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CD 55, Sector I, Salt Lake City, Kolkata 700 064
E-mail: ijoparb1978@gmail.com

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Contents

Editor's Choice

Measurement of Blood Pressure in Hypertensive Disorders of Pregnancy

Prof Dr Gita Basu Banerjee*

Introduction:

Hypertensive disorders complicate 5 to 10 percent of all pregnancies.[1]

The world health organization (WHO) systemically revised maternal mortality world wide, and 16 percent of maternal deaths were reported to be due to hypertensive disorders.[2]

According to ACOG Task force (2013 b)[3] 4 types of hypertensive disorders are: 1) Gestational hypertension, 2) preeclampsia & eclampsia syndrome, 3) chronic hypertension of any etiology, 4) preeclampsia superimposed on chronic hypertension.

Preeclampsia syndrome is potentially more dangerous. Mild to moderate preeclampsia is non-specifically defined under the heading of 'non-severe'. It should be kept in mind that apparently mild disease may progress rapidly to severe variety.

Diagnosis of Hypertensive Disorders: hypertension is diagnosed empirically when Systolic Blood pressure (SBP) is 140 mmHg or more and/or Diastolic BP (DBP) is 90 mmHg or more. (Table 1)

Previously, incremental increases of 30 mmHg SBP or 15 mmHg DBP from mid pregnancy BP values had also been used as diagnostic even if the absolute values were <140/90 mmHg. This is no longer recommended, because they are not likely to experience increased adverse pregnancy outcomes.[4]

Table 1: Diagnostic criteria for Pregnancy Associated Hypertension (ACOG, 2013 b)[3]

Condition	Criteria required
Gestational hypertension	BP>140/90 mmHg after 20 wks in pregnancy in previously normotensive women
Pre eclampsia : Hypertension and Proteinuria	>=300mg/24 hr, or protein : creatinine Ratio>=0.3 or Dipstick 1+ persistent
Thrombocytopenia	Platelets<100,000
Renal insufficiency	Cr> 1.1mg/dl
Liver involvement	Serum trans aminase level twice normal
Cerebral symptoms Pulmonary oedema	Headache, visual disturbances, convulsion

A sudden rise in mean arterial pressure later in pregnancy – delta Hypertension, may also signify preeclampsia even if BP is <140/90 mmHg.[5]

White Coat hypertension describes a group of individual who are normotensive in home environment, but present with a high BP to a health care provider.[6] Diurnal variation of BP is a well documented phenomenon; this change in circadian rhythm may be altered in pregnancy complicated by hypertension or preeclampsia. (Table 2)

So, accuracy of BP measurement in pregnancy is the crucial thing for diagnosis, admission, anti hypertensive therapy and timing of delivery. NICE guidelines7a on Antenatal Care recommends BP measurement in every antenatal visit. But NCE guidelines do not

* Professor, Bankura Sammelani Medical College, Bankura, West Bengal
✉ Dr Gita Basu Banerjee,
E-mail: dr_gita_banerjee@yahoo.co.in

refer to MAP for diagnosing or treating hypertensive disorders in pregnancy.[7]

Table 2: Indicators of severity of Gestational Hypertensive Disorders[1]

Abnormality	Non severe	Severe
Diastolic BP	<110 mmHg	>=110 mmHg
Systolic BP	<160 mmHg	>=160mmHg
Proteinuria	+/-	+/-
Headache	-	+
Visual disturbances	-	+
Upper abdominal pain	-	+
Oliguria	-	+
Convulsion	-	+
Serum creatinine	Normal	Elevated
Thrombocytopenia (< 100,000)	-	+
AST, ALT elevated	-	+
Fetal growth restriction	-	+
Pulmonary oedema	-	+

Auscultatory method is recommended. Following point should be taken care of while measuring BP:

1) Correct size of BP cuff: If the standard cuff is used on a woman with arm circumference of more than 32 cm, BP can be overestimated. This is of concern for women with obesity because they are at higher risk of developing preeclampsia.

   On the other hand BP can be under estimated if a large cuff is used on a woman with normal arm circumference,though the error is much less.[8]

2) Initial inflation of the cuff 20-30 mmHg above the palpable systolic BP and deflation at a rate of 2 mm per second is important. Too fast deflation of cuff may result in underestimation of SBP and over estimation of DBP.[7a]

3) BP is to be recorded to the nearest 2 mmHg. Terminal digit preference (use of 0 or 5 for recordings obtained) is a source of error with auscultatory technique.[9]

4) Korotkoff V: the use of K 5 (Korotkoff phase V, ie. Disappearance of sound) to classify DBP is recommended. It is better reflective of intra arterial pressure and is far more reproducible.[10] Rarely, K4 to K5 range is taken as DBP, if K5 extends to or near zero.

Types of BP instruments used:

Mercury sphygmomanometer is being phased out gradually for environmental concerns.[11] They need regular calibration. Aneroid BP machines have replaced the use of mercury. But these devices need more frequent maintenance and calibration than mercury ones. If they are regularly maintained and calibrated, the can be assumed similar to mercury devices.[12]

In recent years automated BP machine are being used, they don't need trained persons with skill to operate. They detect changes in the amplitude of the intra arterial oscillometric waveform produced during cuff deflation to determine BP.[13] They should also be validated to ensure accuracy; special validation is require for the machines used for pregnant woman.

In preeclampsia, these automated devices tend to under estimate BP because of altered arterial vascular compliance and increased interstitial oedema.

Continuous invasive monitoring is not usually recommended, should be reserved for severe preeclampsia cases with severe cardiac, renal diseases or both, or in cases of refractory hypertension, oliguria, pulmonary edema.[14]

Non invasive continuous monitoring strategy can also be followed for patients needing intensive care.[15]

Automated ambulatory BP devices have been used to assess women at home. In the home setting, it differentiates true white coat syndrome from hypertensive disorders in pregnancy.

The use of self monitoring is simpler, cheaper, is more acceptable to women and provides many of the advantages of ambulatory monitoring.[11]

Management pathway :

Current NICE/ RCOG guidelines[7a] do not recommend treating hypertension of SBP of 140- 149 mmHg or DBP of 90-99 mmHg, except in women with target organ damage secondary to chronic hypertension.

Several studies presses the need of control of SBP over DBP in preventing strokes, and current recommendation is treating SBP of 150 mmHg or above and / or DBP of at least 100 mmHg.

NICE guidelines[7] also recommend keeping DBP above 80 mmHg during pregnancy in women receiving antihypertensive therapy, because of risk of reduced utero placental and feto placental circulations.

Delivery is the mainstay of treatment as maturity is reached, that prevents many complications. In preterm pregnancy corticosteroids may be used in full dose, but in severe cases only initial dose is administered and delivery expedited. Concurrent antihypertensives and seizure prophylaxis (Magnesium sulphate) is used to prevent hypertensive target organ damage. Commonly used antihypertensive medicines are Inj. or Tab labetalol, cap nifeipine , Inj hydralazine.

