3. While over all 182 pregnant women (95.5 %) reported improvement of symptoms also shown in table 8. Total PAQUE score before treatment was as high as 12.35 with standard deviation of 2.13 summarized in table 5, which reduced to 5.72 with standard deviation 2.0908 after treatment of nausea vomiting with doxylamine succinate + pyridoxine combination described in table 6. P value calculated for total PAQUE score before and after treatment is 0.00 calculated via paired sample T test in table 7. While P-value calculated for before and after vomiting is 0.00 via paired sample T test shown in table 4.

Table 1. Age descriptive statistics

	n	Minimum	Maximum	Mean	Std. Deviation
Age	190	20.00	39.00	27.8789	3.79237

Table 2. Base line severity of nausea vomiting of pregnancy

	Frequency	Percent
moderate	91	47.9
Severe	99	52.1
Total	190	100

Table 3. Severity of nausea & vomiting after treatment

	Frequency	Percent
Mild	166	87.4
moderate	22	11.6
Severe	2	1.1
Total	190	100

Table 4. Vomiting before and after treatment paired samples T test

Paired Differences					t	df	Sig. (2-tailed) P- value
Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
			Lower	Upper			
2.24737	1.26695	.09191	2.06606	2.42868	24.451	189	.000

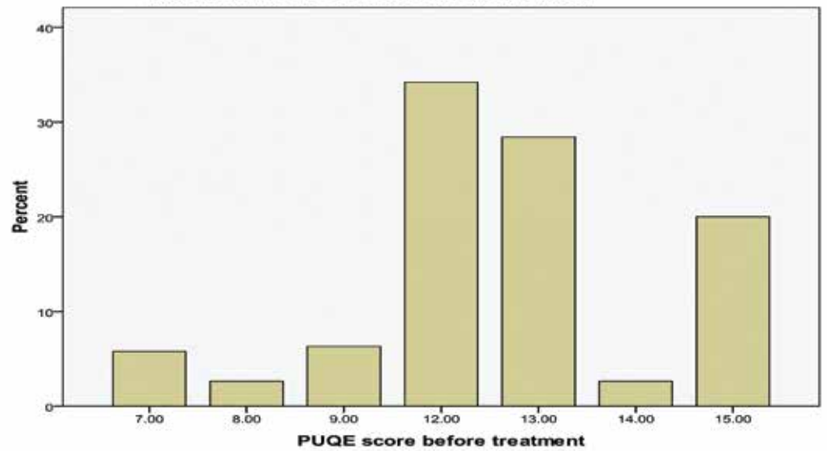
Table 5. Total PUQE score statistics before treatment

	n	Minimum	Maximum	Mean	Std. Deviation
PUQE score before treatment	190	7.00	15.00	12.3526	2.12739

Table 6. Total PUQE score statistics after treatment

	n	Minimum	Maximum	Mean	Std. Deviation
PUQE score after treatment	190	1.00	15.00	5.7211	2.09082

Figure 1. Total PUQE score before and after treatment



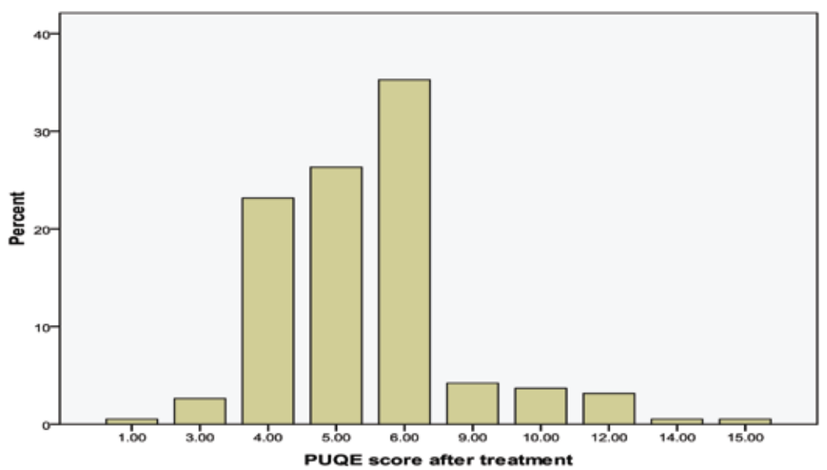


Table 7. PUQE score before treatment - PUQE score after treatment Paired samples T test

Paired Differences					t	df	Sig. (2-tailed) P-value
Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
			Lower	Upper			
6.63158	2.74509	0.19915	6.23874	7.02442	33.299	189	0

Table 8. Efficacy statistics: efficacy of doxylamine succinate+ pyridoxine on nausea vomiting of pregnancy

Symptoms	Frequency	Percent
Aggravated	1	0.5
Not improved	7	3.7
Improved	182	95.8
Total	190	100

Table 9. Base line severity X Severity after treatment X Efficacy Crosstabulation

Base line severity	Severity after treatment			Total
	mild	moderate	sever	
moderate	84	7	0	91
sever	82	15	2	99
Total	166	22	2	190

DISCUSSION

Nausea vomiting of pregnancy is very un pleasant experience.

Incidence of mild to moderate nausea vomiting is 50-90% [1-3] and sever form i.e. hyper emesis gravidarum is 0.5-3% [6,7]. It is less common in developing countries and rural areas but very prevalent in urban area of our country.

In our country 9 million of our women are working.[14] As it is already explained that nausea vomiting of pregnancy affects quality of life, this study is conducted for improvement of quality of and confidence of obstetricians about efficacy of doxylamine succinate with pyridoxine.

In our study patients belong to 20-39 years of age, among them 47.9% presented with moderate nausea vomiting and 52.1% were having severe nausea vomiting which was controlled very effectively i.e. after treatment 87.37% women improved to mild or no nausea vomiting. Results showed that combination of doxylamine succinate and pyridoxine is very effective drug to control nausea vomiting according to results positive efficacy is about 95%. Many clinical trials of doxylamine succinate with pyridoxin (Debendox or Bendectin) have been conducted. A Double-blind placebo controlled with doxylamine succinate +pyridoxine (Bendectin) of 109 patients evaluated, encouraging results obtained that Bendectin improved symptoms upto 94% as compared to placebo that was 65% (P< 0.001). Similar to our study here favorable response was 97%.Another double blind trial conducted in which 41 pregnant women included who received Debendox or placebo. There was an improvement in severity of nausea vomiting of pregnancy upto 70.7% in group who received Debendox while in group who received placebo there was 50.5 % improvement P<0.05.[15] Another research study conducted in 1975 assessed the efficacy of Bendectin with its all contents and pyridoxine alone, also pyridoxine was evaluated with various possible combinations in compression to placebo, in this study around 2300 pregnant women included with symptoms of nausea and vomiting. This research revealed that Bendectin was more effective then placebo in combination with doxylamine; on the other hand it has been observed that pyridoxine is more effective for improvement of nausea then vomiting.[16]

During one of initial prospective studies on effectiveness of doxylamine succinate along with pyridoxine, first interview took place after the onset of symptoms, between six to eight weeks. A second evaluation took place at 20 weeks of pregnancy. During the first follow-up out of 106 patients, 71% reported the improvement in their nausea vomiting symptoms temporally, due to use of Diclectin. 34 patients (23%) reported no improvement and only (1%) 2 patients experienced worsening of their symptoms. These results are also having similarity to our study results. A group of extra 25 of original cohort pregnant ladies used diclectin at 20 weeks of gestation for nausea vomiting of pregnancy; 21 patients (84%) reported improvement of symptoms, 3 pregnant women (12%) experienced no change of their symptoms, while only one patient i.e. 4% suffered worsening of nausea and vomiting. [117] Above findings are noticeably comparable to our study, this study also revealed that around 11 pregnant women increased their dose of doxylamine succinate with pyridoxine which resulted in improvement of symptoms.[15] There are few limitations to our study the main one is that our study was not population based the cases were

selected from Dr. Ziauddin hospitals OPD consecutively; our data may not represent the general population. It can be argued that with lack of control group, it is possible that the improvement merely represents the natural course of nausea vomiting of pregnancy; however follow-up call and improvement in symptoms were noted after 1 week of start of treatment in all cases suggesting that the improvement of symptoms was due to treatment effect. This study can be repeated with control group.

According to Society of Obstetrician and Gynecologist Canada (SOGC) and American collage of obstetrician and gynecologist (ACOG) doxylamine succinate with pyridoxine combination should be considered as 1st line treatment for nausea vomiting of pregnancy. It is easily available all over the country and its purchase price is very cheap i.e. 4 Pakistani rupees per tablet. But before prescription exclusion of other causes must be kept in mind, also electrolyte balance should be checked if a patient comes with intractable vomiting.

It is evident from this study that doxylamine succinate with pyridoxine combination is effective drug to use for nausea vomiting of pregnancy.

CONCLUSION

Nausea and vomiting in pregnancy is affecting quality of life in urban areas of our country so it is necessary for women to get proper treatment so that their daily lifestyles are not hampered.

In order to improve the quality of life and reduction of maternal and fetal complication, education about dietary habits are essential and should be routine part of antenatal care. For the reduction of hospital admissions due to nausea and vomiting in pregnancy women with more severe nausea and vomiting of pregnancy should be individualized and given treatment according to severity of the symptoms dose of doxylamine succinate with pyridoxine should be prescribed as proved by this study. It has been shown that about 97% women improved with this treatment.

In our country where in urban areas treatment facilities are available, in rural areas nausea and vomiting of pregnancy is considered as routine of pregnancy and treatment is neglected. So it is suggested that doxylamine succinate with pyridoxine combination must be used as a drug of 1st choice for control of nausea and vomiting of pregnancy to get maximum therapeutic affect and minimal side effects.

Hence, the overall benefit lies in the significant improvement in quality of life and well being of women treated with doxylamine succinate with pyridoxine combination. Therefore it can be concluded from this study that for nausea and vomiting of pregnancy, doxylamine succinate is effective when given for moderate to severe symptoms. So it should be considered as 1st line of treatment for nausea and vomiting of pregnancy.

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ORIGINAL ARTICLE

ASSESSMENT OF RISK FACTORS FOR GESTATIONAL DIABETES MELLITUS

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ABSTRACT

Background: Gestational diabetes is a condition due to glucose intolerance that occurs in the few of the mothers during gestation. The pathophysiology originates as a result of increased placental hormones which have strong diabetogenic effect. It is strongly associated with multiple problems in mother and the baby and can even leads to unexplained fetal deaths in the end trimesters. So it is important to diagnose and treat females who are at greater risk than the others for developing gestational diabetes mellitus.

Objective: To access the high risk factors associated with the development of gestational diabetes mellitus in 75 GDM diagnosed females

Methods: After screening and diagnoses 75 GDM patients (Diabetic, Group B) and 25 normal healthy patients (Control, Group A) in Lyari General and Mamji Hospital were enrolled in the study. Their detailed history was taken regarding occupation, parity, history of abortions, still births, preterm births and family history of diabetes. Parameters including age, weight, fasting and random blood sugar level and glycated hemoglobin were recorded in a predesigned data form. The results were evaluated using SPSS 16.

Results: Statistically significant difference was found between the mothers of diabetic and normal control group as regards the weight, age (p-value=0.01 and p=0.03) and family history of diabetes (p-value=0.00). Non-significant differences were found in the maternal occupation, parity, abortions, still births and pre-term births between the two groups

Conclusion: Advance maternal age, weight and familial association of diabetes are the risk factors associated with the development of gestational diabetes.

KEY WORDS: Diabetes, Gestational, Risk Factors, Glucose intolerance, Pregnancy trimester

INTRODUCTION

Gestational diabetes is the glucose intolerance that occurs only during pregnancy. Criteria for diagnosis of GDM define by WHO states that pregnant females farther than first trimester having fasting blood sugar equals to or more than 5.5 mmol/l (100mg/dl) and post prandial glucose levels greater than7 mmol/l (126mg/dl) are considered as having gestational diabetes mellitus (GDM). [12] Main factors are the diabetogenic placental hormones, pancreatic beta cell dysfunction; leading to decreased insulin secretion and increase insulin resistance [3]. This predisposes the pregnant females to develop GDM by the second trimester as all these hormones are at highest levels in the second trimester. [4].

The prevalence of GDM is 3.0 to 4.4% worldwide. It is seen in approximately 3-9% of pregnancies. Although the prevalence of gestational diabetes mellitus is 3.2-3.5% in our population but the complications are much higher due to poor glycemic control, lack of awareness and inadequate medical facilities. [5, 6]

Any metabolic change as in Gestational Diabetes Mellitus in maternal blood can affect the mother as well as the baby. [7] Thus to avoid adverse maternal and fetal outcomes such as cesarean section due to macrosomic babies, congenital abnormalities, respiratory distress syndrome, hyperbilirubinemia, polycythemia, and at times unexplained intrauterine death and still births, due importance should be given to the risk factors of GDM. [8.]

As large amount of glucose enter the fetal body, excessive production of fetal insulin occurs resulting in storage of large amount of glucose as glycogen and fats in the fetal cells making these larger than the normal. [9, 10]

Prevalence of GDM has a strong relationship with multiple factors.[11-13] and it can be effectively controlled by identifying the high risk factors to have safe motherhood. This study was carried out to assess the high risk factors associated with the development of gestational diabetes mellitus in our settings.

METHODS

The approval of the study was taken by IRB and ERB, Dow University of Health Sciences. This study was carried out as a clinical trial in Jan 2010- Jan 2011, at Lyari General Hospital and Mamji Hospital, Karachi. Screening was performed

in second trimester by checking RBS of the females using glucometer in the antenatal clinic and then was confirmed by OGCT and OGTT, according to WHO criteria. For OGCT, 50 grams of glucose load was given to the patient and if glycemic values after 1 hour were greater than 7.8mmol/L (140mg/dl), was identified as having GDM [14]. OGTT is a confirmation test in which 75g glucose was given to the patient followed by glucose monitoring for next two hours and any two abnormal blood glucose reading were assenting for GDM. (FBS ≥ 95 mg/dl, 1 hr ≥180 mg/dl, 2 hr ≥155 mg/dl) 14 GDM patients with no other co-morbidity were included in the study. Finally 25 healthy female as control (group A) and 75 diabetic patients (group B) were enrolled in the study following a written informed consent. History was obtained including the age, previous obstetrical history, occupation and family history through interview. Complete physical and obstetrical examination was done in the OPD and all the findings were noted down on a predesigned data form. Data was evaluated using SPSS16 on the computer. The categorical variables were evaluated by using 'chi square test' and for numerical variables 'student's t test' was utilized, and p value less that 0.05 was taken as significant between the groups.