Women having eclampsia should be delivered within 12 hours irrespective of duration of gestation. (Govt. of India guideline)

The role of antihypertensive medicines in mild to moderate (non-severe) gestational hypertension is accepted but burdened with lots of controversies. The disease may progress silently and cause harm to the fetus and mother. But monitoring of BP and investigative parameters can buy some time to attain maturity of the fetus to thrive outside uterus.

Conclusion:

Accurate measurement of BP may not be the only but it is one of the most important time tested clinical methods relied upon in diagnosis, monitoring and managing hypertensive disorders in pregnancy.

Stake holders in health care system should be aware of the need of adequate supply of calibrated and validated BP instruments to reduce maternal and perinatal morbidity and mortality from this disease.

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Views & Reviews

Is Letrozole Better for Ovulation Induction?

Dr. B N Chakravarty, Dr. Shikha Bathwal, Dr. Elavarasan Subramani

Introduction

Over the past five decades, clomiphene citrate (CC) continues to be the first line treatment primarily for ovulation induction and also for ovulation augmentation in unexplained infertility and in intrauterine insemination (IUI) cycles.[1] However, it is reported that 20-25% of women fail to ovulate due to CC-resistance.[2] In view of this, administration of gonadotropins is considered to be the conventional option in such cases. Though use of gonadotropins is highly effective, it is associated with inevitable risk of multiple pregnancies and ovarian hyperstimulation in a significant proportion of women.[3] As an alternative management of gonadotropins, use of laparoscopic ovarian drilling in CC-resistant women has also been advocated.[4] Addition of CC with Gonadotropins (FSH/hMG) helps in decreasing the dose of total amount of gonadotropins required for optimum stimulation and make it more cost-effective in women who fail to respond to only CC treatment.[5] Acceptable pregnancy rates with CC and sequential hMG ovulation induction protocol in IUI following previous CC and IUI treatment failure have also been reported.[6] However, supra-physiological level of E2 is an undesirable consequence of both CC and gonadotropin stimulation. Apart from risk of hyper stimulation and multiple pregnancies, adverse effects of supra-physiological level of E2 have been observed at several levels. These are dys -sync hrony in maturation between endometrial 'stromal' and 'glandular' elements during 'implantation window' period, abnormal expression of endometrial pinopodes, defective endometrial oestrogen – progesterone receptors, abnormal endometrial blood flow and abnormal integrin expression. These are some of the reasons for low pregnancy rate in spite of having good ovulatory response following CC induction in anovulatory infertility.

These limitations motivated researchers to find out an alternative drug which will be less expensive than gonadotropin and at the same time will be safe, simple and equally if not more effective than clomiphene. Letrozole was considered to be an alternative acceptable molecule.

How and why Letrozole?

In women with intact hypothalamic-pituitary-ovarian axis, the commonest cause of anovulation is polycystic ovarian syndrome (PCOS). One of the significant causes of anovulation in PCOS women is 'static' (not pulsatile) elevated or normal level of oestrogen. Static level of oestrogen through 'negative feed-back' mechanism on 'hypothalamic-pituitary (HP) axis' inhibits adequate release of pituitary FSH. Low (not absent) level of FSH results in inadequate growth and development of follicles, - not allowing them to reach maturity and pre-ovulatory follicle leading to non-ovulation. At the same time, tonic elevated level of oestrogen through 'positive feed-back' effect on HP axis results in release of static elevated 'tonic' level of LH. There is no LH surge and therefore anovulation.

Institute of Reproductive Medicine, Salt Lake, Kolkata 700106
✉ Dr BN Chakravarty, E-mail: bncirm@gmail.com

Aromatase inhibitors (letrozole) by inhibiting oestrogen synthesis temporarily release hypothalamic-pituitary block by tonic elevated oestrogen thereby normalizing fluctuating (and not tonic) release of pituitary FSH which helps in restoration of normal ovulatory cycle. Therefore, letrozole was considered to be an effective drug for induction of ovulation.

Literature review:

Several research groups have studied the new group of drugs (aromatase inhibitors) for ovulation induction in the past few years.[7-9] Letrozole, a potent and highly specific nonsteroidal aromatase inhibitor, has been observed to be effective in inducing ovulation in anovulatory and ovulatory infertile women with inadequate response to CC. Initially, letrozole was primarily used as a potent reversible oral aromatase inhibitor which acts a chemotherapeutic agent in postmenopausal women with metastatic breast cancer.[10] Being a chemotherapeutic agent, when the drug was used for ovulation induction, concerns have been raised that it may have some teratogenic effect on oocyte and embryo. Moreover, the resulting hypo-estrogenism may have adverse impact on bone mineral metabolism leading to osteoporosis. The other controversy relating to the use of letrozole as a first-line agent, before CC has been used, is based on the fact that in normo-gonadotropic women, aromatase inhibition is likely to be effective only when baseline estradiol is elevated. The cut-off level of the elevated baseline estrogen is not yet demarcated. Hence use of letrozole as a primary ovulation-inducing drug replacing clomiphene warrants further investigation. An abstract presented at American Society for Reproductive Medicine (ASRM) meeting 2005 regarding increased teratogenic risk of cardiac malformations with letrozole[11] and other safety concerns eventually led to the ban on this drug in India in 2011. Nevertheless, there is an increased concern on the factuality of the observation or a mere co-incidence due to the shortcomings and biases of this study.

In the later years, various studies indicated that letrozole is not associated with increased teratogenic risk.[11,12] Our earlier study showed that the overall rate of congenital malformations among children born to mothers who conceived naturally or after letrozole or CC treatment was observed to be comparable.[13] Our group has conducted one of the largest-ever randomized clinical trials to explore the efficacy of letrozole in ovulation induction on 1387 infertile PCOS women who failed to conceive with CC treatment.[14] This study showed that letrozole appears to be a suitable ovulation inducing agent in polycystic ovary syndrome (PCOS) women with CC failure and is found to be most effective when baseline oestradiol level >60 pg/ml. It is well known that infertility itself is a risk factor and is associated with increased malformation risk as compared to the general population. Several published studies, both controlled and noncontrolled, comparing letrozole with CC alone or in combination with gonadotropins confirm the effectiveness of letrozole as an ovulation inducing agent.[15-18] Based on these various reports, Government of India, Ministry of Health and Family Welfare removed the ban on use of letrozole as ovulation induction agent.

Evolution of aromatase inhibitors for clinical use

Aromatase inhibitors suppress estrogen production by inhibiting the conversion of androgens to estrogens. Letrozole, the drug commonly used in clinical practice, has been developed following extensive trial through three generations of aromatase inhibitors. Third generation aromatase inhibitors like letrozole and anastrozole have been a great leap forward in the treatment of breast cancer. Their clinical efficacy, excellent tolerability and safety profile compare favourably with that of tamoxifen, which has been the cornerstone of endocrine therapy for years.

Concept leading to the use of letrozole for induction of ovulation

The goal of ovulation induction is to induce monofollicular development and subsequent ovulation in anovulatory infertile women. As discussed in previous paragraphs, anovulation in PCOS or any normogonadotropic anovulatory cycle is due to the block of hypothalamic receptors by static elevated supraphysiological level of oestradiol, which is preventing the release of pulsatile luteinizing hormone-releasing hormone (LHRH). Decline in static elevated oestrogen level can help in restoration of synchronized and pulsatile LHRH release. Antiestrogenic effect of letrozole was the concept behind using it for ovulation induction. This was

first reported in literature by Mitwally et al,[19] in anovulatory women resistant to ovulation induction by CC.