RESULTS

IThe results indicated that difference were significant between the mothers of Diabetic and normal control group when their age and weight were evaluated (p-value=0.01 and 0.03 respectively). FBS, RBS and HBAIC were significantly high in the females of GDM group at the time of enrollment in comparison to control (p-value=0.00) (Table 1).Similarly significant family history of diabetes was observed in patients of diabetic group (p-value=0.00). Non-significant differences were found in the maternal occupation, parity, history of still births, history of abortions and history of preterm deliveries between the diabetic and control group. (Table 2)

Table 1. Maternal characteristics, stratified by gestational diabetes

Group A: Healthy control group, Group B: GDM group
Students T test applied accordingly * Statistically significant

Variables	Group A (N=25) Mean± sd	Group B (N=75) Mean± sd	Significance
Maternal Age(years)	29.0 ±4.37	32.16±3.27	0.01*
Maternal Weight(kg)	73.84± 9.97	78.11± 7.82	0.03*
FBS at the time of enrollment(mg/dl)	72.24±9.37	104.4±23.33	0.00*
RBS at the time of enrollment(mg/dl)	126±35.87	186±63.43	0.00*
HBA1C at the time of enrollment (%)	4.84±0.45	5.35±0.41	0.00*

Table 2: Maternal Characteristics

Maternal Characteristics		Group A (N=25)	Group B (N=75)	Sig
Occupation:	House wife	23(92%)	68 (90%)	1.0 ^
	On job	2 (8%)	7 (9.3%)	
Family History Of	Positive	3(12%)	31(41.3%)	
Diabetes:	Negative	22(88%)	44(58.6%)	0.00*
Parity:	More than 3	2(8%)	8(10.6%)	
	Less than 3	23(92%)	67(89.3%)	1.0 ^
History Of Abortions:	Present	14(56%)	51(68%)	
	Absent	11(44%)	24(32%)	0.27
History Of Stillbirths:	stillbirths	2(8%)	12(16%)	0.27
	No stillbirth	23(92%)	63(84%)	
History Of Preterm Births:	Positive	2(8%)	5(6.66%)	1.0^
	Negative	23(92%)	70(93.3%)	

Group A: Healthy control group
Group B: GDM group
Chi square test and students T test applied accordingly * Statistically significant result
^fisher exact test due to decrease cell count (chi square not applicable)

DISCUSSION

Gestational diabetes mellitus is a state of glucose and carbohydrate intolerance in the pregnancy after 22nd week of pregnancy. In our results statistically significant differences were present between the patients in GDM group and controls when comparison was done in mean maternal weight and mean maternal age. This points out that the females with more weight and increased age are more prone to develop GDM making increased maternal age and weight a risk factor. This was similar to study results of Terricco, who observed that maternal age and maternal weight were significantly increased in the GDM pregnancies in comparison to healthy controls. [15] One reason could be that females with increased weight have hidden glucose intolerance. They have border line disease with normal level of fasting and random glucose level. The increase in the levels of pregnancy hormones which are diabetogenic in nature flares-up the hidden disease. Finally these females are diagnosed as having diabetes during pregnancy. GDM is also a critical risk factor for occurrence of diabetes type 2 in GDM females with the advancement of age. [16] Goldman et al. also discuss that the escalation of age can produce bad obstetrical outcomes and development of GDM is one of the complication. [17]

Our results have shown that older females are at higher risk to develop GDM probably due to decrease in insulin resistance along with impaired pancreatic islet cell functioning caused by aging process. Age related insulin resistance is also strongly associated with fat deposition, physical inactivity and decrease in muscular mass. Other factor could be low islet cell proliferative and repairing capability which enhances the effect of already described phenomenon [18]. Sivakumar et al. described that advancement of age along with increased weight, strongly influence the development of GDM and these risk factors are comparable with internationally documented risk factors. [19] These risk factors play an important role in early diagnosis and management of such females

In our study Fasting and random blood sugar levels were significantly different between both the groups. Similar results were documented by Mardi as in his study same groups were enrolled with significant differences in FBS and RBS. His results also showed significant increase in age (p=0.013) and weight (p=0.00) in GDM patients when compared with normal healthy individuals. [20]All these findings are similar to our study results.

Khooshideh et al. stated that history of abortion in previous pregnancy can be a risk factor for development of GDM (p=0.004). Though the results are statistically non-significant regarding history of abortions in our study, but it has been noticed that 68% of GDM females had positive history for abortion, which is an alarming sign. He also pointed out that increased age and positive family history are the strong risk factors for GDM, favoring our results [21].

Tabak et al. pointed out that positive family history is a strong predictor of GDM during pregnancy [22]. There were no significant differences present between the maternal or paternal positive history. Chan et al. had also supported the same results in his study that family positive history should be clearly investigated in antenatal checkup to rule out high risk GDM females.[23]

Al Rowarly studied GDM in Saudi females and concluded that parity is also one of the important risk factor for GDM development. As parity increase the chances of becoming diabetic during pregnancy also increases. [24]

A recent research by Khan et al. stated that including all of other risk factors mentioned above, belonging to Asian population itself is a risk factor for GDM. When more than one risk factor is present the condition worsens and chances get doubled. [25]

There were non-significant differences present between the normal and GDM group when comparison of occupation, parity and history of still births was done. Mardi and Khooshideh have given the same statements that parity and history of stillbirths had not shown significant association with GDM, so the results of these studies are in favor of ours [19, 20].

Advanced maternal age, weight, and familial association of diabetes are strong risk factors coupled with the development of diabetes in pregnancy. Parity, history of abortions and stillbirths although statistically non-significant but numerically were much higher than control group making them probable risk factors for GDM and open venues for future studies with large sample size. Guidelines should be made and measures should be undertaken at the governmental level to reduce the feto-maternal complications arising from diabetic pregnancies and to trim down the occurrence of type 2 diabetes mellitus in forthcoming years in these GDM mothers

CONCLUSION

Advance maternal age, increased maternal weight and familial positive history of diabetes, are strong risk factors associated with the development of gestational diabetes in our females.

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ORIGINAL ARTICLE

LAPROSCOPIC EVALUATION OF PRIMARY INFERTILITY CAUSES AND POST PROCEDURE COMPLICATIONS AMONG INFERTILE FEMALES FROM A TERTIARY CARE HOSPITAL OF KARACHI

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ABSTRACT

Background: Infertility is a common problem globally affecting a large proportion of world population. Laparoscopy provides meaningful information regarding different factors that may cause infertility.

Objective: To determine the frequency of causes of primary infertility in women by diagnostic laparoscopy.

Study Design: Cross sectional study design

Setting: Study was performed at the Department of Obstetrics and Gynecology, Jinnah Postgraduate Medical Centre, Karachi

Duration: September 2011 to February 2012

Subjects and Methods: 86 patients with primary infertility were included in the study and underwent laparoscopy for determining causes of infertility. Data was analyzed on SPSS, frequencies and percentages were determined for qualitative variables while mean and standard deviation was determined for quantitative variable.

Results: Eighty six females were included in the study with mean age of 28.6 + 5.2 years and mean duration of infertility was 4.9 + 1.9 years. Findings on laparoscopy were analyzed and 51.2% of females were found with tubal blockage, while other findings were; hydrosalpinx in 25.6%, PCOs in 22.1%, Ovarian abnormalities in 38.4%, Pelvic adhesions in 38.4% and uterine congenital anomalies in 3.5%.

Conclusion: Tubal diseases found to be one of the major factor causing primary infertility and diagnostic laparoscopy will play a valuable role in early and prompt diagnosis and management of causes leading primary infertility.

Key Words: Primary Infertility, Diagnostic Laparoscopy, Tubal Blockage, PCOs, Pelvic Adhesions, Hydrosalpinx.

INTRODUCTION

Infertility is a unique medical condition because it involves a couple, rather than a single individual. It is defined as failure of a couple to conceive after 12 months of regular intercourse without use of contraception.[1] Incidence of infertility appears to be increasing in developed communities for reasons different from those causing infertility in less advanced countries.[2] The World Health Organization (WHO) has reported major causes of infertility in females on a global scale as being largely due to four disorders: pelvic tuberculosis, post abortal and post partum infections leading to tubal blockade and malnutrition.[3]

Physicians can use multiple modalities to assess the tubes. Direct visualization on laparoscopy (LS) is often used as primary and reference procedures for diagnosing tubal dysfunction. In a local study diagnostic laparoscopy was done and it was found 53% of patients had tubo-peritoneal disease out of these 32% had peritoneal adhesions along with tubal blockage while 21% cases had only pelvic adhesions, Polycystic Ovarian disease was present in 15.7% of patient and endometriosis was found in only 9% of patients. Fibroids of uterus was found in 6% of patients and 16.5% had no abnormality.[4]

Laparoscopy (peritoneoscopy) is a transperitoneal endoscopic technique that provides excellent visualization of pelvic structures and often permits the diagnosis of gynecologic disorders and pelvic surgery without laparotomy. [5] Laparoscopy was the final diagnostic procedure of the female fertility exploration, as outlined by the American Fertility Society in 1992 and by the WHO guidelines (Rowe et al., 1993). In 1997, Glatstein et al. (1997) reported that 89% of all reproductive endocrinologists in the USA routinely performed a laparoscopy in the diagnostic work-up of infertility.[6]

Advantages include the possibility to perform both

diagnostic and therapeutic procedure at the same time, all as part of day care surgery.[6] Local data is deficient on this topic, especially on diagnostic findings of laparoscopy for causes of infertility in women. Therefore this study will be undertaken to see the burden of causes of infertility. This data could be utilized for resource allocation & improvement in management strategies. This study is planned with the objective of highlighting the relative importance of laparoscopic evaluation in the etiology of primary infertility in women. Infertility is a major problem affecting women's health and quality of life leading to social and psychological upsets and bringing misery and insecurity to many women.

METHODS

This Cross Sectional study was conducted from September 2011 to February 2012 at the Department of Obstetrics & Gynecology, Jinnah Post Graduate Medical Center-Karachi. The sample size was calculated by using WHO sample size determination software with 80% power of the test and 95% confidence interval. Taking anticipated population proportion (P) of fibroids of uterus in 6%4 of sub-fertile women & margin of error (d) of 5% the sample size was calculated as (n) 86 women. Data was collected by Non-probability (purposive) sampling technique. All females of child bearing age with infertility presented in infertility clinic with negative pregnancy test were included in the study while those females were excluded who had recent history of salpingitis or other infections, obvious hormonal problems, sever cardio pulmonary diseases, large abdominal mass, massive absolute or relative contraindications for laparoscopy, diaphragmatic hernia, massive intraperitoneal hemorrhage, paralytic ileus, generalized peritonitis, male factor infertility, bowel obstruction and gross obesity. Pregnant females were also not included in the study.

The sample subjects were selected through outpatient department or infertility clinic of Gynaecology and Obstetrics Unit of JPMC. The patient who fulfilled the inclusion criteria was enrolled in the study. The purpose, procedure, risks and benefits were explained and informed consent was taken. All the patients were admitted a day before the procedure, preferably in the pre-menstrual phase. Pre-anesthetic evaluation was carried out in the evening. Prophylactic antibiotic was injected and diagnostic laparoscopy was carried out under general anesthesia. The patency of the fallopian tubes was ascertained by injecting methylene blue dye into the uterine cavity through uterine cannula or a Foley's catheter and observing its spill through fimbrial ends. Dilatation and curettage was carried out in patients with menstrual abnormalities or suspected endometrial tuberculosis and endometrium was sent for histopathology. All information was entered on a predesigned proforma.

Data was entered and analyzed by SPSS version 17. Mean ± standard deviation was calculated for age of the patient. Frequencies and percentages were calculated for causes of infertility found on diagnostic laparoscopy. Stratification was done with regards to age of women and duration of infertility to see the effect of these on outcomes. Chi square test was applied to find association between categorical variables and p- value less than 0.05 was taken as significant.

RESULTS

Eighty six primary infertile females were included in this study and underwent diagnostic laparoscopy. Ages of patients investigated were ranging from 20 – 40 years and mean age was 28.6 + 5.2 standard deviation. Patients were arranged into groups according to age and 29 (33.7%) of the females were in age group 25-29(Table 1)

Duration of infertility among females was ranging from 2 to 10 years with mean of 4.9 + 1.9. Patients were also grouped according to duration of infertility (Table 2). Out of 86 females 24 (27.9%) had regular menstruation and 62 (72.1%) had irregular menstruation.

Causes of primary infertility investigated by laparoscopy were PCOs, tubal blockage, hydrosalpinx, ovarian abnormalities, pelvic adhesions and uterine congenital anomalies, among them most common finding was tubal blockage which account for 44 (51.2%). Other findings are presented in Table 2.

Among ovarian abnormalities most of the abnormalities were hemorrhagic cyst and endometriotic cyst while congenital anomalies were absent uterus, didylphus uterus and two uteri.

Out of 44 patients with tubal blockage, 10 (22.7%) had unilateral tubal blockage and 34 (77.3%) had bilateral tubal blockage. Hydrosalpinx was found in 22 (25.6%) patients and of those 17 (77.3%) had bilateral hydrosalpinx and 5 (22.7%) had unilateral hydrosalpinx.

Out of 44 (51.2%) patients who had tubal blockage and 22 (25.6%) who had hydrosalpinx, 19 (22.1%) were those who had both tubal blockage and hydrosalpinx. Chi square test was applied on these two categorical variables and p-value was found significant as it is 0.000 which is <0.05. (Table 3)

Association between tubal blockage and pelvic adhesions was also analyzed Out of 44 (51.2%) patients who had tubal blockage and 33 (38.4%) who had pelvic adhesions, 27 (31.4%) were those who had both tubal blockage and pelvic adhesions. Chi square test was applied and p-value was found significant as it is 0.000 which is <0.05. (Table 3)

There were no complications in 78 (90.69%) patients, while other complications were fever, shoulder tip pain and abdominal pain. (fig 1)

Table 1. Age groups and Infertility duration of women with infertility at the time of laparoscopy

		Number of Cases (n=86)	Percentages (%)
Age Groups	20 – 24 years	14	21.1
	25 – 29 years	29	33.7
	30 – 34 years	22	25.6
	35 – 39	12	14
	40 – 45	4	4.7
Duration of Infertility	2 – 4	41	47.7
	5 – 7	36	41.8
	8 – 10	9	10.5

Table 2: Laparoscopic findings among Primary Infertile Females

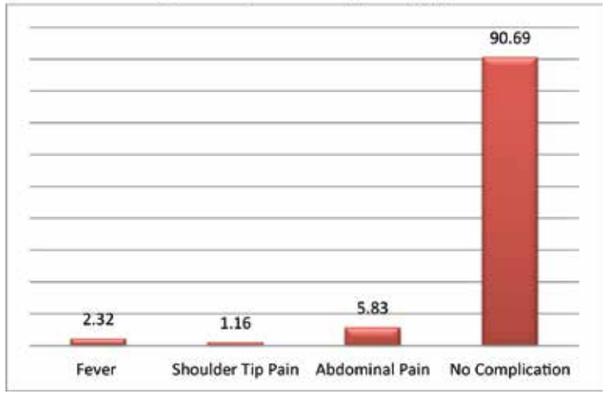
Laparoscopic Finding	Number of Cases (n=86)	Percentages (%)
Tubal Blockage	44	51.2
Ovarian Abnormalities	33	38.4
Pelvic Adhesions	33	38.4
Hydrosalpinx	22	25.6
PCOs	19	22.1
Uterine Congenital Anomalies	3	3.5
Normal Findings	9	10.7

Table 3. Association of Tubal Blockage with Hydrosalpinx and Pelvic Adhesions

	Tubal Blockage		
	Number of Cases (n=86)	Percentages (%)	P-Value*
Hydrosalpinx	19	22.1	0.0001
Pelvic Adhesions	27	31.4	0.0001

P-value <0.05 is considered significant. Chi square test was applied for categorical variable

Figure 1: Complications of Laparoscopy (%)



DISCUSSION

Infertility is among one of those medical problem which mostly a challenging task for gynecologists. Laparoscopy is a mandatory and essential procedure for complete and detailed assessment as well as treatment of infertility. [7,8,9]

This technique is successfully investigate and provide information about tubal condition, pelvic adhesions, ovaries, uterine pathologies and so replaced certain old procedures like gas insufflations and even HSG in assessing the tubal patency. [10,11]

Infertility may be due to primary and secondary reasons. Most of the studies till now investigate both primary and secondary infertility and used laparoscopy as one mean of investigation. In this study the primary focus was only assessing causes of infertility among primary infertile patients with the help of laparoscopy.

Female age is one of most important determinant of spontaneous as well as treatment related conception.[12] NICE recommendations states that women over age of 35 years should be referred early from primary care for investigation and treatment. [13,14]

Mean age of females diagnosed at the time of research was 28.6 + 5.2 years and Aziz N in her research at LUMHS also mentioned mean age as 28 years.7, [11, 12] In this research primary infertility was found more in age group between 25 to 29 years i.e. 33.7% and other research also showed the prevalence of infertility more in this group[12] but in another research primary infertility was more in age group 18 to 25 i.e. 55%.[15]

In this research mean duration of infertility found 4.9 + 1.9 years and it was found as 3.7 years in one research and 3.2 years in another research.[8, 12] Duration of primary infertility was more from 2 to 4 years and it was also stated by Aziz N and Naz T that duration of infertility was more from 5 to 10 years.[15,16]

Most common finding on laparoscopy in this study was tubal blockage (51.2%) while in other studies Aziz N also reported it was most common cause (21.9%) [15]. Haider G reported tubal blockage in only 10% cases and Naz T also reported it only in 6 % cases.[15] In a study conducted at Mayo hospital Lahore and at Holy Family Hospital Rawalpindi the incidence of tubal factor was 30% and 47.8% respectively.[17] In this study it was noticed that those who had tubal blockage were also had hydrosalpinx and pelvic adhesion, so to find out association test of significance was applied and according to p-value < 0.00 for both cases tubal blockage is associated with hydrosalpinx and pelvic adhesions. Hydrosalpinx was found in 25.6% of cases and it was observed that both tubal blockage and hydrosalpinx was 77.2% presented as bilateral.

Other findings on laparoscopy were ovarian abnormalities and pelvic adhesions, both were found in 38.4% females. PCOs was also found in 22.1% females and other studies also mentioned it as one of the common cause among primary infertile patients.[18,19]

Interestingly 3 cases were found with uterine congenital anomalies that were absent uterus, didylphus uterus and two uteri. Congenital uterine abnormalities were more frequent in primary infertility and Naz T; et al. also reported 2 cases of double uterus in their study.

Most of the cases were found without any abnormalities and many studies showed that there were certain unexplained reasons for primary infertility as their laparoscopic findings were normal.[20, 21]

In this study only 10% were found with normal physiology while others were found with some pathology whether they were uterine, tubal or ovarian. Laparoscopy is a very powerful tool that not only helps in early diagnosis of primary infertility but also help in management of infertility.

CONCLUSION

Among various causes of primary infertility, tubal disease found to be the commonest factor responsible for primary infertility.

Laparoscopy is a valuable, more convenient, more precise technique and is a mandatory procedure for detailed and complete assessment and diagnosis of female infertility. In primary infertility this technique should be pertain properly and promptly, without delay in trials and blind management.

More effective treatment decisions and interventions can be made according to the particular cause of infertility in the light of laparoscopy findings.

CONFLICT OF INTEREST

Author declares no conflict of interest

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ORIGINAL ARTICLE

CHEMICAL CHARACTERIZATION OF SILORANE BY FTIR AND RAMAN SPECTROSCOPY

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ABSTRACT

Background: Silorane, introduced to the dentistry recently. It is named after the functional groups present in the material i.e. Siloxane and Oxirane. It is introduced in the market to overcome the main problems of composite resins i.e. Polymerization shrinkage. Claims are being made that the polymerization shrinkage have been overcome in the material and the material results in less than 1% polymerization shrinkage. The material claims to have properties which may fulfil the criteria of being the ideal restorative materials of all times.

Objective: : To confirm the presence of Siloxane and Oxirane in the chemical structure of the Silorane by Fourier Transform Infra-red (FTIR) and Raman Spectroscopy.

Methods: Solvation of Silorane was done in Tetrahydrofuran (THF) using the magnetic stirrer. After the evaporation of THF, the resultant powder was then evaluated under the FTIR and Raman Spectroscopy.

Results: The FTIR spectrum of Silorane shows some primary reference bands in the spectrum of Silorane and shows the absorption of primary oxirane bands. The peaks indicated the presence of Siloxane bands and CH groups.
Raman spectrum of Silorane confirming the presence of v phase of Siloxane. The peaks show the presence of O-Si-O and C = C group.

Conclusion: The FTIR and Raman spectrums confirms the presence of Siloxane and Oxirane bands which results in low polymerisation shrinkage due to the cationic ring opening mechanism when compared with methacrylates which polymerises via a free radical mechanism.

KEY WORDS: Silorane, Fourier Transform Infra-red, FTIR, Raman Spectroscopy

INTRODUCTION

Silorane has been introduced to the dentistry recently. Claims have been made by the manufacturer that the novel material shows less than 1% of the polymerization shrinkage. It is named after the functional groups presents in the materials, Oxirane and Siloxane. The hydrophobic behaviour of the material is characteristic feature of siloxane which helps in the long term intraoral physical strength of the composites. Moreover, the hydrophobic material tends to absorb very low amount of pigments of daily nutrition resulting in less exogenic staining when compared with hydrophilic material. The polymerisation mechanism of Oxiranes is by a cationic ring opening mechanism which results in low polymerisation shrinkage when compared with methacrylates which polymerises via a free radical mechanism. The polymerisation starts when acidic cation initiates, which opens the oxirane ring and forms a new carbocation, a new acidic centre. After an oxirane monomer has been added, the epoxy ring is opened to form a chain and if there are multifunctional monomers a network is formed. [1, 2] The polymerization reaction is activated by the light source and there is no difference found the transmission of light between Silorane and the conventional composites. [3] Attia et al. used Silorane based restorative material for one year clinical followup and suggested that the materials is found acceptable even after one year of clinical application. [4]

Fourier Transform Infrared (FTIR) Spectroscopy is a type of infrared (IR) spectroscopy. FTIR can be used to recognize the chemical structure and considered a useful tool for recognizing the functional groups. IR rays are passed through a sample which absorbs some rays and some rays are transmitted, which produce a unique wavelength for each molecular structure to form a spectrum. Chemical structure and bonds can be determined by interpreting this spectrum. The spectrum produced for each molecule is so unique that they are called "molecular fingerprint".

FTIR is the qualitative technique widely used for the identification of polymers. [5] There are a few types of FTIR, like FTIR-ATR (Fourier transform infrared attenuated total reflection) spectroscopy, FTIR-PAS (Fourier transform infrared photo acoustic spectroscopy) and FTIR-RAS (Fourier transform infrared reflection-absorption) spectroscopy. FTIR-ART technique can provide data on the process of releasing drugs in formulations and become a usual protocol to study the drug-penetration and drug release in membranes from pharmaceutical products. FTIR-PAS is capable of providing chemical information of transparent to opaque samples. FTIR-RAS is used for the measurement of thin films; up to the depth of 50 µm can be reached by certain ranges by this technique. (6) Fourier transform Raman Spectroscopy is one of the spectroscopic techniques developed with FTIR for the confirmation of the molecules order. It is usually used to characterize the molecular structure of the compound. [6] It characterizes the vibrational, rotational and other low frequencies in a compound.

The objective of the study was to recognize the chemical structure of Silorane by confirming the presence of Siloxane and Oxirane.

METHODS

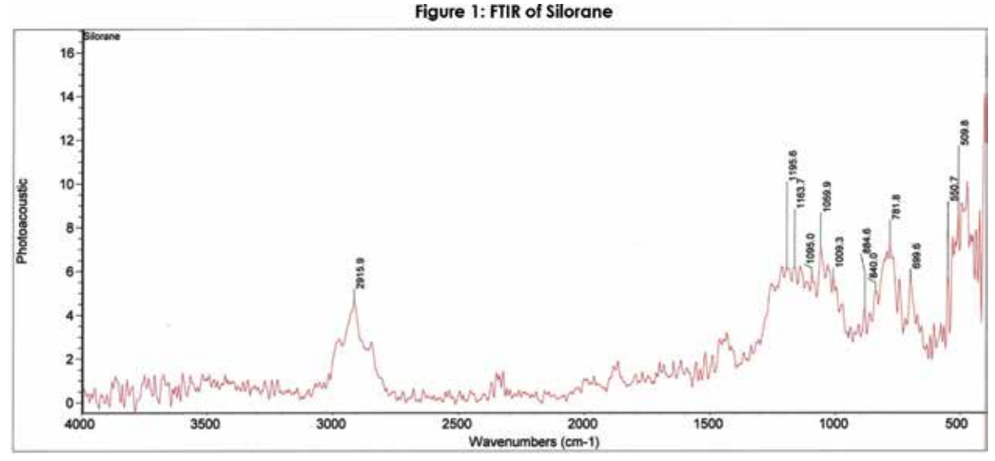
SOLVATION OF SILORANE

Silorane was obtained from 3M ESPE UK, Solvation of Silorane was done in Acetone, N, N dimethyl formamide (DMF) and Tetrahydrofuran (THF) initially. 10 ml of the solvent was taken in the glass beaker and 1 gm of Silorane was added in the beaker. The beaker is then placed on the magnetic stirrer (Model - IKA C-MAG HS 7) with a magnetic stir bar in the beaker. Silorane is then allowed to dissolve in the solvents. After the evaporation of the solvents, samples were analysed by FTIR spectroscopy. FTIR spectrum of Silorane dissolved in THF shows the close resemblance to the Silorane spectrum, showing no chemical changes.

Silorane was dissolved in THF. After the evaporation of THF, the resultant powder was then evaluated under the FTIR and Raman Spectroscopy.

Nicolet Amelga XR dispersive Raman spectrophotometer has been used for Raman spectra. And FTIR spectra were obtained by using a Nicolet 8700 FTIR spectrometer (Thermo Electron Corporation, UK) in combination with a photo acoustic sampling (PAS) cell.

Figure 1: FTIR of Silorane



RESULTS & DISCUSSION

Figure 1 shows the FTIR spectrum of Silorane. The fine structure in 884 – 886 cm^{-1} region shows some primary reference bands in the spectrum of Silorane and shows the absorption of primary oxirane bands. [7] The peak at 2915 cm^{-1} indicated the presence of CH group. Different Siloxane bands can be seen in the region of 770 – 3000 cm^{-1}. Peaks at 781, 848, 1059, 1095, 1195, 1259 and 2915 cm^{-1} indicates the v SiCH3, (SiOSi, CO) and CH3 respectively. [8]

Figure 2: Raman Spectrum of Silorane

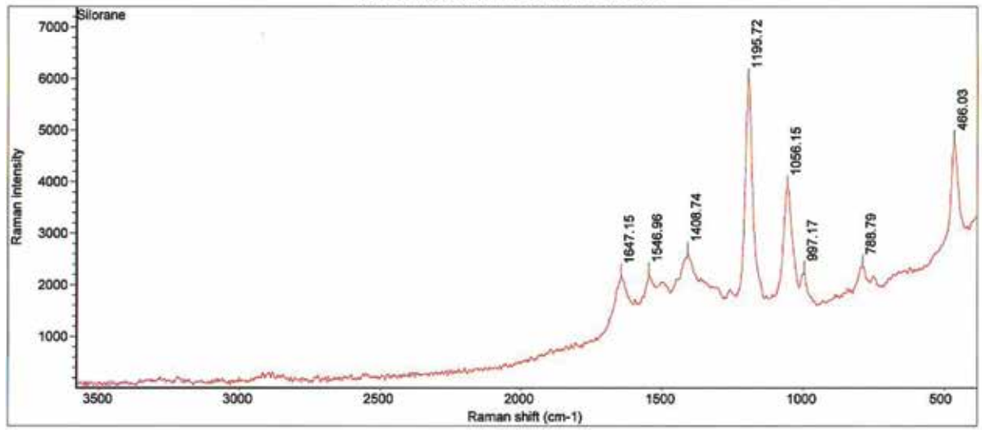


Figure 2 shows the Raman spectrum of Silorane confirming the presence of v phase of Siloxane. Strongest infrared absorption of siloxane is a sharp bend occurring at 1056 cm^{-1}. The peak at 1640 cm^{-1} shows the presence of C = C group. The peak at 1195 and 466 cm-1 indicates the presence of O-Si-O [9, 10]

CONCLUSION

This study confirms the presence of Siloxane and Oxirane in Silorane by confirming the presence of Siloxane and Oxirane bands. The polymerisation mechanism of Oxiranes is by a cationic ring opening mechanism which results in low polymerisation shrinkage when compared with methacrylates which polymerises via a free radical mechanism. The polymerisation starts when acidic cation initiates, which opens the oxirane ring and forms a new carbocation, a new acidic centre. After an oxirane monomer has been added, the epoxy ring is opened to form a chain and if there are multifunctional monomers a network is formed. Dental composites are the most commonly used restorative materials because of their excellent mechanical and aesthetic properties, but the low polymerisation shrinkage of the Silorane is an added advantage on the composite restorative materials. The novel material is fulfilling all the criteria of being an ideal restorative material except being bioactive.

ACKNOWLEDGEMENTS

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ORIGINAL ARTICLE

EFFECTS ON BLOOD GLUCOSE, GLUTATHIONE AND LIPID PROFILE BY MURRAYA KOENIIGI IN EXPERIMENTAL ANIMALS (RABBITS)

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ABSTRACT

Background: Obesity is responsible for beta dysfunction and insulin resistance. This is main cause of type 2 diabetes and excess in glycosylated hemoglobin. The concentration of glycosylation is directly proportional to the amount of blood glucose. It is investigated that oxidative stress can play a major role in the destruction of tissue that directly link with diabetic complication. This condition also associated with elevated level of lipid peroxidation. Murraya leaves may cause hypoglycemic and hypolipidemic effects and thus reduce lipid peroxidation in experimental animals.

Methodology: The animals (rabbits) were randomly divided into three groups of equal size; a control group that did not receive any sort of modification in diet throughout the study while the group 2 and 3 were orally administered 10gm of fructose and 6gm of butter in addition to normal animal chow. While a dietary modification by addition curry leaves , was made in group 3 and it received 10g curry leaves per day for the next 45 days. The blood levels of glucose, glutathione and lipid profile were measured.

Results: After consumption of Murraya leaves concentration of blood glucose and LDL-C, TC, TG was significantly decreased and increased HDL-C. Glutathione evaluation was used as a parameter for the oxidative stress showed a mark decline.

Conclusion: Murraya leaves acted as anti-diabetic because it is also responsible to decrease the absorption of the glucose from gastrointestinal tract and anti-hyperlipidemic effects.

KEY WORDS: Murraya Koeniigi, diabetes mellitus, hypoglycemic, anti-hyperlipidemic

INTRODUCTION

The prevalence of obesity is increasing worldwide. Obesity is responsible to increase adipose tissue mass lead beta dysfunction and insulin resistance. Insulin resistance resulting from increased adipose tissue mass has been identified the main factor that could drive the rise in type 2 diabetes mellitus prevalence. Thiazolidinediones, a class of oral anti-diabetic agents that reduce insulin resistance and improve beta-cell function and these effects are produced by regulating adipocyte-derived factors, in particular TNF-alpha and free fatty acid.[1] The main cause of diabetes is the excess amount of glucose present in blood which reacts with hemoglobin to produce glycosylated hemoglobin. The concentration of glycation is directly proportional to the amount of blood glucose[2,3]. In diabetic rats evidences show that glycation is responsible for the production of oxygen derived free radicals. It has been investigated that oxidative stress can play a major role in the destruction of tissue that directly link with diabetic complication. [3,4] Diabetes mellitus is associated with elevated level of lipid peroxidation also enhanced the formation of reactive oxygen species. Murraya leaves cause decrease the blood glucose level and lipid profile[5] Phytotherapy has a promising future in the management of diabetes, considered to be less toxic and free from side effects as compared to the use of synthetic drugs. Antioxidant protein derived from curry leaves having molecular weight 35 kDa (Murraya koenigii) [6]. The mahanimbine from Murraya koenigii possess anti-hyperglycemic and anti-hyperlipidemic effects. Thus results suggesting mahanimbine has beneficial effect in the management of diabetes associated with abnormal lipid profile and related cardiovascular complications[7]. Both the Murraya Koeingii and Olea europaea possess a potent anti-hyperglycemic and hypolipidemic effect, which may be due to the presence of antioxidants such as carbazole alkaloids and polyphenols[8,9].

The significant prediction of its anti-hyperglycemic and anti-hyperlipidemic activity of Murraya leaves will be explored on rabbits in this study.

The purpose of this study was to determine the strength of Murraya leaves against diabetes mellitus induced hyperlipidemia and hyperglycemia in experimental rabbits.

METHODS

The animals (rabbits) were randomly divided into three groups of equal size; a control group did not receive any

sort of modification in diet throughout the study while the group 2 and 3 were orally administered 10gm of fructose and 6gm of butter in addition to normal animal chow for 45 days. While a dietary modification was made in group 3 and it received 10g curry leaves per day for the next 45 days. Initial glucose, glutathione and lipid profile was done from blood. After feeding them crushed murrayya leaves for 45 days again blood levels of glucose, glutathione, and lipid profile was done.