Need of an alternative drug for ovulation induction other than clomiphene citrate

Several drawbacks with CC had been the reason for lookout for an alternative ovulation inducing agent in certain cases. CC remains bound with oestrogen receptors for 60 days because of its long half life. In case, CC fails to induce ovulation or establish pregnancy, other ovulation inducing drugs cannot be initiated before 60 days. It is thought that dose of 150 mg or more will confer no benefit. CC induces ovulation in 70-85% of patients while only 20-40% will conceive. The pregnancy rate per cycle is around 10-20%. About 20-25% anovulatory women are clomiphene resistant.

CC has unfavourable effects on endometrial thickness and cervical mucus due to its anti-estrogenic effect. The incidence of miscarriage after CC therapy has been reported to be about 23.6%. It has been shown that with prolonged CC use, along with low endometrial thickness, there is also decreased uterine blood flow during early luteal and peri-implantation phase. There have been evidences suggesting that supra-physiological serum luteinizing hormone (LH) level from day 9 until the LH surge, together with premature luteinisation and higher serum oestrogen levels throughout the cycle can lead to higher chances of either non-conception or miscarriage.

Difference in mechanism of action of CC and letrozole

In CC, hypothalamic receptors are bound to oestrogenic component of CC and therefore these receptors become unaware of presence of supra-physiological levels of circulating estrogens, allowing hypothalamus to release effective synchronized pulsatile LHRH, thereby leading to LH surge and ovulation.

Letrozole causes direct inhibition of oestrogen synthesis thereby allowing follicle-stimulating hormone (FSH) to induce active folliculogenesis. This hypo-estrogenic state is quickly reversible due to the short half-life of letrozole (45 hours). There is no anti-oestrogenic effect on endometrium. Also there is temporary elevation of testosterone to an optimum level which is beneficial as it increases the follicular sensitivity to gonadotropin. Excess levels of androgen cause detrimental effects whereas a very low level of testosterone impairs follicular development.

Common features in mechanism of action of CC and letrozole

Though the drugs act in different ways, there are some common features in their mechanism of actions. These are: (a) Release of hypothalamus from negative tonic feedback effect of static normal or elevated level of oestrogen (b) Allowing release of pulsatile gonadotropin-releasing hormone (GnRH) (c) FSH & LH ratio is synchronized (d) LH surge is effective for ovulation. These have been illustrated in Fig-1 & Fig-2.

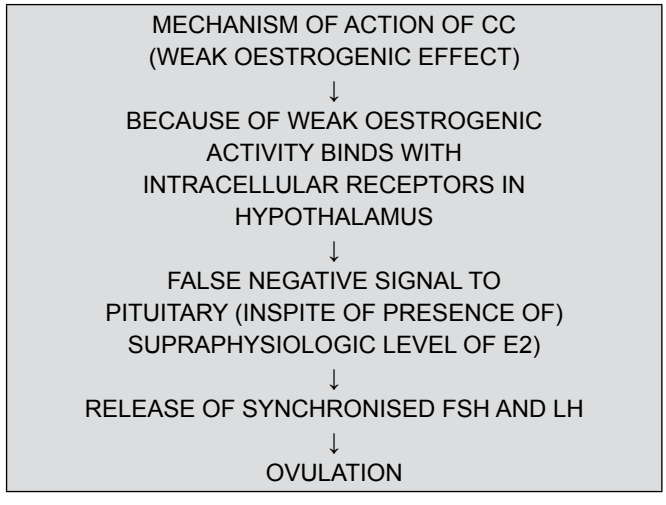

Fig 1: Mechanism of action (ovulation induction) with CC

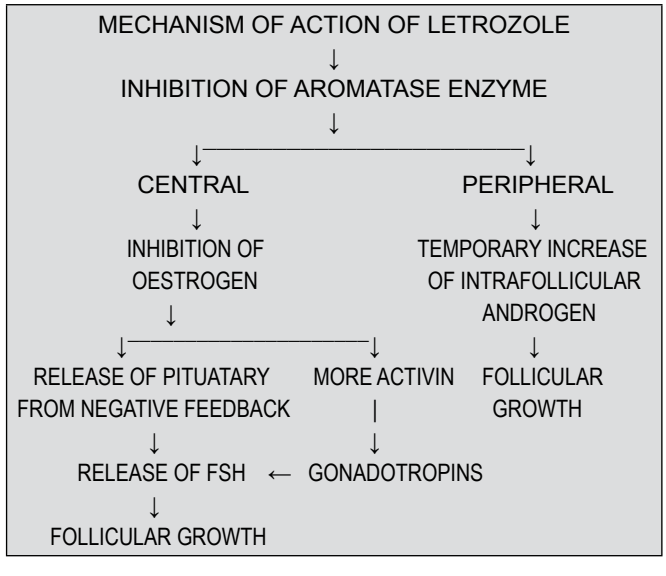

Fig 2: Mechanism of action (ovulation induction) with letrozole

Role of aromatase inhibitors in different types of infertility

Ovulation induction in anovulatory women with PCOS

Letrozole versus CC in PCOS women has been tested in several randomized trials.[14,20-23] However, the efficacy of letrozole in ovulation induction remains unclear. One of the largest randomized controlled trials conducted in our institute comparing efficacy of letrozole with continuous gonadotropins and CC-gonadotropin combination for ovulation induction in 1387 PCOS women after clomiphene citrate failure concluded that the ovulation and pregnancy rate with letrozole was significantly higher with letrozole compared to CC-rFSH combination (79.30% vs 56.95%, p value <0.0001 and 23.39% vs 14.35%, p value <0.0001 respectively).[14] Also there was a significantly lower cycle cancellation rate with letrozole compared to CC-rFSH (20.70% vs 43.05%, p value <0.0001). Another group had reported comparable pregnancy rate with letrozole and CC-hMG therapy in a pilot study.[24] An analysis of four early randomized studies had observed a significantly higher pregnancy and delivery rate in women treated with aromatase inhibitor compared with CC.[25] Nonetheless, the trials involved were heterogeneous with a limited number of patients.

A recent well-designed double blind multicentre randomized control trial comparing letrozole versus clomiphene for infertile PCOS women has concluded that letrozole was associated with higher live birth and ovulation rates. Therefore, letrozole is considered to be superior than CC as a treatment for anovulatory infertility in women with PCOS.[26] Similar findings were observed by other studies.[27,28] A meta-analysis published in 2015 analysed 4999 ovulation cycles (2455 with letrozole, 2544 with CC) indicated that live birth and pregnancy rates were higher in patients with PCOS following treatment with letrozole as compared to CC. However, there was no difference in ovulation rate/cycle, miscarriage rate or multiple pregnancy rate between the two drugs.[29] A study by Liu et al. on 141 CC-resistant PCOS women showed comparison between letrozole and laparoscopic ovarian drilling (LOD). They found letrozole had superior reproductive outcomes compared with LOD in women with CC resistant PCOS and that letrozole could be used as 1st line treatment for women with CC-resistant PCOS. The number of cycles with synchronised follicular and endometrial growth was also significantly higher in letrozole group.[30] A study comparing efficacy of letrozole with tamoxifen observed that tamoxifen was inferior to letrozole in terms of ovulation and pregnancy rate.[31]

Ovulation induction/stimulation in unexplained infertility

Aromatase inhibitors are recommended as an alternative drug to CC in women with unexplained infertility, either alone or with gonadotrophins. Nonetheless, it is likely to be less efficacious compared with treatment in PCOS women. Letrozole results in lesser number of mature follicles (mono-ovulation) in comparison to CC because it has less anti -estrogenic effects in the later part of follicular phase. Thus, it may not be the first choice in patients with unexplained infertility. A meta-analysis of seven randomized control trials showed comparable clinical pregnancy rates between aromatase inhibitor and CC in women with unexplained infertility.[32] These findings are in good agreement with another large trial where no statistically significant difference was observed between 100 mg of CC versus 5 mg of letrozole in terms of clinical pregnancy rate in unexplained infertility.[33] A recent large multicentre trial on 900 women with unexplained infertility concluded that letrozole resulted in lower frequency of multiple pregnancies but also lower live birth rates as compared to gonadotropins. However, when letrozole was compared to clomiphene alone, pregnancy rates were similar.[34]

Safety concerns with letrozole

Concerns had been raised regarding the use of letrozole for ovulation induction, as it might interrupt the normal aromatase function in tissues during early fetal development and can be potentially teratogenic.[35] This issue was discussed in the Annual Meeting of the American Society for Reproductive Medicine in 2005. An abstract presentation by the authors discussing the use of letrozole for infertility treatment may be associated with a higher risk of congenital cardiac and bone malformations in the newborns.[11] Following this, Novartis Pharmaceuticals, the company that developed letrozole for breast cancer treatment, issued

a warning to infertility clinics asserting that it does not advocate letrozole's use for infertility treatment. In October 2011 the Ministry of Health and Family Welfare, India issued a directive to suspend the use of letrozole in infertile women with immediate effect citing concerns regarding its safety. A study analysing 911 newborns born after infertility treatment with either CC or letrozole found no difference in overall rates of major and minor congenital malformations between the two groups.[36] In a recent retrospective trial from Asian sub-continent analysing 646 women, congenital malformations were found to be comparable following natural conception, letrozole and CC.[12] Most recent trial by Tatsumi et al (2017) reported that no increase in the risk of major congenital anomalies or adverse pregnancy or neonatal outcomes was observed in letrozole treated women compared with natural cycles in women undergoing ART.[37] Considering these reports, Indian Health Ministry has recently removed the ban on letrozole for use in infertility. Therefore, letrozole may be considered as a safe option for ovulation induction.

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Potential Areas of Litigation in Obstetrics

Dr Alka Mukherjee,[1] Dr Apurva Mukherjee[2]

Modernization and Consumer Protection Act (1986) converted our noble medical fraternity into a business community. The continuously increasing cost of medical treatment, patient's demand of well constructed and fully equipped hospitals with quality care, made us sitting on the fence of uncertainty. Compared to other professions, medical profession is bit complex. Outcomes are not always favorable as per the expectations of patients and their relatives and this gap between reality and their expectations give ample opportunity for litigations. But the question – will vandalism or litigation improve medical services? Still unanswered.

As per ACOG survey

- An obstetrician can expect an average of 2.5 liability claim over the course of his or her career.
- 80% of obstetricians can anticipate being sued one or more times in career.
- 25.6% of surveyed obstetricians have decreased their high risk obstetrics practice.
- 7.2% quit obstetrics practice.
- 28.5% who continue to deliver patients have high cesarian rates.
- 26.4% not preferring VBAC.

Reasons for litigation in obstetrics are:

1. Obstetricians have two precious and potential litigants – Mother – seen clinically Fetus – wellbeing depends on electronic gadgets eg CTG, Doppler, USG.
2. Pregnancy and childbirth are perceived as physiological processes, so patients and relatives expect everything as normal and any untoward incidence is unacceptable.
3. Obstetric patients are usually young healthy patients and free from obvious disease, hence relatives find it difficult to accept any mishap because of emotional connect.
4. Booked patients stay with obstetrician for a prolonged period – 40+6=46 weeks with rapidly changing physiology. Any pathologic condition can arise.

DUTIES OF AN OBSTETRICIAN

Aim of good care in all three phases

- Antenatal period – counseling regarding diet, rest, immunization, precautions, investigations, medications, possible complications, delivery process, postpartum care and breastfeeding is must.
- Delivery
- Postpartum period – importance of balanced diet, immunization of newborn, importance of exclusive breast feeding for six months, postpartum exercises and contraceptive options.
- Inform patient and relatives about diagnosis, management, investigations, alternative

1. MBBS, DGO, ICMCH, Mukherjee Multispeciality Hospital, Nagpur
2. MBBS, Mukherjee Multispeciality Hospital, Nagpur
✉ Dr Alka Mukherjee, E-mail: mukherjeehospital@yahoo.com

management options, probable cause and prognosis of disease process.

- In case of surgery, type of surgery to be performed – conservative / radical, what will be the cost and what are the potential complication, all the details should be told to the patient and her family.
- During labor – information about progress of labor from time to time.
- In case of operative intervention, can discuss for the option of second opinion.
- All queries of patient and relatives should be solved till their satisfaction in a sympathetic manner.
- In case of adverse outcome transparency and honesty should be maintained.
- Non attending booked patient in labor / emergency without appropriate reason can land in sue.

AREAS OF SUE –

- History taking – the age of patient with relevant complaints and relevant past and family history with special reference to obstetric history is very important. History provides many important clues for diagnosing and treating cases of BOH, infertility, genetic disorders, congenital malformations, DM, HT, multiple gestation etc. Improper history can lead to act of omission on our part. Nowadays the concept of pre-conceptional care is given more importance than the antenatal care.
- Diagnosis – Clinical diagnosis of pregnancy must be supplemented with urine pregnancy test or serum beta HCG or ultrasound, if necessary.
- Investigations – HB%, ABO Grouping & RH typing, blood sugar, sickling, VDRL, HbsAg and HIV is must. HIV testing must be done after informed consent – otherwise patient may sue. High risk pregnancies are only picked up through history taking, routine examinations and investigations. Failure of identifying and failure of timely referrals of high risk patients can lead to medico-legal problem.
- Subsequent visits –

▪ Antenatal screening for congenital abnormalities– Patients having history of congenital abnormal babies (Down's syndrome, Anencephaly, Hydrocephalus and child with genetic diseases) – basic screenings by ultrasound, CVS, Amniocentesis or some biochemical investigations is must as per the individual case. Counseling regarding false positive / false negative is very important.

▪ Intrauterine growth restriction (IUGR) –

With clinical suspicion, doing ultrasound, CTG, Doppler studies to detect end diastolic blood volume flow are very important otherwise there can be IUD and may have to go to the court.

▪ Multiple pregnancy – high risk pregnancy involving two fetal lives. There can be fetal problems – potential for litigation.