At the beginning of the study, body weight of all the animals was measured.

Later on, a fasting blood sample from all the animals was collected in two test tubes, while using heparin as an anticoagulant. A single tube was used for the determination glutathione levels and hemoglobin. A lysate of red cells was prepared by adding 20 µL of whole blood to 2 ml distill water. The hemoglobin concentration was determined by using Drabkin's reagent on an automatic hemoglobinometer. 2ml of hemosylate was added to 3ml of metaphosphoric acid and incubate (50-60minutes). Added 2ml of filtrate to 0.8ml of 0.3 Na2HPO4 solution.

Took another reading (OD2) by adding 80µL(0.08ml) of DTNB (5,5'-thiobenzoic acid)reagent.

$$\text{Glutathione} = \frac{(OD2 - OD1) \times E\ (0.542) \times 101}{\text{Hemoglobin(mg/dL)}}$$

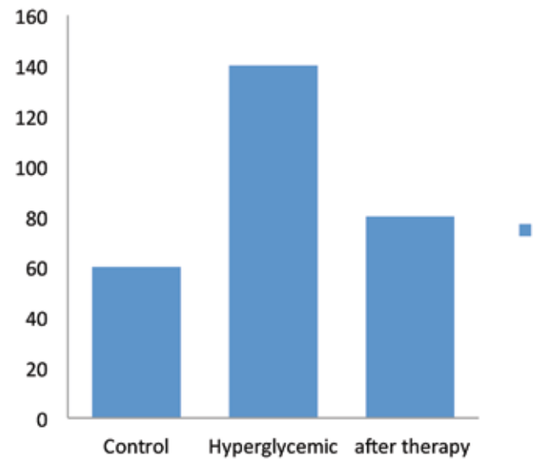
Also the measurements were done for each group of total Serum Cholesterol, LDL-C, HDL-C, Triglycerides and blood glucose levels. Approval of study was taken from physiology department ethical review committee.

RESULTS

Concentration of serum glucose showed a marked decline. In lipid profile LDL-C, TC, TG was significantly decreased and increased HDL-C. Glutathione evaluation was used as a parameter for the oxidative stress showed a mark decline oxidative stress. No physical parameter changed except drastic effect of weight loss. Graph 1 shows glucose levels in control, hyperglycemia and after therapy. Graph 2 shows glutathione levels in control, hyperglycemia and after therapy. Levels of glutathione were 3.5 nmol/L in therapy animals as compared to 2.5 nmol/L in hyperglycemic animals, showing reduction in oxidative stress.

Table 1 shows comparison of lipid profile of controls and hyperlipidemics. Table 2 shows the comparison of hyperlipidemic and treatment group, p-value was significant. Graph 3 shows LDL-C, HDL-C and TG of hyperlipidemics and after treatment. Graph 4 represents the total cholesterol in control, hyperglycemia and after therapy.

Graph 1. Glucose levels in control, hyperglycemia and after therapy.



Graph 2: Glutathione levels in control, hyperglycemia and after therapy.

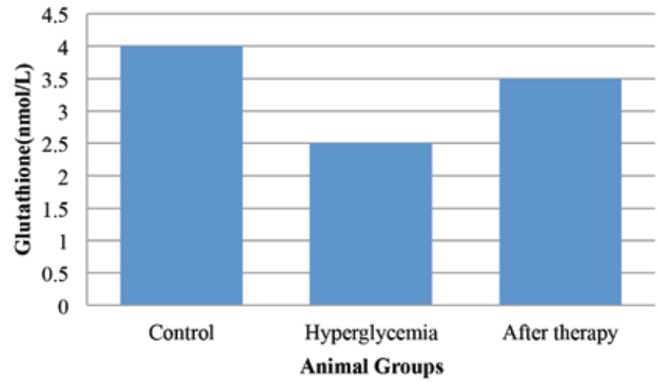


Table 1. Control vs Hyperlipidemic

Lipid Profile	Control	Hyperlipidemic	p-value
TC(mg/dL)	98.2	367	0.013
HDL-C (mg/dL)	27.2	15.9	0.05
LDL-C(mg/dL)	30.5	58.5	0.05
TG(mg/dL)	33.8	63.6	0.025

	Point estimate	**Point estimate**	**Point estimate**
	(p-value)	upper bound	lower bound
TC (mg/dl)	367(0.013)	367.1	366.9
HDL-C(mg/dl)	15.9(0.05)	15.95	15.85
LDL-C(mg/dl)	58.5(0.08)	58.58	58.42
TG(mg/dl)	63.6(0.025)	63.62	63.57

Table 2. Hyperlipidemic vs Treatment

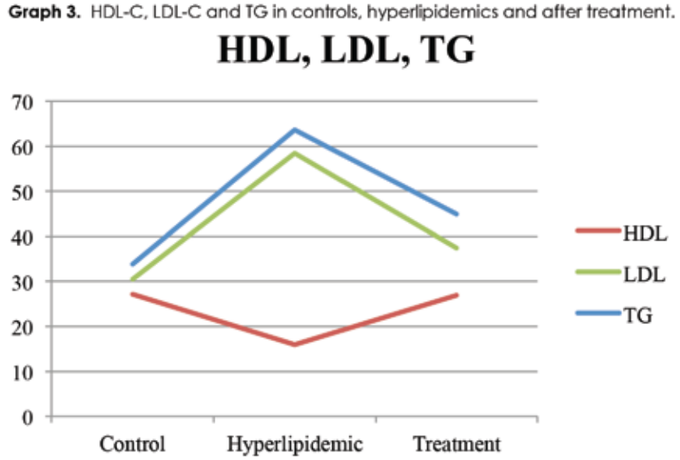
Lipid Profile	Hyperlipidemic	Treated	p-value
TC(mg/dL)	367	117.6	0.022
HDL-C(mg/dL)	15.9	26.9	0.05
LDL-C(mg/dL)	58.5	37.4	0.05
TG(mg/dL)	63.6	44.9	0.05

	Point estimate	Point estimate	Point estimate
	p-value	upper bound	lower bound
TC mg/dl	117.6(0.022)	117.62	117.57
HDL-C mg/dl	26.9(0.05)	26.95	26.85
LDL-C mg/dl	37.4(0.05)	37.45	37.35
TG mg/dl	44.9(0.05)	44.95	44.85

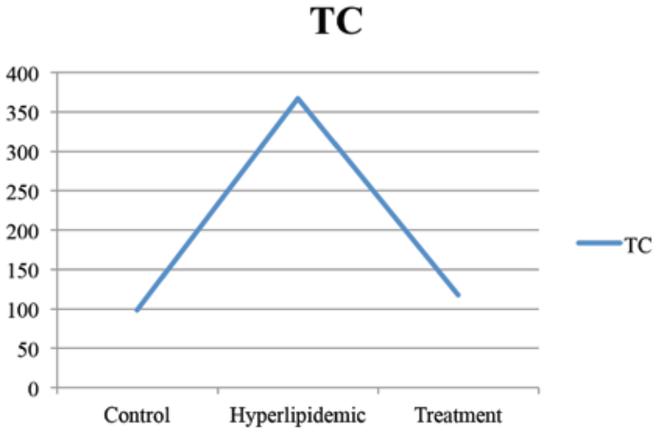
Table 3. Control

	Point estimate p-value	Point estimate upper bound	Point estimate lower bound
TC(mg/dl)	98.2(0.05)	98.25	98.15
HDL-C(mg/dl)	15.6(0.05)	16.1	15.1
LDL-C(mg/dl)	30.5(0.60)	31.1	29.9
TG(mg/dl)	33.8(2.2)	36	31.6

Graph 3. HDL-C, LDL-C and TG in controls, hyperlipidemics and after treatment.



Graph 4. TC in control, hyperlipidemics and treatment groups



DISCUSSION

The study showed significant anti-hyperglycemic and anti-hyperlipidemic activity of Murraya koenigii. Kesari et al. results revealed a defined role of the water extract of Murraya koenigii leaves in suppressing blood glucose level [10]. Lipid peroxidation of unsaturated fatty acids is commonly used as an index of increased oxidative stress and subsequent cytotoxicity[11]. Murraya koenigii hypoglycemic and anti-hypolipidemic effects may be due to presence of antioxidants such as carbazole alkaloids and polyphenols[8]. Another Study has shown that mahanimibine (carbazole alkaloid from Murraya koenigii) has anti-hyperlipidemic and hypoglycemic effect thus mahanimibine has beneficial use in diabetes associated with abnormal lipid profile and cardiovascular complications[12].Hypoglycemic effects of Murraya koenigii were comparable to Glibenclamide[13]. Murraya koenigii thus seems to be a promising plant with respect to its hypoglycemic effect and may be prescribed as adjunct to dietary therapy and drug treatment for controlling diabetes mellitus.

CONCLUSION

This result showed that the Murraya Koeniigi have potent antioxidant activity due to the presence of biological active components such as carbazole alkaloids, glycoside, and phenolic compounds due to this Murraya leaves acted as anti-diabetic because it is also responsible to decrease the absorption of the glucose from gastrointestinal tract and inhibits the lipid peroxidation.

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ORIGINAL ARTICLE

IMPACT OF ACADEMIC INTERVENTIONS ON STUDENTS PERFORMANCE IN ELECTIVES

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ABSTRACT

Background: Elective clinical rotations have become a significant part of most of the medical educational curricula. Evaluation of electives is imperative to assess their usefulness in achieving the objective of improving the competencies of graduating students. Results of these evaluations can be used to guide future academic developments.

Objective: The purpose of this study was to assess the change in the performance of medical students after academic intervention based on the results of evaluation of previous year electives.

Methods: Students' performances in elective rotations were evaluated in the year 2012 and again in 2013 after bringing modifications in teaching / learning program. The data collected was from 60 students. Students consisted of two sets, those who completed their electives in the country while the other completed their electives abroad. Scores were calculated in three distinct domains of education i.e knowledge, attitude and ethical behavior. Independent Sample T test was applied to compare the scores.

Results: Findings suggest that as a result of the academic interventions carried out in 2013 in the educational program by the combined efforts of the faculty and students, the scores for all the three educational domains in both the local and abroad groups improved considerably.

Conclusion: Study findings conclude that active curricular interventions play important role in improving the outcomes of teaching programs.

KEY WORDS: Knowledge, attitude, participatory action research, ethical behavior

INTRODUCTION

Since the last century, traditional medical curricula for bachelor's degree programs were mostly prescribed and students found minimal opportunity to select courses of their own choice. Hence cohorts of medical students were exposed to similar learning opportunities and experienced the same learning settings.

Medical education being a dynamic field has witnessed revolutionary changes in its curricula throughout its long history. Harden et al. presented the concept of SPICES Model of medical curriculum in 1984 which represented a spectrum of curricula ranging from standard programs to those having elective courses.[1]. Another model of medical curriculum designed for the twenty-first century was conceptualized by Bligh, Prideaux, & Parsell. It has the acronym PRISMS which suggested multisite learning experiences for medical students. These changes in curriculum were proposed with the aim to develop physicians for the 21st century who possess the knowledge, skills, and attitudes that satisfy the societal expectations and meet the requirements of national and international health care systems. [2,3,4,5].

Presently, most of the Medical education institutions are providing some dedicated time to the students to experience medicine in a diverse clinical setting. [6] The objectives for providing electives in medical curricula vary from institution to institution; the most common one being to improve the clinical skill and knowledge of the students [7] . Electives can be internal or external. Internal electives are the ones in which students gain firsthand experience in their selected disciplines within their parent institution while in external electives learning takes place in a clinical/ research set up outside the parent institute. Due to internationalization of medical education, it is becoming increasingly important for the medical schools and residency programs to provide opportunities for learning other than the ones in the local/community settings. Students are also realizing the need to improve their professional competence by working at other health care facilities. In this wake, students from developing countries are making efforts to travel abroad and gain experience in technically advanced countries offering highly sophisticated learning environments. [2] Most often these electives are unilateral arrangements made by the students and result in improvement of professional competence and effect career choice. [3, 4, 5,6,7,8]

At Ziauddin Medical College the students of fifth year are provided a dedicated one month's duration to pursue medical electives. In most of the medical education programs, electives are placed in the later clinical years so that the students have a better opportunity to improve academically as well as clinically. Four weeks time for electives is enough to enable the students to get used to the change in culture and environment and assimilate new learning. 10 Selection of elective is totally a self directed activity at the college so students have the freedom to choose and decide for the training site themselves. Almost all the ZMC students opt for external electives; some manage for electives outside the country while a large number take elective clinical rotations in medical institutions within the country. Evaluation being essential to establish the reliability of any educational activity, student's performance in electives at Ziauddin Medical College is evaluated externally by the supervisor or the incharge of elective rotation in the host institution.

METHODS

Participatory Action Research was carried out on the basis of analysis report of elective evaluation forms submitted by the final year students of 2012 batch and was used to find out the weaknesses in their performance in order to guide the future. [11]

At Ziauddin Medical College fifth year medical students going for electives are mandated to get Elective Evaluation forms filled and signed by the supervisor/ incharge of elective rotation at the host institute and submit them to their clinical coordinator. These evaluation forms are designed on Likert scale and evaluate medical student's core competencies under the subdivision of knowledge & skills, attitudes and ethical behavior [12]. Every year, analysis is done and reports are generated which are used to identify the weaknesses in the afore mentioned domains and improvements are planned accordingly.

Keeping in view the findings of the elective evaluation report of 2012, following steps were taken to improve the future performance of the students in the electives:
1. In the beginning of the year 2013, a meeting was organized with the 5th year students and the clinical faculty involved in their teaching. Elective evaluation report of the year 2012 was shared and discussed at length.
2. Didactic teaching sessions were reduced in number and lectures were scheduled strategically to cover the core curriculum only.
3. Emphasis on teaching of clinical skills was increased and sessions for clinical examination were increased in number.
4. Major changes in clinical rotation schedule were carried out and more time was dedicated for rotations in high density units and Emergency Rooms.
5. Frequent student teacher meetings were carried out throughout the year. These were aimed to provide feedback to the students.
6. It was decided by the Board of Studies of Ziauddin Medical College that student assessment will be carried out at the end of each clinical rotation in the 3rd and 4th year and weightage of 5% and 10% respectively, will be carried forward to the result of summative assessment at the end of 5th year.

In 2013, after the completion of elective rotations, evaluation forms were collected from the students and data analysis was done.

The primary purpose of this study was to assess the effectiveness of academic interventions carried out in the educational program of final year after identifying the weaknesses in the previous electives evaluation report.

DATA ANALYSIS

Data from the evaluation forms was based on scores secured by students who had completed their electives and were evaluated by their supervisors in three different educational domains for two different years i.e in 2012 and 2013.

Analysis of data was carried out using Statistical software "Statistical Package for Social Sciences" version-20. Secured score was presented in terms of Mean±SD. Independent Sample T test was applied to compare the secured scores in the three given domains i.e. knowledge & skills, attitude and ethical behavior for each year. In order to compare the secured scores for each year, the students were further divided into two groups i.e those who have done the electives locally and those who did it abroad. Furthermore, Local and abroad groups were compared regarding the above mentioned three domains for both years separately.

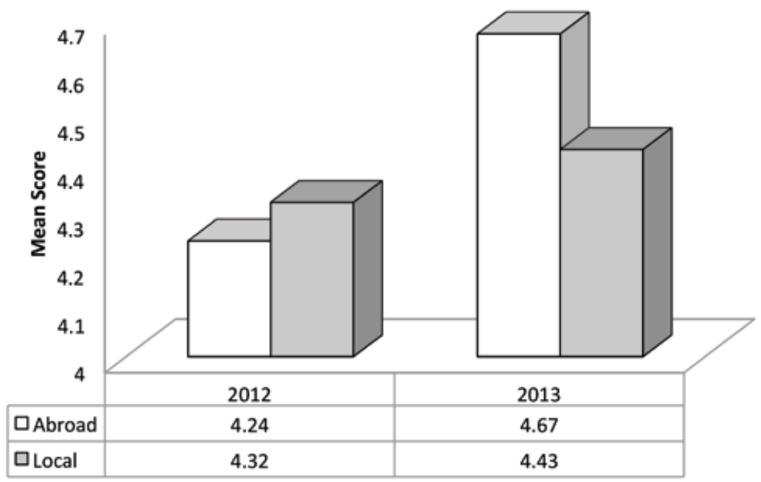
RESULTS

It was observed from the findings that secured scores for all three educational domains were significantly higher in year 2013. Among all the three domains, students secured highest score in ethical behavior for year 2013 with mean 4.58 and SD 0.407. Difference between secured scores for year 2012 and year 2013 was also highest in ethical behavior and is 0.37 (Considering significance level 0.05).

Comparing local and abroad groups, it was evident from the data that there was no significant difference detected between the secured scores of local and abroad student groups in year 2012 while in year 2013, statistically significant difference was observed among the two groups (P-value 0.026). Both groups improved their overall secured score i.e. difference between scores of both the years was 0.12 and 0.44 for local and abroad ones respectively. Overall highest scores were secured by abroad group in year 2013 (Considering significance level 0.05).
was used as a parameter for the oxidative stress showed a mark decline oxidative stress. No physical parameter changed except drastic effect of weight loss. Graph 1 shows glucose levels in control, hyperglycemia and after therapy. Graph 2 shows glutathione levels in control, hyperglycemia and after therapy. Levels of glutathione were 3.5 nmol/L in therapy animals as compared to 2.5 nmol/L in hyperglycemic animals, showing reduction in oxidative stress.

Table 1 shows comparison of lipid profile of controls and hyperlipidemics. Table 2 shows the comparison of hyperlipidemic and treatment group, p-value was significant. Graph 3 shows LDL-C, HDL-C and TG of hyperlipidemics and after treatment. Graph 4 represents the total cholesterol in control, hyperglycemia and after therapy.

Fig. 1. Comparison of Mean scores secured by students of year 2012 and 2013



In group of students who completed their electives abroad in the year 2012, scores for attitude and ethical behavior were significantly different from those of the local group with P-value 0.017 and 0.010 respectively. On the other hand, secured scores for knowledge and attitude in 2013 were significantly different among students in region wise elective groups i.e. P-value 0.039 and 0.020 respectively.

Table 1. Comparison of Objectives

Attributes	Year-2012 Mean ± SD	Year-2013 Mean ± SD	P-value
Score	4.23±0.432	4.52±0.403	<0.01**
Knowledge Skills	4.14±0.524	4.31±0.466	0.045*
Attitude	4.32±0.467	4.58±0.407	0.001**
Ethical Behavior	4.25±0.662	4.62±0.491	<0.01**

Table 2. Group wise comparison of Objectives for students of 2012

Objectives	Local Mean ± SD	Abroad Mean ± SD	P-value
Knowledge Skills	4.15±0.58	4.12±0.42	0.763
Attitude	4.23±0.50	4.48±0.36	0.017*
Ethical Behavior	4.12±0.72	4.49±0.47	0.010*

Table 3. Group wise comparison of Objectives for students of 2013

Objectives	Local Mean ± SD	Abroad Mean ± SD	P-value
Knowledge Skills	4.47±0.543	4.2±0.372	0.039*
Attitude	4.74±0.47	4.49±0.32	0.020*
Ethical Behavior	4.75±0.517	4.53±0.464	0.097

DISCUSSION

In this study participatory action research was used to assess the difference in the performance of students in elective rotations after launching planned changes in the teaching/ learning methodology. In action research actual educational problems are discussed for the purpose of rectification of the existing ones and strengthening the program for future. The participants of action research use reflective strategies to propose new changes [13]. Students of ZMC who entered final year in 2013, and all the faculty involved in their teaching participated in the discussion for finding out means to improve learning in the fields identified in the previous year's elective evaluation report.

With the encouragement to become responsible for their own learning, students actively contributed in decision making regarding the teaching schedule and teaching/ learning methodologies. Studies have shown that a learner centered approach to curriculum improves academic performance as well as the quality of learning [14, 15, 16]. Retention of knowledge in the long term memory is enhanced if the students are actively involved in their learning program [17, 18].

Lectures in large groups are notorious as there is little interaction with the students and passive learning takes place [19]. During the student faculty interaction it was suggested that the number of lectures was to be reduced and more time should be provided for learning in wards and emergency rooms. This combination of active learning and student centered instruction acted as a strong motivating force for the students and the improvement became evident from the results of performance of the batch of 2013 in their elective rotations [20]. Statistically significant difference between the scores of the two years and between the two groups of the year 2013 clearly depicts that the student centered approach in instruction as well as the participation of the students in improving their academic performance facilitated them in achieving the objectives of the elective rotations.

Students going outside the country for electives in 2013 probably took the challenge of performing more seriously than the previous year group and got the highest scores among all the groups of the two years.

In the year 2012, analysis of elective evaluation forms showed that students possessed good clinical knowledge but were weak in clinical skills. Learning of facts is different from learning of skills and to enable skill's learning practicing of the required skill is imperative [21]. During faculty student meeting in 2013, the teaching program was revisited. More time was allocated for student interaction with the patients and performing and practicing clinical skills by increasing the time spent in the clinics and wards. Duvivier et al. very aptly stated "repitition itself is not enough; progress depends on sustained efforts to purposefully enhance particular aspects of performance." [22, 23]

Students going for clinical electives outside their parent institution face challenges of language barrier that may affect communication with the patients and their families, as well as of cultural change and professional attitude [24]. Ethical considerations to healthcare though not much emphasized in our national medical curriculum, are given paramount importance internationally. Medical Ethics as a topic is not explicitly taught at Ziauddin Medical College but is learnt by the students implicitly. More often than not, the students try to emulate their teachers in professional behavior and handling of ethical issues. Ethical behavior and professional conduct are also assumed to be the tacit traits of clinical practice at Ziauddin hospitals. [25, 26, 27,28] Students of the class of 2012 who were going abroad were probably cognizant of the importance of ethical behavior and made conscious efforts to develop themselves as compassionate and culturally competent healthcare providers.

CONCLUSIONS

Involvement of students and teaching faculty in Participatory action research helps in improving the results, as in this study in the performance of students in elective clinical rotations [29]. Use of Quantitative assessment data of the previous year can be used to highlight the weaknesses in learning and provide directions for forthcoming educational programs.

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ORIGINAL ARTICLE

MEDICAL MANAGEMENT WITH VAGINAL MISOPROSTOL VERSUS SURGICAL MANAGEMENT FOR FIRST TRIMESTER PREGNANCY FAILURE

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ABSTRACT

Background: The incidence of clinically recognized miscarriages remains around 10-20%.The most common type of early pregnancy failure include spontaneous abortion, anembryonic gestation and embryonic or fetal death (missed miscarriage).In this study we compared the effectiveness of vaginal misoprostol for the management of first trimester pregnancy loss in obtaining adequate evacuation of uterus as an alternative to surgical evacuation in a tertiary care hospital.

Methods: This was a Quasi experimental trial conducted at Ziauddin University Hospital and the study participants were 180 women who presented with first trimester miscarriage upto 12 weeks of gestation. The women were divided into two groups according to their choice (90 women in each). Group one named Misoprostol group who received tablet Misoprostol 800mcg vaginally, two dose 6 hours apart. Group two named surgical evacuation group, who underwent surgical evacuation under general anesthesia.

Results: The success rate in achieving complete evacuation of uterus was 82.8% in misoprostol group in the current study while in surgical evacuation group it was 100%.No serious side effects were encountered in misoprostol group.

KEY WORDS: Misoprostol, Medical management, Miscarriage

INTRODUCTION

The incidence of clinically recognized miscarriage remains around 10-20%.[1] The most common types of early pregnancy failure include spontaneous abortion, anembryonic gestation and embryonic or fetal death (missed miscarriage). Approximately one in four women will have an early pregnancy loss during her life time.[2] It is estimated that 89,000 women present with miscarriages annually in Pakistan and the estimated annual miscarriage rate is 29 in 1000 women between the ages of 15-49years.[3] The management options to evacuate the uterus are expectant, medical and surgical.

Expectant management for incomplete abortion in the first trimester after use of misoprostol or after spontaneous abortion may be practical or feasible, although it may increase anxiety associated with impending abortion.[4,5] The period to spontaneous expulsion is unpredictable, and it may take up to four weeks. Medical management with misoprostol for early pregnancy loss appears to offer more prompt expulsion of products of conception and has become an increasingly popular method.[6] Surgical evacuation of retained products of conception (RPOC) was the mainstay of treatment for a long time to reduce complications such as infection and hemorrhage. However, surgical management may be complicated with infection, uterine perforation or bowel damage.[7] This draw more attention to medical and expectant management. In a recent prospective comparative study vaginal surgical evacuation was successful in 100% of cases, while medical management with misoprostol was successful in 79.6% of cases.[8]

In spontaneous end of pregnancy before fetal viability up to 12 weeks of gestation, patients may present with or without p/v bleeding, while ultrasound show early pregnancy failure with no cardiac activity. Diagnosis of incomplete miscarriage is made when there is a history of passage of tissue or heterogenous echogenic material in uterine cavity with a thickness of>15mm on ultrasound. A missed abortion is diagnosed when an intrauterine gestation with a fetal pole measuring > 6mm is demonstrated with no cardiac activity. An anembryonic pregnancy is diagnosed when the diameter of gestational sac was >20mm with no visible foetal pole.

On the whole the success rate of medical management (72–93%) is almost similar to that of expectant management (75 – 85%),[9] but the advantage of medical management is that patient can control the course of events by timing medication to allow the miscarriage to take place. However, success rates are dependent on how much time has passed following treatment: the longer the duration, the higher the success rate. When compared with surgical management, medical management is associated with significantly more blood loss but no increased requirement for blood transfusion.[10]

When compared with placebo vaginal misoprostol speeds up the miscarriage process and reduces the need

for surgical evacuation. Vaginal misoprostol 800mcg is more effective than oral misoprostol 400mcg. There were no serious side effects with the use of vaginal misoprostol. A single dose of 800mcg appeared more effective than lower doses.[11]

Pharmacokinetics studies comparing oral and vaginal administration have shown that vaginal misoprostol is associated with slower absorption, lower peak plasma levels, and slower clearance, similar to an extended-release preparation.[12,13] Vaginal misoprostol is also associated with a greater overall exposure to the drug (area under the curve [AUC]) and greater local effects on the cervix and uterus.[13] There is, however, a wide variation in the absorption of misoprostol through the vaginal epithelium among different women. There is no clinically significant difference between vaginal misoprostol that is administered dry and vaginal misoprostol moistened with water, saline, or acetic acid.[12,14,15]

In most studies misoprostol was used by the oral route and there are indications that the vaginal use may be more effective. For this reason misoprostol is used through vaginal route in the current study for the medical management of miscarriage.

METHODS

This Quasi experimental trial was conducted in the department of obstetrics and gynaecology, Ziauddin University Hospital, for a period of six months from 1st August 2014 to 31st January 2015. The calculated sample size was 90 women in each arm, calculated through Gehan tables using a difference in cure rates of 20% at 95% confidence level and 80% power.(total sample size 180).The Sampling Technique was non probability consecutive sampling. The Inclusion Criteria was women who presented with Incomplete, missed miscarriage and anembryonic pregnancy up to 12 week gestation, Haemodynamically stable,willing for medical management.

Exclusion Criteria was Hypersensitivity to misoprostol, heavy bleeding requiring immediate evacuation, second trimester miscarriages, women with inevitable abortion, history of more than one previous caesarian section.

Data Collection Procedure: After approval from ethical committee of Ziauddin University Hospital, all eligible females fulfilling the inclusion criteria were provided necessary information about the study protocol and both the options available for the treatment and written consent was taken. The eligible women were divided into two groups according to patients choice, group (1) named misoprostol group, received tablet misoprostol 800mcg vaginally and repeated in a dose of 800mcg after 6 hours if needed(total two doses 200mcgx4),while group(II) named surgical evacuation group undergone surgical evacuation of uterus under general anesthesia by the standard technique of the hospital. Both groups were remain admitted in hospital and were followed for the first 24 hours for abdominal pain(pain was assessed by using visual analogue score) ,vital signs, presence of excessive bleeding defined as vaginal bleeding more than menstrual blood with or without presence of blood clots. Patients were observed for passage of products of conception per vagina as well as for severity of vaginal bleeding .Patients with no excessive bleeding were discharged home after 24 hours in misoprostol group after confirming complete evacuation of uterus by transvaginal scan. In group II patients had surgical evacuation of uterus by conventional method. The patient were kept postoperatively for 12 hours and then discharged if stable. Both groups were called for follow up on 10th day of treatment and were assessed by transvaginal scan for complete of evacuation of uterus. If endometrial thickness was less than 15mm no treatment was required, if it was more than15mm surgical evacuation was offered to the patient.

STATISTICAL ANALYSIS

Recognizing that the success rate of medical treatment is unlikely to exceed that of surgical treatment for early pregnancy failure, we designed the study as a non-inferiority trial. Success is defined as complete uterine evacuation without the need for surgical evacuation in the medical management group. Data was be entered, edited and analysed using SPSS (Statistical Package for the Social Science) version 20. Descriptive analysis was carried out with frequencies and percentages for categorical variables. Chi square test was applied. P value less than 0.05 was taken as statistically significant.

RESULTS

A total of 180 women were recruited in the study, 90 in misoprostol group, and 90 in surgical group .The age range of study participants was 18-39years and mean age was 26-years. Results of current study showed that both groups were similar with respect to age, parity, gravidity, number of previous miscarriages, and clinical symptomatology with no statistically significant difference. In the study participants 56.7% had missed miscarriage, 35.6% had incomplete miscarriage and 7.8% had diagnosis of anembryonic pregnancy. The total dose of misoprostol required for successful treatment in medical group was 1600mcg i.e. four tablets of 200mcg (800mcg) administered vaginally 6 hours apart.

Table:1.Clinical Outcomes Of Study Groups

	Misoprostol group n=90 (%)	Surgical group n=90 (%)	P-value
Success of treatment	74(82.8%)	90(100%)	--
Patient satisfaction Yes No	 84(93.3%) 6(6.7%)	 90(100%) 0(0.00%)	 0.014
Recommend to others: yes No	 78 (89%) 9 (10.3%)	 90 (100%) 0 (0.00%)	 0.001
Incidence of moderate pain	39 (43.3%)	30 (33.3%)	0.004
Blood loss more than menstrual loss less than menstrual loss	 57 (63.3%) 33 (36.6%)	 15 (16.6%) 75 (83.3%)	 0
Endometrial thickness <15mm >15mm	 74(82.2%) 13(14.4%)	 90(100%) 0(0.00%)	 0

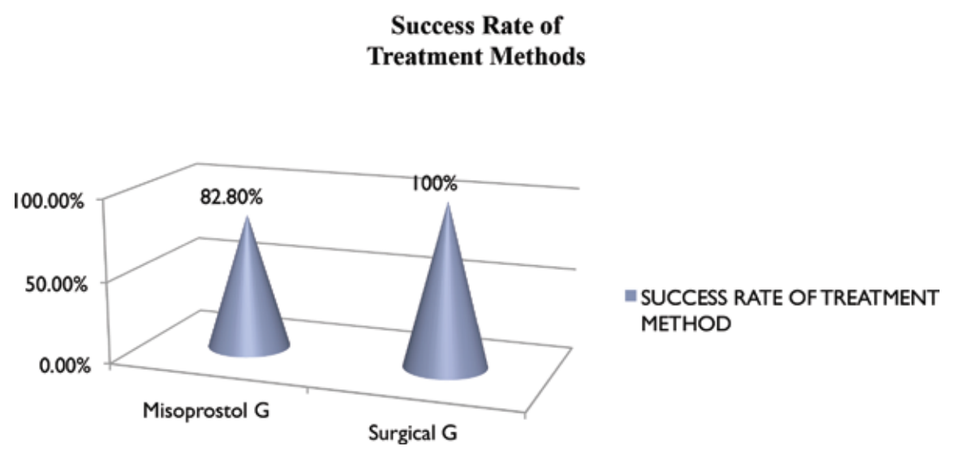
Figure 1: The overall satisfaction was slightly higher in surgical group but most of the women in misoprostol group expressed their satisfaction about treatment.