▪ Intrauterine fetal death – very sensitive issue. Cause must be explored as routine autopsy in India not performed and unexplained fetal death may impose problem of medical litigation.

▪ Sex selection and PNDT Act – PNDT Act (1994) – misused for sex determination under the pretext of identifying genetic and congenital abnormalities in relation to sex – resulted in falling sex ratio because of selective female feticide all over India. Doctors if found guilty are liable for serious punishment.

- Intra-partum care – in order to have healthy mother and healthy baby, proper intra-partum management is the key. In 78% patients – spontaneous onset of labor. Injudicious administration of oxytocics – can be one of the cause for litigation.

RCT of EFM and only auscultation of fotal heart found only an increased incidence of caesarian section and decreased neonatal seizures in the EFM group but no effect on cerebral palsy or perinatal death. Fetal electrocardiogram can prevent birth asphyxia and can minimize litigations.

- Mode of delivery :

▪ Cesarean Section (CS) – incidence increased from 10% to 30%. Increased incidence of cesarean section because of CPA. But it does not help in improving pregnancy outcome, rather there is increased maternal morbidity and mortality and

low birth weight babies. Decision of cesarean section, if delayed, can lead to maternal and fetal complications, one of the leading cause of litigation. If mishap happens due to unnecessary section, again mother can sue you. In London 31% patients prefer to deliver by CS for fear of damage to perineum.

- Difficult vaginal delivery
- Shoulder Dystocia – timely identification of high risk factors like DM is must in order to predict and prevent this condition and preventing complications arising out of it. A senior experienced obstetrician is must for such complicated delivery.
- Breech – timely decision for route of delivery – normal or cesarean section is very important.
- Multiple pregnancy – too much risk involved and modern dictum is to deliver by CS.
- Instrumental delivery – (forceps/ventouse). Commonly low forceps / outlet forceps are to be applied if indicated. High forceps must be avoided. Ventouse must be avoided in prematurity and fetal distress. Doctor may land up in medicolegal case if there is any untoward complication like facial palsy or visceral injury to baby or perineal injury to mother.
    - Emergency obstetric care – EMOC. All over world maternal mortality is around 5 lakhs. The MMR in India is about 174/100000 live births as per 2015 data. (Far behind than our millennium goal of achieving MMR of 109 by 2015). In India more than 70% people live in rural areas, effective implementation of EMOC is mandatory. FOGSI and ICOG has laid down guidelines about the infrastructure but till date unfortunately these are not implemented, forcing our doctors prone to litigation.
    - Postpartum care –
- Postnatal complete perineal tear – Obstetric anal sphincter injuries (OASIS) – Patients must be counseled about the risk of OASIS in instrumental delivery eg forceps.
- Perinatal morbidity
- Brain Damage- Any neurological and psychological deficiencies in the newborn can become a major litigation issue where compensations are claimed. A doctor will be sued if it can be proved in the court that brain damage has occurred during intra-partum period due to negligence of the doctor.
- Damage to Bones and Viscera- This may occur specially during breech delivery. Doctors must be very conscious during face, legs and arm delivery in breech.
- Analgesia and anesthesia - Anesthetist must be experienced, competent and senior to avoid complications in patients and thereby litigations.
- Drugs in pregnancy and lactation - FDA recommendation of drug use must be followed. The doctor must not use off-license drugs. If damage occurs; he will be blamed of negligence when a licensed alternative drug is available. It is a vise precaution to avoid vast majority of drugs, if not genuinely indicated. One should keep in mind "Thalidomide Disaster".
- Ethical issue in Surrogacy- Patient without uterus but functioning ovaries can have her child with the help of surrogacy and it is possible by AID and IVF. According to fertilization act 1990, the carrying mother is the mother in law. Genetic mother can get legal parenthood by legal procedures only. Surrogacy when the woman is physically capable of bearing a child, just for convenience, is unethical.
- Special conditions – Obstetricians usually face cases of battery. Battery is usually defined as unwanted, harmful or offensive bodily contact that occurs without consent. In cases of surgery, the legal burden falls on the doctor to prove that a proper informed consent was obtained or that the clinical circumstances were such that consent was implied though was not taken on paper. The prevention of potential claims of battery in surgery depends on the content of consent. This requires appropriate communication between the treating doctor, patient and family. This situation arises in cases of instrumental delivery, episiotomy complication, PPH, cesarian section, removal of ovaries, doing onco surgeries and laparoscopic procedures.

- Standard of care - Standard of care defines a management protocol or prescription for specific medical condition that is rationally accepted as best practice by a medical faculty. Like we have the practice guideline of FOGSI, ICOG, RCOG, ACOG. Other sources for standards of care are those derived from data in government regulations, the opinion of learned bodies of the profession, textbook chapters and articles in scientific literature, institutional protocols as well as the Acts of Legislature. There are advances in medical practice particularly in prenatal diagnosis and reproductive technologies, new legal theories of physician liability have developed and so also the type of novel legal problems.
- Errors in antenatal screening and diagnosis can lead to claims.

  Wrongful birth – birth of an infant with serious or disfiguring disabilities such as, CNS defects – hydrocephalous, meningomylecoele, encephalocoele or various chromosomal abnormalities eg:trisomy 21, Tay-Sachs disease or cystic fibrosis. Allegation usually the genetic or hereditary basis for potentially serious condition was not recognized by the clinician or appropriate screening was not advised early enough to prevent or terminate the pregnancy. Parents must prove that if they had been informed of the potential for the defective fetus prior to pregnancy or the existence of an abnormal infant during pregnancy, they would have sought to avoid the pregnancy altogether or to terminate the affected pregnancy. Hence it is very important to obtain a complete family or genetic history and inform the women of available methods for genetic testing. At-risk families are often referred to prenatal centers for genetic testing and evaluation by perinatal geneticists. Routine referral to a genetic counselor for evaluation is not yet considered as standard of care.

- Wrongful life – is an action claiming that negligent prenatal testing on the part of healthcare provider resulted in a birth of 'damaged child'- physically/ mentally disabled child. Such claims usually involve devastated infants with serious genetic disorders or those born with major injuries as a result of undiagnosed maternal disease or early pregnancy drug exposure. The legal theory for these claims is that the duty of clinician owned to the unborn child is similar to that owned to the parents.
- Wrongful conception – claims are brought by the parents of a healthy, normal, unwanted infant born after failed sterilization or contraceptive method eg pregnancy in women after postpartum tubal ligation or women who undergoes tubal ligation was already pregnant at the time of surgery.
- Wrongful death – is a cause of action arising when an otherwise normal pregnancy, which has reached viability, is terminated because of misdiagnosis eg Misdiagnosis of renal agenesis resulting in pregnancy termination.
- Recent guidelines by ACOG – offer antenatal screening for chromosomal abnormalities to all pregnant patients regardless of age. The broader availability of nuchal translucency screening establishes a standard of care in which most patients should be offered the opportunity for first trimester screening. Obstetrician failing to offer patients such diagnostic testing are at risk for suit.
- Measures for prevention of law suits –
- RECOGNIZE, RESPOND, RESOLVE – 3 'R' for dealing with some mishap condition. It helps to preserve the doctor-patient relationship through clear, concise communication regarding treatment related injury. In case of adverse event doctor must discuss with patient and her family addressing her concerns and questions in a frank and open manner. Early and clear communication can reduce litigation exposure.
- Proper patient selection as per one's knowledge and capabilities.
- Good counseling and proper informed and documented consent.
- Good record keeping and documentation in hospital case record.
- Preservation of medical record for an appropriate period of time – in case of childbirth one may even need to preserve the records till the child becomes a major.