Out of 90 study participants (84/90) 93.3% required two doses of 800mcg vaginal misoprostol given 6 hours apart for successful expulsion of products of conception, while (6/90) 6.6% required single vaginal dose of 800mcg.Mean induction expulsion time was 12 hours.

Most of the subjects expelled products of conception in 8–16 hours. The overall success rate was 82.8 % in Group 1 (misoprostol group) and 100% in Group 2 (surgical group). Out of 90 women in Group 1, only15 i.e. 17.2% had to undergo surgical evacuation due to excessive bleeding or incomplete expulsion of products of conception.
Repeat evacuation was not required in any patient in surgical group. The side effects during and after treatment were minimal in both the groups. Pain scores were slightly higher in misoprostol group but most of the women experienced moderate pain and did not required analgesia.

In misoprostol group 15 patients i.e.17.2% required analgesia and 82.8 % did not require any analgesics. In surgical evacuation group 9 out of 90 women required analgesia. Post abortive blood loss was heavy in misoprostol group as compared to surgical evacuation group but none of the subjects required blood transfusion. Women in misoprostol group told that the blood loss was more than menstrual loss. (soaked more than 3-4 pads per day).

Figure 2. Misoprostol group: 82.80% success rate. Surgical group: 100% success rate.



The endometrial thickness on TVS ultrasound was more than 15mm in 13 women and less than 15mm in74 women (85%) in group 1 which was considered a cut off value for complete evacuation of uterus.

The mean duration of hospital stay was 30 hours in misoprostol group and 24 hours in surgical evacuation group. Only 1 patient (1.1%) had signs and symptoms of vaginal infection after medical management, came with complaint of pain in lower abdomen, and discharge p/v.

DISCUSSION

Medical management of miscarriage is becoming

increasingly popular. The current study demonstrated that vaginally administered misoprostol in a dose of 1600mcg (four tablets of 200mcg repeated after 6 hours) is efficacious. The primary outcome measure of the study was to achieve complete evacuation of uterus and expulsion of products of conception without surgical evacuation .The secondary outcome measures included the number of doses of misoprostol, duration and amount of post abortive bleeding, incidence and severity of cramping abdominal pain, need for analgesia, the duration of hospital stay, patients satisfaction with the treatment method and future choice of patients, and whether they will recommend the method to a friend or relative or not. The success rate with Misoprostol has varied from 13-25% with single oral dose of 400µg to 88% with single vaginal dosage of 800µg.[16,17] Three major randomized controlled trials comparing misoprostol with surgical evacuation have been carried out. The success rate with vaginally administered Misoprostol ranged from 53-83%, whereas that with surgical evacuation ranged from 96-100%.[16, 18, 19]

Medical management with Misoprostol was found successful in 82.5% of subjects as compared to 100% of subjects managed surgically (Demetruolis et al., 2001).[16] Inanother study by Zhang et al., 84% of subjects were

successfully treated with Misoprostol as compared to 97% with vacuum aspiration.[20]Amanda et al., M. Creinin et al. and Gilles et al. have also observed similar success rates.[21,22,23] The results of the present study are also comparable with these studies and the success rate observed was 82.8% in medical group with two doses of vaginal misoprostol and 100% in surgical evacuation group.

The presence of symptoms like abdominal pain and heavy vaginal bleeding significantly affected the success rate of medical management with misoprostol. The women in misoprostol group who had under gone surgical evacuation were mostly due to heavy bleeding p/v and intact gestational sac after completion of treatment with two doses of 800mcg vaginal misoprostol. We did not observe any significant relationship between gravidity or gestational age and success rate. We also found that success rates vary with the type of miscarriage and maximum success rates were seen in cases of incomplete miscarriage.

Past studies established no specific sonographic criteria of endometrial thickness to label as failure of medical management. Graziosi et al., Nielsen et al. and Luise et al. [24,25,26,27] have used an endometrial thickness of 15mm as cut- off for success, while Zhang et al. defined endometrial thickness >30mm as incomplete abortion.[20] M Creinin et al. found endometrial thickness an important measure to assess the completion of abortion.[21] They noted a wide variation in endometrial thickness after expulsion of gestational sac. None of the subjects in their study with an endometrial thickness less than 15mm required surgical evacuation.[21] In the current study I also considered an endometrial thickness of 15mm as cut off value for success of medical management and my study also confirmed the same findings and none of the patient with endometrial thickness 15mm or less than 15mm required surgical evacuation. Although an endometrial thickness less than 15 mm was found to predict successful medical management, clinical indicators such as a closed cervical os and cessation of bleeding were also considered important prognostic markers. It was therefore concluded that all subjects with an endometrial thickness 15mm or <15mm should be labelled as having complete evacuation after 24 hours of treatment. Further course of treatment should be decided by clinical and ultrasound findings on follow up visit after ten days.

We discharged the patients after completion of treatment with misoprostol in whom endometrial thickness was found to be less than 15mm on TVS .None of these women presented with heavy bleeding p/v within 24-48 hours of misoprostol administration.

Vaginal and oral misoprostol are equally effective although the oral regimen has higher gastrointestinal side-effects. Nynde et al.[28] compared oral and vaginal administration of 200 micrograms of misoprostol given 6 hourly for up to four doses. The induction to expulsion time was significantly shorter in the vaginal group which was nearly 8 hours. The current study also demonstrated that vaginal route of misoprostol has minimal and tolerable side effects and higher success rates.

The data available about the timing of repeat dosage include intervals as frequently as 3 hours and as long as 24 hours. The reports that described the shortest interval from induction to expulsion included regimens in which doses repeated every 4 to 6 hours.[29,30] In the current study we also used misoprostol at an interval of six hours and found it very effective as expulsion of products of conception was completed after 12 hours of administration of 2nd dose of misoprostol in majority of study participants.

CONCLUSION

Vaginal administration of Misoprostol is safe, effective and cheap when used as alternative to surgical evacuation or when facilities for surgical evacuation are not available.- No serious adverse effects are observed with a vaginal misoprostol and many disadvantages of surgical evacuation are avoided. The option of medical management should be given to all women presenting with early pregnancy failure as it significantly decreases the need for surgical intervention and also reduces the risks related to general anaesthesia.

RECOMMENDATIONS

The development and implementation of national guidelines regarding medical management of miscarriage or adoption of an international guideline might prevent women from undergoing unnecessary curettage. It could improve overall treatment results, enhance satisfaction in women treated with misoprostol and reduce practice variations.

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CASE REPORTS

BIRTH OF QUINTUPLETS A GREAT CHALLENGE

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ABSTRACT

Different names have been used for multiple births depending on the number of offspring of which common multiples are 2 and 3, in our case we have 5. They are associated with high rates of complications like: preterm labor, pre eclampsia, low birth weight and significant perinatal mortality and morbidity. Quintuplets occur rarely making the survival of infants even rarer. We here report a case of non-booked woman who presented in her third trimester of gestation. Who on ultrasound was found to be having 4 babies but surprisingly at the time of delivery,5 babies were delivered by caesarean section, of which one was IUD (intrauterine death) and another baby expired on the second day of operation due to interventricular hemorrhage as the infant was of low birth weight and premature. The remaining infants were kept in NICU. This is a very precious pregnancy and since we found out that the frequency of multiple pregnancies with more than two fetuses has increased considerably since the introduction of methods of ovulation induction the case was looked on carefully according to the requirements.

KEY WORDS: Quintuplets, antenatal care, caesarean section, perinatal mortality, perinatal morbidity, IUD(intrauterine death)

DISCUSSION

Gestational diabetes mellitus is a state of glucose and A dramatic increase in the incidence of high multiple pregnancy since mid-seventies has been well documented and found in medical literature [1-4]. In addition to economical and logistical problems associated with them, these infants have a high rate of mortality and morbidity. [3-6]. Firstly we will present an account of surviving quintuplets and their occurrence, followed by the medical issues involved in the management and care of such cases.

CASE REPORT

A 30 year old woman, married for 16 years, G3 Para 0+2, presented at 27th week of gestation with quadruplets as a result of ovulation induction treatment. She has pregnancy induced hypertension and is referred from a private hospital in Quetta, for good antenatal care and management. On admission, the husband was counseled completely about the status of the babies, need of ICU, NCU and further complications were explained. High risk consent was taken.

Physical examination revealed a young woman, looking-pale, sitting uncomfortably due to huge edematous abdomen and pedal edema.She was hospitalized immediately for blood pressure and fetal growth monitoring. Corticosteroid Betamethasone was offered for lung maturity. On admission her BP was 160/100mmHg, pulse 88bpm, Oxygen saturation was 98%.

On abdominal examination, height of fundus was more for gestational age due to multiple pregnancies, fetal heart sounds were audible and multiple fetal parts were palpable. Abdomen was very edematous.

Ultrasound examination further revealed quadruplets, but quintuplets could not be ruled out. The presentation was both breech and cephalic. Fetal heart activity was present. Initially the amniotic fluid was adequate but later it decreased in amount. No gross fetal abnormality was noted.

Her Hemoglobin was found to be 6.8g/dL,platelets were 248×10^9/L, urea 20 mg/dL ,uric acid 7.65 mg/dL, creatinine 0.48 mg/dLand urine albumin was positive 100mg/dL. Coagulation profile was within normal range.Anemia was corrected by blood transfusion. Hemoglobin was checked weekly while renal functions were also monitored on alternate days that were gradually increasing. Proteinuria was also increasing when investigated on daily basis. Physician was involved.Fetal monitoring was done by CTG twice a day that was normal. Doppler Ultrasound was also performed on alternate day that showed mild placental insufficiency. On the 30th week, one of the infants on monitoring was found IUD. After which the parents were again counseled and informed about all the possibilities which may occur and affect others as well since her blood pressure was high and that she should be operated immediately. They were counseled about the elective caesarean section.Both the patient and husband agreed.

During caesarean section,surprisingly the quintuplets were revealed, one was IUD and four were alive. Three female babies had breech presentation of weight 1.3kg, 1kg and 1.3kg respectively, one male of 1.5kg was cephalic, and female IUD of 0.6kg had an oblique lie. Apgar score of 2 was 6/1, 2nd was 8/5 ,third was resuscitated due to respiratory distress syndrome who was then moved to the ventilator and eventually died on the second day of operation due to prematurity as mentioned above. The pregnancy was di-amniotic and di-chorionic and placenta was delivered one by one. Liquor was found to be clear. Uterus was very large for which a B-Lynch suture was applied prophylactically to prevent the postpartum hemorrhage. Oxytocin and Misoprostol were given to prevent the postpartum hemorrhage as an active part of management. Intraoperatively one packed cell and 6 FFPs were transfused.

DISCUSSION

Quintuplets are rare and unique because "quintuplets pregnancies are associated with high rates of obstetrics complications and significant perinatal morbidity and mortality" [8].

Literature and Web were searched for more data regarding quintuplets in general and those who survived. The first quintuplets that are known to have survived infancy are Dionne quintuplets born 28th May 1934 in Corbeil, Ontario, Canada (Figure 1).

Figure 1.Quintuplets born on 17th September 2014, Karachi

Figure2.The Dionne sisters in 1947.

Before the Dionne, the world record for surviving quintuplets had been 55 days, born to mother in Lisbon, Portugal in 1866.[7]Other well followed up and well described quintuplets include the Whalen quintuplets and the Brooks quintuplets [7].

In Pakistan, there has been one previously reported case of a woman giving birth to three boys and two girls in Karachi through caesarean section. We know a case born through normal vaginal delivery and without treatment in Quetta in 2008.
In a report by Schenker et al. [9] above five quintuplet pregnancies, 3 delivered by caesarean section at 33 to 35 week gestation, of the 15 children born, 13 survived. In another report, quintuplets are reported to have survived the perinatal period. [10]. The largest report comes from Francois et al. [8], who reviewed 36 cases of quintuplets arising from ovulation induction (5cases) and hormonal stimulation and assisted reproductive technologies (31cases).

Regarding complications, in this largest dataset, all pregnancies, as in this case, were complicated by preterm labor: 6 delivered before 24 week (Group A) and 30 delivered after 24 weeks of gestation (Group B) [8] .One from A and all from B were done by Caesarean Section. This case was also done by Caesarean Section. Other complications in those pregnancies that were delivered after 24 weeks include: anemia (13%), preeclampsia (57%) and vaginal bleeding (3%). [8]

The perinatal mortality reported in study by Francois et al. [8] was 253 per 1000 pregnancies. It was further compounded with neonatal morbidity within neonatal period. Minor morbidities such as patent ductus arteriosus responsive to medicine and necrotizing enetrocolitis that too responds to medical therapy were approximately 20% while the major one include abnormal neurological examination result and interventricular hemorrhage were found to be approximately 10% [8]. In our case the infant that died on the second day of operation had interventricular hemorrhage.

A review of 96 twin pregnancies was done in another city of Pakistan that showed that the patients coming from rural areas often present late in pregnancy leading to high rate of complications compared to those that came earlier [13]. Other study in Pakistan, the perinatal mortality rate in twins versus singletons was found 108 versus 82 per 1000 births that shows higher risk of antepartum and intrapartum complication in women with multiple gestations[12].Through this case we would like to highlight the need to focus on the delivery of women's health care services and to recognize the importance of antenatal care in the community so that burden of lives is reduced .[13]

Before the advent of fertility drugs, triplets were rare, quadruplets and quintuplets were never heard of. With spontaneous pregnancy rate for a quintuplets gestation is estimated as 1in 65,610,000 pregnancies by Hellin Law [8]With the advent of assisted reproductive technologies, these have now become so much common that the concern about obstetric implication has increased. The chance of identical quintuplets being born as in case of Canadian Dionnes sister is 1 in 57 million. Rate of quintuplets studied in Japan over a 12 year period was found to be approximately 0.77 per million births [14]. At the same time, as rightly pointed out by Babay et al. [15], multiple pregnancies carry a high risk and women with multiple pregnancies should be offered extra care during antenatal with specific objective of early diagnosis and timely treatment of complication. Specifically with reference to preterm labor, surveillance for sign and symptom should be undertaken at an early gestational age as compared to other pregnancies [8].

In the case presented, the babies are still in NCU and tolerating feed and doing fine. Mother is now normotensive.

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CASE REPORTS

UNDIAGNOSED CERVICAL ECTOPIC PREGNANCY IS A THREAT TO LIFE

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ABSTRACT

Cervical ectopic pregnancy implants in the lining of endocervical canal. Cervical ectopic is rare form of ectopic pregnancy and incidence of cervical ectopic pregnancy is 1:9000 pregnancies .We are reporting a case report of a 35 years old female P1+0 was presented in OPD with continuous per vaginal bleeding since 3 months. MRI pelvis showed 4.8x4.5x4.2 cm lesion involving the entire cervix including stroma with partial obstruction of endocervical canal. Growth was removed digitally with difficulty and was sent for frozen section & biopsy. Hemostasis was secured with great difficulty by taking sutures & cervix was packed. Report of frozen section showed products of conception. Injection Methotrexate was given intramuscularly.

Cervical ectopic pregnancy was associated with significant hemorrhage which led to hysterectomy in the past. Mortality is limited and fertility is preserved by improved ultrasound resolution, MRI and earlier detection of these pregnancies which has led to the development of more conservative treatments.

KEY WORDS: Cervical ectopic pregnancy, Methotrexate, endocervical canal, frozen section

INTRODUCTION

Ectopic pregnancy is any gestation that implants outside the uterine cavity.[1] Cervical ectopic implants in the lining of endocervical canal. Cervical ectopic is rare form of ectopic pregnancy in which .Incidence of cervical ectopic pregnancy is 1:9000 pregnancies .[2] Mortality is limited and fertility is preserved by improved ultrasound resolution, MRI and earlier detection of these pregnancies which has led to the development of more conservative treatments. [1] In this case we were unable to diagnose preoperatively as it was mimicking neoplastic lesion on history , examination and ultrasound.