- Ensure that in case a patient is managed by a multi-specialty approach or in operative cases where two or more doctors may be present such as surgeon(s) and anesthetist, there should not be any contradiction in documentation by different individuals which may complicate the issues in the court of law.
- Regular checking of expiry dates of medications, specially in OT and to preserve the empty vials, ampoules, injectable medications in case of a mishap to avoid allegation of a cover – up.
- Provide standard medical care as per existing guidelines.
- Timely referrals if required.
- Awareness of potential litigation areas.
- Self and professional auditing.
- Regular updating of medical and legal knowledge.
- Medical indemnity insurance is must.
- Fully equipped hospital with availability of qualified, experienced and appropriately trained doctor.
- Risk management strategies: it is a prospective process which identifies factors prompting legal action and attempts to improve the medical system to prevent future losses. Risk management involves the participation of health care providers of all types, attorneys, various technicians, health insurance providers, hospital administrators and many others. When a potential risk is identified, there are several possible resolutions. Like development of education programs, a review of the performance of clinicians, the purchase of new equipment or changes in existing protocols and practice guidelines.

Conclusion

Medical profession is always exposed to the threat of litigation. But practicing defensive medical is not the solution. It hampers professional confidence and brings about a sense of dissatisfaction among patients. The most important aspects of preventing litigation is to practice contemporary, evidence-based medicine, with compassion and excellent communication and adoption of every possible precaution and professional updating. If suit occurs, the best defense entails comprehensive documentation, particularly in recognized areas of risk. Hence an obstetrician must be aware of the potential areas of litigation so that he or she can face the situation successfully.

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Original Article: Obstetrics

Efficacy of Ramosetron and Ondansetron for Prevention of Nausea and Vomitng after Cesarean Section under Spinal Anesthesia

Dr Utpal Kumar Roy,[1] Md Aftabuddin Mondal[2]

Abstract

Introduction: Postoperative nausea and vomiting (PONV) after spinal anesthesia for cesarean delivery are distressing to both patients and surgeons. Spinal anesthesia has been shown to be easy, safe, rapid and safe technique for cesarean section. Both Ramosetron and Ondansetron are increasingly being used for prevention and treatment of nausea and vomiting.

Objectives: To evaluate the efficiency of ramosetron and ondansetron in prevention of nausea and vomiting intra-operatively and post-operatively in LSCS patients under spinal anesthesia.

Materials & Methods: This was a randomized, double-blind study with 60 female patients. They received either ondansetron (4 mg) or ramosetron (0.3 mg) intravenously 10 mins before the administration spinal anesthesia. All the patients were subjected to elective caesarean section under spinal anaesthesia. They were randomly allocated into two groups namely study group A (30 patients received inj. ramosetron 0.3 mg I.V) and B control group (30 patients received inj. ondansetron 4 mg. I.V). Patients were observed intra-operatively, in the recovery room and the ward upto 24 hrs. for episodes of nausea and vomiting. Rescue anti-emetic was given if the patients had PONV score 2 and was recorded. All the patients were observed for side-effects such as dizziness, headache, sedation or extra pyramidial reaction upto 24 hrs.

Results: Incidence of nausea and vomiting in immediate post-operative period was 10% in study group compared to 20% in control group. Dizziness, headache, were comparable in both the groups.

Conclusion: Ramosetron is quite effective to prevent nausea and vomiting in LSCS patients under spinal anesthesia. It reduces the incidence of nausea and vomiting intraoperatively and in the immediate postoperative period.

1. Assistant Professor, Dept. of Anesthesiology, Murshidabad Medical College
2. Assistant Professor, Dept of Obstetrics and Gynecology, Calcutta National Medical College and Hospital

✉ Dr Md Aftabuddin Mondal, 29/1 Doctor Lane, Kolkata – 700014, Email – aftabudinmondal5@gmail.com; Ph: 9434101777 / 9804692902.

Keywords: Spinal anesthesia, Cesarean section, Ramosetron, Postoperative nausea and vomiting, Ondansetron.

Cesarean section in spinal anesthesia has become increasingly popular in recent years and is now commonly performed surgical procedure. Regional anesthesia is performed in 80% of anaesthetized patients compared to 20% who received general anaesthesia.[1,2] Consciousness allows the patients to enjoy the early immediate contact with the newborn child. The procedure may be associated with various important problems,[3] like arterial hypotension, headache, insufficient anesthesia and psychologicdistress.[4] A common problem in cesarean section is intra and postoperative nausea and vomiting under regional anesthesia.[5,6] About 72% of patients are afraid of nausea and vomiting and 71% feel significant discomfort. Previous reports suggest both nausea and vomiting as frequent phenomenon, with the incidences upto 80%.[7,8] The major risk factors for nausea and vomiting during or after spinal anesthesia in cesarean section is arterial hypotension due to blockade of the sympathetic nerve system.[9] Critical anesthesiological complications suchas airway obstruction, aspiration pneumonitis, and wound dehiscence are rare and mainly related to postoperative nausea and vomiting in general surgical patients.[10–12] Nausea and vomiting may be influenced by hormonal changes in pregnancy, which alter the sphincter tone of the esophagus and the stomach and the activity of small bowel and esophagus, as well as adverse effects of uterotonic drugs, intraoperative manipulation of the uterus and psychological distress aggravated by insufficient anesthesia.[13–15]

The goal of our present study was to compare the effectiveness of Ramosetron and Ondansetron in LSCS patients for prevention of intra-operative and post-operative nausea and vomiting under spinal anesthesia.

Objectives

To evaluate the efficiency of Ramosetron and Ondansetron in the prevention of nausea and vomiting intra-operatively and post-operatively in LSCS patients under spinal anesthesia.

Methods and Materials

In this randomized, double-blind study, 60 female patients were divided into two groups. Gr. A Ondansetron (4 mg) or Gr. B control group Ramosetron (0.3 mg) intravenously 10 mins before the administration spinal anaesthesia. The study was done at Murshidabad Medical College & Hospital for one year from July 2016 to June 2017. All the patients were subjected to elective cesarean section under spinal anesthesia. Patients with H/O diabetes mellitus, allergic to local anesthetic hepatic disorders and those taking antiemetic medication were excluded from the study. After Pre-anesthetic evaluation and investigation, the patient was explained about the procedure. Informed consent was taken. Baseline vital parameters were recorded. All the patients were preloaded with RL10ml/kg to prevent intraoperative hypotension followed by nausea and vomiting. All patients were given premedication with midazolam 3.75 mg orally 1hr. before transfer to the operating theatre. Spinal anesthesia was induced in sitting position between L3/L4 with 0.5% hyperberic bupivacaine with 25/26G spinal needle.Dosage depended on the body height. Body height 150 cm resulted in 1.8 ml bupivacaine 0.5%, every 5 cm additional height resulted in an additional 0.2 ml bupivacaine dosage.

Patients were observed intra-operatively, in the recovery room and the ward upto 24 hrs. For episodes of nausea and vomiting or retching which were evaluated on 3 point PONV score 0-no nausea and vomiting, 1-episode of nausea, 2-retching and vomiting) for next 24 hrs. Rescue anti-emetic was given if the patients had PONV score 2 and was recorded.All the patients were observed for side-effects such as dizziness, headache, sedation or extra pyramidial reaction and treated accordingly upto 24 hrs.

Data were analyzed usingunpaired "t" test and p value <0.05 was considered statistically significant. Data was presented as mean ± standard deviation and percentage. A statistical analysis was done Epi Info 7, WHO CDC Atlanta, Georgia, USA. χ^2 test was done at 5% significants level.

Results

There were 60 patients in the study with 30 patients in each group. The demographic data with respect to age, sex, height and weight were comparable in both groups (Table 1). There was no statistically significant difference in respect to duration of surgery and duration anaesthesia in both the groups.

When PONV score 2, rescue anti-emetic was given in 2 cases in the study groups and 4 cases of the control groups. Incidence of side effects (headache, constipation and dizziness) was comparable in both the groups (Table 4).

In the early postoperative period (immediately) the incidence of nausea was 20% in the control group and was 10% in study group.Within 0-3 hrs, the incidence of nausea was10% in control group and 6.66% in study group. Within 12-24hrs, the incidence of nausea was 6.66% in control group and 3.3% in study group.

PONV score 0 (no nausea & vomiting) was observed in 53.34% in control group and 73.34% in study group. PONV score 2 (Episode of retching, vomiting) was13.33% in control group and 6.66% in study group.

Dizziness was 30% in control group and 36.66% in study group. Patient's satisfaction was 80% in study group and 60% in control group.

Discussion

The aim of our study was to find a highly efficient anti-emetic and anesthetic procedure to reduce the incidence of intra and postoperative nausea and vomiting in 60 female patient exposed to cesarean section surgery under spinal anesthesia.The study was conducted on the background that an optimal perioperative patient comfort is of outstanding interest and nausea & vomiting with average incidence of 30% is rated as one of the most undesirable events in the context of surgery and anesthesia.[16–18] Therefore, every attempt should be made, especially in context of birth, to avoid this complication, which is an unpleasant adverse effect, but also may cause severe complications such as wound dehiscence, dehydration, aspiration or pneumothorax.[10,11] There were no definite study performed regarding comparison of ramosetron and ondansetron in LSCS patients under spinal anesthesia.

Table 1 : Demographic Profile

Study Group n=30		Control Group n=30	P Value
Age (Years)	24.22±2.56	24.66±2.62	P>0.05NS
Height (Cms)	154.36±8.86	157.42±9.56	P>0.05NS
Weight (Kgs)	65.2± 4.8	64.2±4.6	P>0.05NS
Duration of Surgery (mins)	40.26±6.6	41.43±6.8	P>0.05NS
NS-Not Significant			

Table 2 : PONV Score

PONV Score	Study Group	Control Group	Total
	(n=30)	(n=30)	n=60
0	22	16	38
1-2	8	14	22
Total			

χ^2 (1) = 2.58, p = 0.108 not significant

Table 3 : Distribution of patients experiencing nausea and vomiting in first 24 hrs

Nausea and vomiting	Study Group	Control Group	Total
	(n=30)	(n=30)	n=60
Immediate to 6 hrs	5	11	16
> 6 hrs	1	2	3
Total	6	13	19

Fisher Exact Test p = 0.704 NS

Table 4 : Side effects of antiemetic drugs

Side effects	Study group	Control Group	Total
	(n=30)	(n=30)	(n=60)
Dizziness	11	9	20
Nausea and vomiting	6	5	11

χ^2 (1) = 0.00, p = 0.98 not significant

Table 5 : Patient satisfaction with antiemetic drugs

Patients satisfaction	Study group	Control group	Total
	(n=30)	(n=30)	(n = 60)
Satisfied	24	18	42
Unsatisfied	6	12	18

χ^2 (1) = 2.86, p = 0.09 not significant

In our study, We have observed 60 patients for episodes of nausea and vomiting in LSCS patients under spinal anesthesia.

Ramosetron, recently developed elective 5HT3 receptor antagonist. It shows significantly greater affinity for 5HT3 receptors, resulting in more potent, longer receptor antagonizing effects compared to older 5HT3 antagonist.[19–21]

Ramosetron is more potent and longer duration of action than granisetron in prevention of emesis after cis-platin therapy and prevention of PONV.[22]

Choi and Colleagues reported that Ramosetron I.V. was better than Ondansetron I.V. in reducing the severity of nausea, incidence of vomiting and the rescue antiemetics at 6-24 hrs. after operation in patients who undergone spinal surgery.[23]

PONV score was 0 in 73.4% patients in study group (Ramosetron group) compared to 53.4% patients in control group (Ondansetron group) in our study. It suggests that ramosetron is quite effective in controlling nausea and vomiting in both intraoperative and postoperative period.

Fujii et al reported that Ramosetron is effective in preventing PONV after major gynecological surgery.[24]

In our study, Ramosetron 0.3 mg was effective in reducing the incidence of PONV (26.66% in study group versus 46.66% in control group).

Kim et al performed similar study in gynecological surgery and they have observed similar results as well.[25]

The most frequently reported adverse events of 5HT3 receptor antagonists are dizziness and headache.[26] Adverse events observed in our study were similar in both study and control group.

Conclusion

On the basis of the present study it can be concluded that inj. Ramosetron 0.3 mg I.V is much more effective for prevention of postoperative nausea and vomiting in LSCS patients under spinal anesthesia.Ramosetron seems to be useful alternative and relatively safe drug for effective anti-emetic prophylaxis. It also reduces the PONV score and incidence of nausea in both the groups.

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Case Report: Obstetrics

Management Dilemmas in Placental Chorioangioma Presenting as Polyhydramnious – A Case Report and Literature Review

Dr Sandhyasri Panda,[1] Dr Poornima Kunchi Paramban,[2] Dr Durga Devi Meda,[3] Dr Shashi Kumari Goppisetti,[4] Dr Mahalakshmi[5]

Introduction

Chorioangiomas are benign non trophoblastic placental tumors histologically corresponding either to hamartomas derived from primitive chorionic mesenchyma or placental hemangiomas arising from chorionic plate.[1] Placental chorioangiomas occur in approximately 1% of pregnancies, is seen more frequently in multiple pregnancies and in female babies.[2,3] Most placental chorioangiomas are small and are not clinically important. In chorangiomas larger than 4 cm, there can be significant effects on the hemodynamic and circulatory processes of the fetus, leading to grave clinical consequences, such as IUGR, fetal anemia, hyperdynamic circulation, congestive heart failure and polyhydramnios.[4] Different types of chorioangiomas are associated with varied maternal complications like Preeclampsia, diabetes and mirror syndrome.[5] Early diagnosis by routine placental mapping can detect the presence and progression of chorangioma. Multi modality imaging can predict fetal complication, can help in planning intra uterine intervention to prevent morbidity and timely termination of pregnancy for fetal salvage.