Previous cervical and uterine surgery seems to be predisposing factors. In vitro fertilization, Asher man's syndrome, prior instrumentation, infertility and prior ectopic pregnancy have also been implicated as predisposing factors.[3]

CASE REPORT

A 35 years old female P1+0 was presented in OPD with continuous per vaginal bleeding happening since 3 months .She gave the history of admission 5 days back to another tertiary care hospital where 3 units of packed cell transfused because of severe anemia as result of heavy per vaginal bleeding. In that hospital her ultrasound pelvis was done which showed normal sized uterus with echogenic mass measuring 2.8x2.5cm in cervical canal most likely cervical polyp.

At the time of presentation in our OPD, patient was vitally stable with no positive findings on abdominal examination. Speculum examination was not possible because of heavy bleeding per vagina.

We advised her to get MRI of her pelvis done which showed 4.8x4.5x4.2 cm lesion involving the entire cervix including stroma with partial obstruction of endocervical canal, most likely neoplastic lesion of cervix .Her CBC was repeated which was within normal limits.

Examination under anesthesia, frozen section and biopsy of cervical growth was decided after obtaining written consent.

Intraoperative findings showed necrotic growth lying inside the cervix more on right side about 3x3 cm .Growth was removed digitally with difficulty and was sent for frozen section & biopsy. Hemostasis was secured with great difficulty by taking sutures and cervix was packed. Report of frozen section showed products of conception .Her βHCG was immediately sent after getting report of frozen section which was 1856iu/ml. Injection of Methotrexate was given intramuscularly.

After 2 days her βHCG was repeated the results of which were was 365 i.u/ml. The patient became well and was discharged after 3 days. She was subsequently followed up with final report of histopathology which showed cervical tissue exhibiting multiple chorionic villi covered by cytotrophoblast and syncytiotrophoblast. Findings were suggestive of cervical ectopic pregnancy.

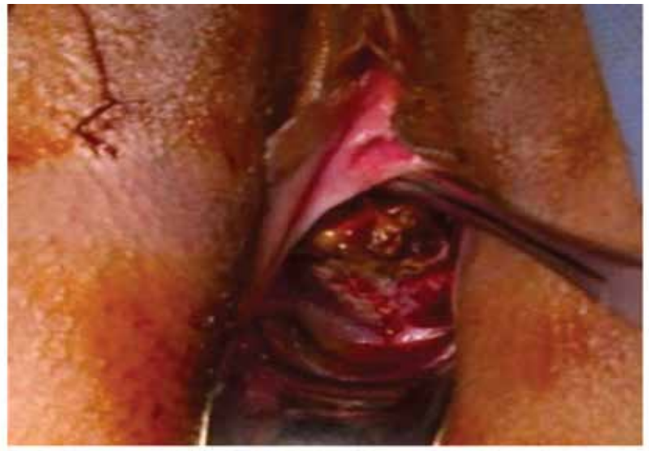

Fig.1 Necrotic growth lying inside the cervix more on right side about 3x3 cm

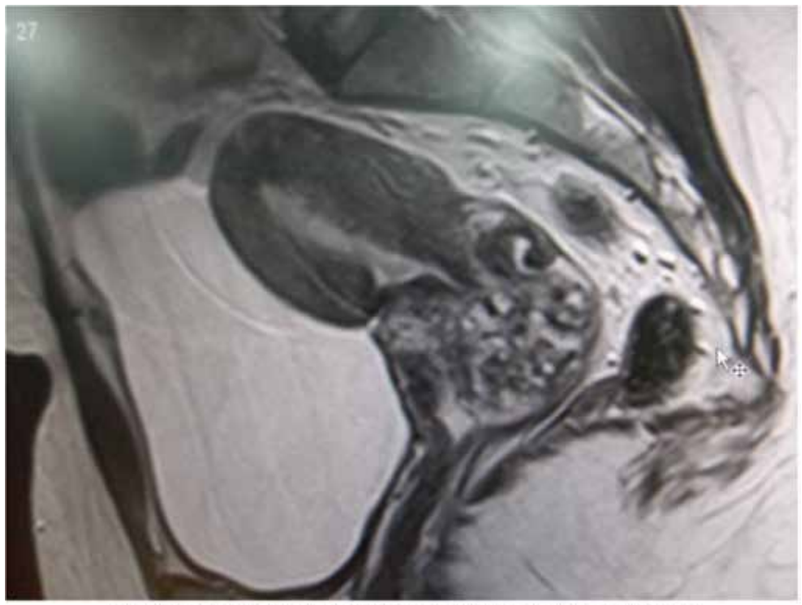

Fig.2 MRI showing empty uterine cavity & cervical ectopic pregnancy

Fig3. MRI showing cervical ectopic pregnancy as rounded cervical growth

DISCUSSION

Typical symptoms of cervical ectopic pregnancy are abnormal bleeding as in our patient and lower abdominal pain. 5 clinically practical criteria for the diagnosis of this condition were proposed by Palman and McElin.[2]

1 Following a period of amenorrhea uterine bleeding without cramping pain.
2 A soft but enlarged cervix equal to or larger than the fundus resembling the hour glass uterus.
3 Products of conception entirely confined within and firmly attached to the endocervix.
4 Internal cervical os is close.
5 External os is partially opened.

Clinical and ultrasound findings can lead to correct diagnosis but not in our case. In 81.1 %of patients sonography has led to more correct diagnosis.[3] Forthe early detection of cervical pregnancy ultrasound seems to be integral. Findings characteristic of cervical pregnancy include the so-called hourglass uterus or dilated cervix. Abortions in progress can be distinguished from those with vascular implantation in the cervix by Doppler flow sonography. Molinaro et al. has mentioned siding sac sign as a sign of cervical pregnancy that helps to distinguish it from an abortion in progress.[4]

Minimising the risk of severe haemorrhage, and to preserve the patient's future reproductive potential should be the goal to treat cervical ectopic pregnancy.

Medical management options include methotrexate (a folate antagonist) either administered systemically or by direct injection, or potassium chloride (direct injection).[5] Alternative therapy could be the use of curettage followed by locally acting hemostatic agents . Flystra et al. reported two cases in which pre curettage, vasoconstriction was obtained with local injection of vasopressin. Postoperatively a Foley balloon was placed to mechanically tamponade the operative site. Bagga et al. described cervical stay sutures as an additional method of cervical tamponade as we did in this patient of cervical ectopic pregnancy so her life and fertility was preserved[7]. Adjunctive techniques to control hemorrhage from curettage procedures are uterine artery ligation and embolization (UAE).[8]

UAE after methotrexate injection was reported by Cosin et al. to control bleeding with success[9]. UAE was used by Suzumori et al. to preserve the uterus of a woman who failed methotrexate combined with cervical sutures . I Infection, uterine infarction, sciatic nerve injury, and necrosis of the bladder or rectum could be the complications after UAE.[10]

Life threatening haemorrhage can be the result of surgical curettage. For reduction of haemorrhage risk, preoperative uterine embolization is an option.[5]

In our case examination under anesthesia frozen section was detrimental in diagnosis and hemostatic sutures and packing were life saving.

CONCLUSION

Cervical pregnancy is a rare condition if not diagnosed and treated early during the course of pregnancy, can be life threatening. Primary care providers who are involved in obstetric care should be very vigilant. They should include this entity in the differential diagnosis of women presenting with bleeding and cramping early in pregnancy. Early diagnosis and use of interventional management is necessary in preserving patient's fertility without significant complications.

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REVIEW ARTICLES

EPICARDIAL ADIPOSE TISSUE AND ITS EMERGING IMPORTANCE

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ABSTRACT

It is an emerging concept now a day that epicardial adipose tissue (EAT) thickness has an essential character in the progression for cardiac risk profile. It is now consider as a new and consistent cardiovascular risk factor. EAT thickness is the indicator for cardiac adiposity. It modifies the cardiac morphology and function. It has close anatomical relation to myocardium. It causes local paracrine interactions between myocardial tissues. It causes enlargement of left ventricle with its diastolic dysfunction.

Measurement and assessment of epicardial adipose tissue thickness is now done by new method echocardiography. It appraises visceral adiposity and inflammation. Association of EAT location and its physiological or pathological importance requires advance research. EAT in future may replace waist circumference, as a marker of abdominal obesity.
This article briefly discussion the structure of epicardial adipose tissue and its function. It also describes the method for its assessment.

KEY WORDS: Epicardial adipose tissue thickness, Cardiac adipose tissue, Brown adipose tissue, Visceral adipose tissue

INTRODUCTION

Knowing the importance of epicardial adipose tissue thickness and its cut off value will help the clinician for the early diagnosis and prevention of coronary artery disease. Therefore latest research from the current years showed that distribution of visceral fat causes the development of metabolic and cardiovascular risk factors [33]. Visceral adipose tissue is reliable predictor than generalized fat distribution for the identification of cardiovascular and metabolic risk profile [1]. Visceral adipose tissue has potential importance because of anatomical closeness to those viscera, especially of the heart [2]. EAT thickness is emerging as new concept for cardiovascular risk factor and indicator [3]. EAT modulates the morphology and function of the heart. It is dependable indicator for beneficial intervention [2, 3].

In latest research new interest is developing for studying and reliably quantifying adipose tissue [4].Most important technique for the accurate quantification of subcutaneous, visceral and therefore cardiac adiposity is Magnetic Resonance Imaging (MRI) [5].MRI is more expensive than echocardiography for research and clinical application[4]. Echocardiography can directly measure the EAT thickness [6].Echocardiography is widely available and is a commonly used radiological tool for the quantification of epicardial fat, and it is also less costly.

This article briefly discussion the structure of epicardial adipose tissue and its function. It also describes the method for its assessment.

Objective of the Study: This article will briefly review the epicardial adipose tissue and its emerging evidence to its specific role as cardiac risk factor marker and its budding role in the development of cardiac pathology.

Review Criteria: We searched MEDLINE, Google Scholar and Pub Med for original articles published between 1999 and 2013, focusing on epicardial adipose tissue. We gathered 120 articles on this topic among them we selected 36 articles for detail study. We selected these articles because these articles full fill our objectives of review. The search terms we used, alone or in combination, were "epicardial fat", "epicardial adipose tissue", "subepicardial fat", "visceral fat" and "echocardiography". All articles identified were English-language, full-text papers. We also searched the reference lists of identified articles and our own database for further relevant papers.

What is Epicardial Adipose Tissue?

The visceral fat is composed of adipose tissue [9]. Histologically adipose tissues are classificified into white adipose and brown adipose tissues [9]. It is the storage area for visceral fat of heart [7]. Brown adipose tissue is embryological origin for both epicardial and intra-abdominal adipose tissue [2].

Location of EAT

It occupies the atrioventricular and interventricular grooves [10]. Its small amount is also located subepicardially on the atria and auricles [11]. It occupies the space between ventricles and occasionally covers the entire epicardial surface in hypertrophy [2]. It also coves the coronary arteries and over the right ventricle [15] .This fat around the coronary arteries might have interesting importance because of its secure anatomic relation with the coronary arteries [36]. 80% of the heart's surface is covered by EAT and 20% of total heart weight is because of it. Metabolically it is active and

has anatomical and functional contiguity to the myocardium [12]. EAT thickness has important independent association with the myocardial fat [13]. It causes interaction of heart and its visceral adipose tissue stores because of its close relation with myocardium [14]. Its normal range is from 1mm to 23mm. [16].

Link of EAT Thickness with Obesity

As the visceral obesity increases it also increse the EAT thickness then it possibly contributes to obesity-associated cardiac changes [13]. Obesity develops in two different ways. Hypertrophic obesity results from the accumulation and storage of fat in unilocular fat cells. Hypercellular obesity results from an over abundance of adipocytes [9]. A study states that obese subjects have commonly increased amount of EAT [7].

Functions of EAT:

Recognized functions of epicardial adipose tissue include:

- It buffers coronary arteries torsion induced by the arterial pulse wave and cardiac contraction [15].
- It helps coronary artery remodeling [15].
- Protect the heart against high fatty acid levels by absorbing excessive fatty acids [16].
- In coronary microcirculation it regulates fatty acid homeostasis [15].
- It is local source of energy to cardiac muscles [15].
- Defending the myocardium against hypothermia [17] .
- It releases anti toxic substances for the neutralization of toxic end products of fatty [18].
- Provides several proinflammatory factors and anti-inflammatory adipokines [18, 35.]
- It also secretes adiponectin which is a serum protein [20, 35.]
- It actively produces several bioactive adipokines [21].

Biochemical Properties of EAT

Epicardial adipose tissue has a number of biochemical characteristics. It affects the energy metabolism besides its vascular, immunologic and inflammatory responses. It releases allots of inflammatory mediators [22]. The expression of these inflammatory mediators is perhaps because of the presence of inflammatory cells in epicardial adipose tissue. It releases adipocytes-derived tumor necrosis factor-α, which increases lipolysis via impairing insulin receptor signaling [22]. This fat also has adiponectin, an adipocytes-derived protein, which has profound anti-inflammatory and antiatherogenic properties [26]. Its levels were found to be low in CAD patients as compared to healthy adults [23]. Another factor resistin, an adipocyte secreted factor, was found in human epicardial fat [23] Presence of increased number of inflammatory cells in the region of advance arthrosclerosis also favors the inflammatory response [23].

This fat has the capability of amplifying vascular inflammation, plaque instability via apoptosis, and revascularization because of presence of tumor necrosis factor-α [22]. EAT has potential to accelerate the angiogenic response, that leads to the development of collateral circulation in patients with obstructive coronary artery disease [22].

Echocardiography

The echocardiogram is an extremely useful test for studying the heart's anatomy by ultrasound. The echocardiography when interpreted by a well-trained cardiologist is a very accurate tool for the assessment of epicardial adipose tissue thickness [16]. It is a useful diagnostic test for evaluation of patients with cardiovascular diseases because it provides reliable structural, functional, and hemodynamic information about the cardiovascular system. The major advantages of echocardiography include virtual absence of contra-indications, safety and its unparalleled temporal and spatial resolution. Echocardiography is the most frequently used cardiovascular diagnostic test only after electrocardiography. In less than five decades, the evolution in this technique has made it the basic part of cardiovascular medicine [8]. In addition to providing single-dimension images, known as M-mode echo that allows accurate measurement of the heart chambers, the echocardiogram also offers far more sophisticated and advanced imaging, which is known as two- dimensional (2-D) Echo [8].

Measurement of EAT Thickness using Echocardiography

Transthoracic echocardiography is non-invasive safe method for the measurement of EAT thickness (39). It is the part of routine investigation in patients with suspected cardiovascular risk factors that is why it has cost and time effectiveness. Recent studies shown that echocardiographically done EAT thickness is a reliable marker for visceral adiposity and adiposity related metabolic and cardiovascular risks [24, 25.] The direct association of epicardial fat thickness has been shown with metabolic syndrome features, increased low density lipoproteins (LDL) cholesterol, increased fasting insulin, increased left ventricular mass and diastolic blood pressure, and decreased adiponectin [25].

VAT is recognized as an important risk factor for cardiovascular disease [26]. Measurement of VAT helps clinicians as a diagnostic tool in patients at high risk for cardiovascular disease. Clinician normally measure visceral fat by waist circumference or waist to hip ratio. Therefore, there is now an undeniable need and growing interest for less costly and more reliable imaging markers of visceral adiposity is upcoming [27]. Therefore much attention is now focusing on the measurement of nontraditional visceral fat depots, such as epicardial fat.

Iacobellis et al. first proposed and validated that two-dimensional (2D) echocardiography is commercially available equipment for the measurement of EAT thickness [27]. Accurate measurement of EAT thickness by 2D echocardiography on the right ventricle is done by standard parasternal long-axis and short-axis views with optimal cursor beam orientation in each view. It is generally identified as an echo-free space between the outer wall of the myocardium and the visceral layer of pericardium. In 3 cardiac cycles EAT thickness is measure perpendicularly on the free wall of the right ventricle at end-systole [28]. To prevent its compression during diastole, epicardial fat thickness is best measured at end-systole at which the ultrasound beam is oriented in a perpendicular manner [28].

There is not established upper normal limit value for epicardial fat thickness. Its wide range reflects the substantial variation in abdominal visceral fat distribution. Iacobellis et al. found median epicardial fat thicknesses in a large population of patients who underwent transthoracic echocardiography for standard clinical indications [29]. Jeong et al. reported a mean epicardial fat thickness of 6.3 mm in coronary angiography patients [29]. Natale et al. set the normal upper limit to 7 mm (30).

EAT thickness …. An index for evaluation of high cardio metabolic risk

- Measurement of EAT thickness by echocardiography provides a more receptive and precise assessment of true visceral fat content.
- Echocardiography can accurately quantify visceral cardiac fat.
- Epicardial fat is a direct measure of fat deposition, whereas anthropometric measures also related with the presence of fat.
- Epicardial fat can be quantified with other parameters of traditionally associated cardiovascular risk such as LV mass and ejection fraction.
- It can be used as consistent quantitative therapeutic marker for intervention of visceral obesity.

Limitations of Echocardiography for the measurement of EAT thickness

Possible limitations of echocardiography include;

- Epicardial fat thickness is usually less in the mid right ventricular free wall and greater in the distal portion of the right ventricular free wall [30].
- EAT has a obvious distribution around the heart and 2D echocardiographic assessment may not give accurate estimate of the total amount of fat [31].
- Epicardial fat volume relatively than its thickness may be the most consistent measure [31].
- Echocardiographically there are difficulties in differentiating between EAT thickness and pericardial effusion.

CONCLUSION AND PERSPECTIVE

Although there is few data available on epicardial adipose tissue, therefore the evidences suggested that it has anatomical and clinical relation to cardiac morphology and function. Epicardial adipose tissue has bioactive power and it affects cardiac functions by the release of some active substances. It acts as paracrine gland and regulates the functions of myocardium because of its close anatomical relations. This fat depot reflects intra-abdominal visceral fat, therefore its assessment by echocardiography might serve as a reliable marker of visceral adiposity. Further studies of this neglected tissue and its relationship with cardiac function, as well as of its use as a marker of metabolic and cardiovascular risk, should be encouraged.

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REVIEW ARTICLES

OCT – A WINDOW TO RETINA

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ABSTRACT

Optical coherence tomography (OCT) is a non-contact, non invasive imaging modality that helps diagnosing a variety of diseases involving the eye. It provides quantitative measurements of retinal nerve fiber layer (RNFL), optic nerve head and macular thickness parameters [1, 2] and can be used as a valuable tool in many intraocular surgeries.
This article discusses the applications of different OCT systems available commercially for diagnosing and managing various ophthalmic conditions. Furthermore, future directions of OCT technology, clinical uses and benefits are also discussed.

Different articles published till year 2014 majorly in between 2005 to 2014, obtained from online search engines Pubmed and Google Scholar were used in preparation of this review. Those articles were included that contained information regarding OCT and its uses in various ophthalmologic conditions and its future advancements. We excluded those articles that did not contain relevant information regarding OCT and its uses.

Due to advancements in OCT technology, it is now possible to reveal the structural changes associated with retinal diseases that help in improving early analysis and monitoring of disease progression and response to treatment.

Three generations of OCT have been introduced till date. Early versions of this technology i.e. OCT 1 and OCT 2 are relatively slow, limiting both the amount of data to be captured and the quality of image. The older versions required dilation of the pupil but the latest version, the Stratus OCT can be used without dilating the pupil.[3]

Commercially, OCT is employed in diverse applications including diagnostic medicine, interventional cardiology and art conservation. Ophthalmology is still the most important field of OCT application because of transparent ocular structures.

KEY WORDS: Optical Coherence Tomography (OCT), Retinal Nerve Fiber Layer (RNFL) thickness, Glaucoma, Diabetic Retinopathy.

INTRODUCTION

In the medical field, optical techniques are of great importance because these are low cost and safe, offering good therapeutic prospective. Advancements in OCT technology have made it possible for its relevance in an extensive diversity of applications but its medical application is still dominating.[4-6]

OCT was first introduced by Huang et al. in 1991. [7] It allows in vivo imaging of ocular tissue to a very high magnification, making it an easy method of assessment of internal eye structures. It helps in obtaining retinal images from which retinal estimates can be made which have been proved to be helpful in diagnosing various diseases.[8, 9]

SD-OCT known as OCT-3, is 100 times faster than older versions. This increased rate diminishes the possibility of motion artifacts, decreases the chance of missing lesions and enhances the resolution. Advancements in SD-OCT also permit precised choroidal thickness measurements that was not possible with older versions. The choroidal changes observed by SDOCT are now being appreciated. As a result it is now the emerging point of interest for research. [10-13]

Apart from commercially available OCT systems, prototype OCT systems have added to an ever-growing research body. It includes ultra high-resolution OCT (UHR-OCT), SD-OCT with longer wavelength light making deep tissue penetration easy, and swept-source OCT (SSOCT). [14]

It is quoted in a paper that the SS-OCT is 5 to 10 times faster than that of the SD-OCT, and can achieve more accurate axial resolutions in tissue. [14]

OCT – PRESENT APPLICATIONS

By using ultra-speed high-resolution OCT, three-dimensional OCT imaging can be obtained providing wide-range mapping and visualization of retinal microstructure. The high-data obtaining speeds allow data sets of high-density with large numbers of slanted positions on the retina reducing the possibility of missing any focal pathologies.[15, 16]

OCT is used widely to obtain high-resolution images of both the anterior and posterior eye segments. Nowadays, various diseases are evaluated by using OCT. It also provides assessment of axonal integrity as in macular degeneration and multiple sclerosis. Many researches indicate that OCT may be used as a consistent tool for observing the disease progression involving the eye. Differ-

ential diagnosis is made easy by imaging structures at such levels that were not possible previously such as in differentiating retinal detachment from retinoschisis. [17]

Estimates of retinal thickness is significant in monitoring various diseases such as macular edema, glaucoma, macular holes, optic disc pit maculopathy etc. OCT plays an important role in recognizing retinal nerve fiber layer (RNFL) loss long before the appearance of symptoms leading to better prognosis of the disease.[18, 19] The early detection of changes in retina helps clinicians to identify the cause potentially before the patient suffers objective limitations.
Measurements of RNFL thickness is dependent on transparency of the anterior and posterior retinal planes. The OCT software has a predefined algorithm that identifies the outer limits of retina at the inside of a greatly reflective layer possibly the retinal pigment epithelium (RPE) and the choriocapillaries. Two laminae are seen at the interface. The internal streak may signify the reflective part or the neurosensory retina whereas the outer line is considered to relate histologically with RPE. [20]

OCT & glaucoma:
Glaucoma shows gradual loss of retinal ganglion cells (RGCs) leading to reduced retinal thickness. [21] It has been found that before the visual field defect is clinically symptomatic, 30% or more of RGCs are already lost. Significant loss in thickness may lead to visual field defects and optic disc cupping. [22] It is reported that thinning of retina starts in the initial stages of glaucoma, therefore, it can be used as a predictive indicator for glaucomatous damage.

OCT was found to be more sensitive to detect early nerve fiber layer loss than other techniques such as visual fields or red-free photography.[23] It has the ability to spot focal defects in the RNFL occuring in early glaucoma with high accuracy.[24]

It is now possible to perform automatic measurements of circumpapillary RNFL thickness with the recent development of OCT. [1425] Kafieh et al. in their study have suggested that even earlier than noticeable changes in the visual field occur, there is reduction of RNFL thickness in diseased eyes which is observed by using OCT.[26]

OCT & maculopathy:
OCT can help in diagnosing and quantifying various macular diseases, including idiopathic macular hole, maculopathies, macular pits etc. [27, 28] While talking about macular diseases the first thing coming to mind is macular edema in which macular thickness can be easily assessed by OCT rather than by biomicroscopy which has a limited extent to which edema can be detected.

For visual loss, macular edema is found to be one of the major causes in which there is abnormal fluid buildup within the retina with increase in retinal thickness usually from the break in blood-retinal barrier.[29, 30] This is found in diabetic retinopathy, retinal vein occlusion, uveitis etc.

Conventional methods for evaluating macular edema, like slitlamp biomicroscopy, stereoscopic photography and fluorescein angiography, are found to be relatively insensitive to tiny changes in retinal thickness. OCT has facilitated the clinicians to spot and assess even minute changes in macular thickness.[31]

Imaging of macular holes and other pathologies in the vitreofoveal interface has also become feasible with high-speed OCT offering three dimensional images to facilitate further precision and minute observations of the intraretinal structural changes.[32] OCT has also shown its significance in differentiating neurosensory layer and retinal epithelial layer detachment. [33] Measurements by this technique are found to be highly accurate. [34, 35]

Owing to the defined resolution of OCT, it may possibly be a supportive device to track anatomical features of idiopathic macular holes longitudinally over time. Recently, OCT has been used to follow the sequence of events leading to macular hole formation. In a research by Shimozono et al. in 2011, it is stated that due to vitreofoveal traction, the anteroposterior powers result in splitting of retina, following full-thickness macular hole documented longitudinally by OCT. [36]

OCT may aid discriminating actual holes from partial thickness holes, macular pseudo-holes and cysts. It helps in staging the hole and quantifying the diameter of the hole and in assessing the risk of hole formation in the fellow eye. [37]

In age-related maculopathy, retinal thinning and an increased reflectivity of the choroid due to lack of pigment in the retinal pigment epithelial layer is identified easily by OCT. These areas are seen as regions of increased reflectivity on the tomogram. [38]

Thus, OCT is able to validate the anatomical configurations. Macular examination by using OCT helps in the diagnosis and allows follow-up of the macular pathologies after surgical repair.[37]

OCT & diabetic retinopathy:
OCT can detect significant variation of retinal thickness in patients with diabetic retinopathy even when macular edema is not clinically significant. [39] Goebel et al. in their study suggested that OCT plays major role in evaluating retinal thickness of diabetic patients with excellent reproducibility and great reliability.[40] Another study by Roy Beck et al. concluded that OCT was found to be very helpful in evaluating the three crucial changes in diabetes which include macular edema, retinal swelling and detachment of retina.[41]

Furthermore, OCT is stated to be useful for diagnosing and differentiating tractional retinoschisis from retinal detachment in patients with proliferative diabetic retinopathy and macular elevation.[42]

OCT & retinal vascular diseases:
A detailed analysis of retinal structure is obtained by 3D cross-sectional retinal levels at high resolution.[43] Retinal vessels can be visualized because of the high resolution imaging leading to more objective diagnosis in retinal vascular diseases including retinopathy of prematurity, hypertensive retinopathy etc. Moreover, vessel visualization also allows to follow fundus color changes for better understanding of the structure and localizing retinal lesions.[44]

Preeclampsia and eclampsia cause retinopathy similar to hypertensive retinopathy with papilloedema, hemorrhages, cotton wool spots, retinal detachment, and lesions of the retinal pigment epithelium (RPE) which can be easily detected by using OCT.[45]

OCT & optic neuritis in multiple sclerosis (MS):
Optic neuritis (ON) is a very common presentation of multiple sclerosis (MS). It occurs often as the initial symptom of CNS demyelination. RNFL is that part of brain where nerve fibers are not enclosed with myelin sheath because it develops from optic cup, thus making the OCT examination particular for demyelinating nerve injury contrasting to brain MRI changes, which reflect a range of various types of tissues in the brain.[46]

The measurement of RNFL thickness represents a feasible way of monitoring axonal loss in MS patients as RNFL comprises of unmyelinated axons.[47], [48]Studies have suggested that eyes with a history of optic neuritis revealed reduction in RNFL thickness, showing occurrence of axonal loss. [49-51]

OCT & visual disorders in Alzheimer's Disease (AD):
Visual disorders are usually noted in patients with Alzheimer's disease affecting the visual field. Many studies have suggested that the visual field defects are probably due to nerve degeneration in the visual cortex.[52, 53] Recent studies have suggested that retina and optic nerve degeneration also add to the occurrence of such disorders in AD patients.[54, 55]

In an OCT based study by Yan Lu et al. in 2010, the RNFL thickness was measured in normal individuals and patients with Alzheimer's disease and was found to be reduced in patients with Alzheimer's disease. Reduction in RNFL thickness might be due to loss of nerve leading to neuronal cell body loss.[54] It is suggested that OCT is a simple method and this technique could be used in improving the diagnosis of individuals who are affected clinically by memory disturbances.[56]

Miscellaneous:
In Parkinson's disease, visual impairment is due to loss in dopaminergic neurons in retina. This loss is believed to alter visual process by altering the axons that form the RNFL. OCT is found to be an efficient tool in ruling out such disorders.[57]

The choroidal tumor appears similar to normal choroid when the overlying retina is normal and appears less reflective than normal when the overlying retina is not normal. These small alterations in tumor appearance can easily be diagnosed by using OCT. [58, 59]

OCT also accomplished its name in localizing laser scars, disciform scars, chorioretinal atrophy, and choroidal neovascularization and many other retinal disorders. Other retinal diseases like X-linked retinitis pigmentosa, juvenile macular retinoschisis, idiopathic polypoidal choroidal vasculopathy, idiopathic juxtafoveolar retinal telangiectasis and pigment epithelial hyperplasia can also be diagnosed by OCT.

Comparison of OCT with older modalities:
Comparing the Retinal Thickness Analyzer (RTA) and OCT Scanners for retinal thickness measurements in macular diseases, it is noted that media opacities produce less hindrance for OCT than for RTA which is helpful in a way that in populations with frequent occurrence of media opacity, images can be achieved in a larger fraction of eyes by OCT than by RTA. [60]

Ophthalmoscope, the most commonly used instrument showed many limitations while compared with OCT. Different researches were conducted to compare its validity and it was found to be inferior than OCT.[61, 62] Another study by Hibbs et al. stated that OCT alongwith fundoscopy is valueable.[63]

OCT is different from ultrasound B-scan which uses sound waves rather than light rays in providing higher resolution. It is also found to be helpful in detecting the detachments of retinal layers which are not easily observed by biomicroscopy.

Oct & Its Future:
While talking about the future of OCT, it is an excellent option to be used in medical diagnosis. It can be fiber optic based, allowing inexpensive incorporation with endoscopes and catheters. It is compact and portable and can be done without direct contact with the tissue. It is comparatively fast, allowing real time imaging of tissues at a rate not available with MRI or CT scan. [17, 64]
Recent advancements in SD-OCT have now helped imaging the choroid which was not possible earlier.[10] Further advancements are expected to offer enhanced understanding of choroid involvement in retinal diseases using various techniques.

SS-OCT & Longer wavelength OCT
An exact choroid estimation by OCT should be made by measuring upto the interface of choroid and sclera.(59) Studies using Cirrus OCT suggested almost accurate revelation of the choroid by looking upto choroid–sclera interface in just 70–75% of included eyes. [10, 12, 13] Eyes with even clear choroid–sclera interface have not been reported with Spectralis OCT but prototype OCT using longer wavelength have verified an improved estimation of the choroid, also through opaque media . SS-OCT is also anticipated to be of great help in visualizing the choroid.[14]

The visualization of choroid–sclera interface is expected to improve because of longer-wavelength OCT systems including SS-OCT. This can be helpful in conditions in which the choroid is thicker than normal, and it is difficult to assess the entire thickness

Doppler optical coherence tomography
Traditional examinations like, indocyanine green (ICG) and fluorescein angiography are now taken inferior to Doppler OCT which is a promising technology that localizes the accurate position of vascular abnormalities using cross-sectional imaging. Doppler OCT can assess the flow and volume of blood and evaluate the abnormalities in retinal and choroidal vasculature [65].

CONCLUSION

Modifications in OCT software, enhancement and competent data processing are essential for valuable assessment of retinal and choroidal changes in posterior segment diseases. OCT technology offers enhanced understanding, proper monitoring of disease progression and its response to various treatment modalities employed in eye diseases especially chorioretinal diseases. This expansion has updated the ophthalmic practice over the period of last ten years. Further advancements in OCT technology are expected to be of greater help in assessing diseases more easily and in more depth.

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