Case Report

A 23 year-old gravida two para one live one with previous term cesarean delivery presented to OPD (8.9.17) with breathlessness, not perceiving fetal movements at 30 weeks gestation with unremarkable past medical, surgical and family history. She was referred to our hospital in view of severe hydramnios and a placental tumor, which was diagnosed at 28wks of gestation. Her SFH was 42 cm, and abdominal girth was 37 inches with an AFI of 40cm (> 95th percentile for that gestational age) and DVP of 15cm (severe polyhydramnious) On USG placenta was in upper segment on posterior uterine wall with 7.7x6.3 cm heteroechoic, hypervascular and nodular lesion in the lower end of placenta projecting into the amniotic cavity, and fetal growth was more by 2 weeks than clinical GA with neither structural abnormalities nor hydrops fetalis and normal umbilical artery doppler (25.8.17). Rpt USG showed consistent finding on placenta but increased umbilical S/D to 4.1 and MCA PSV 45 (11.9.18). She was advised a fetal echo and while awaiting appointment she was put on low dose indomethacin 25 mg bid for 3 days. She showed symptomatic improvement, SFH and abdominal girth reduced. One course of antenatal steroid was administered. Fetal echocardiogram

1. MD, FICOG, Professor and Unit Head (ll), Maharajah's Institute of Medical Sciences, Vizianagram, A.P.
2. PGT 2nd Year, Dept of OBGYN, Maharajah's Institute of Medical Sciences, Vizianagram, A.P.
3. MD, Asst Prof, Dept of OBGYN, Maharajah's Institute of Medical Sciences, Vizianagram, A.P.
4. DGO, DNB, Asst Professor, Dept of OBGYN, Maharajah's Institute of Medical Sciences, Vizianagram, A.P.
5. G. DGO, SR, Dept of OBGYN, Maharajah's Institute of Medical Sciences, Vizianagram, A.P.

✉ Dr Sandhyasri Panda, E-mail: dr.sandhyasree@gmail.com.

reported (14.9.17) as thrombosis of the pulmonary artery and partial thrombosis of right ventricle with interval development of tricuspid regurgitation and signs of cardiogenic failure. Interval absence of intra tumoral vascularity in the chorioangioma suggesting possibility of tumor vascular thrombosis.

Immediate decision to terminate pregnancy was taken but in view of CCF in premature fetus patient was reluctant for emergency cesarean delivery. She was induced with 25 mcg misoprostol four hourly intravaginally with continuous intrapartum CTG. She was delivered by VBAC with assisted breech delivery of a fresh still born male baby weighing M, 1.7 kg; placenta wt 1.9 kg; with large thrombus on chorioangioma portion. HP study of tumor showed numerous proliferative thin walled capillaries consistent with capillary angiomatous type of chorioangioma.

Discussion

Placental chorioangioma is a benign vascular tumor detected in 1% of placentas after systematic examination. Only 10% of these are macroscopically visible. Most of these tumors are small and discovered only by microscopic examination and have no adverse impact on the fetus. Larger tumors are rare and when above 4-5 cm in diameter (one in 9000 to 1 in 50000)[1] they probably act as arteriovenous shunts and cause complications. Around 50% of large chorioangioma cases develop fetal and maternal complications that required either elective delivery or intervention for tumor-related effects.[5,6] Large or giant chorioangiomas have 30% to 40% perinatal mortality.[5] The vascularization of the tumor is a determinant for perinatal outcome. Where the tumor is avascular, no specific complications should be expected.[7]

Chorioangiomas may act as peripheral arteriovenous shunts, leading to left to right shunt, increased cardiac output, cardiomegaly and finally heart failure and hydrops, additionally complicated by fetal anemia secondary to fetomaternal hemorrhage, or blood sequestration in the tumor; resulting in thrombus and thrombocytopenia.[6,7] Maternal complications are preeclampsia, preterm labor, placental abruption, polyhydramnios and mirror syndrome. Of the various reported clinical complications, the correlation of chorioangioma with hydramnios and preterm delivery is significant, latter being a sequelae of hydramnious.[8]

They can be diagnosed prenatally by ultrasound, color Doppler imaging, and magnetic resonance imaging (MRI).[3] When the tumor is vascularized, and in particular, if it contains numerous large vessels, serial ultrasound and Doppler examinations are warranted to detect early features of fetal congestive heart failure.[7] Generally small placental nodules pass unnoticed by USG but larger ones are easily diagnosed by their characteristic appearance. The tumor may remain static or grow in size during pregnancy; which decides the clinical features.

Large tumors are often symptomatic and present with features of polyhydramnious which can be managed by amnioreduction. The pathogenesis of polyhydramnious is increased transudation across the membrane from the dilated veins and hyperdynamic circulation at the placental bed due to arteriovenous shunts. The resultant placental insufficiency could be other aetiology of polyhydramnious. There are instances of symptomatic resolution of polyhydramnious following conservative management and amniocentesis[9] if the tumor stays static and rest of the placenta grows in subsequently. Therefore, the relative surface of the placental tumor to the overall surface of the placenta is decreasing, and this may decrease the transudation process and at the same time increase the absorption rate of the amniotic fluid by the more viable placenta.

Other presenting feature of chorangioma is preterm labor secondary to maternal polyhydramnious. Therefore treatment is aimed at amnioreduction by therapeutic amniocentesis and/or maternal indomethacin therapy. Steroid administration for acceleration of fetal lung maturity before 34 weeks is indicated.[8]

In the present case a low dose protocol of indomethacin was followed at 25mg bid in view of controversy and caution regarding its use after 31weeks of gestation due to its reversible association with premature closure of ductus arteriosus.[10] After 48hours she showed symptomatic improvement. Indomethacin was stopped after three days of treatment. Fetal echocardiography was done after two days revealed evolving thrombus at chorio angioma, umbilical vein, right ventricle and pulmonary artery, tricuspid regurgitation, cardiomegali and signs of RVF. Although literature is rich with evidence showing sequestration and thrombus at large placental tumor is

Fig 1: USG showing vasular nodular growth

Fig 2: Placental tumor

Fig 3: Thrombus in chorioangioma

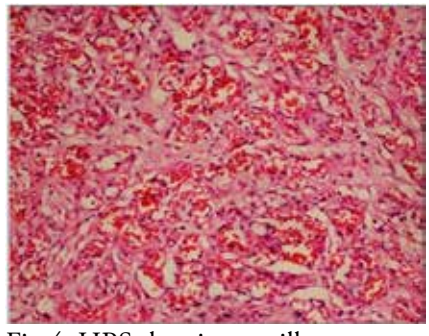

Fig 4: HPS showing capillary type angioma

a consequence of A-V shunts, fetal cardiac echo report was consistent with indomathacin induced closure of PDA which has resulted in congestive cardiac failure; causing a management perplexity.

The patient was explained about the prognosis of the baby after birth; she opted to go for a vaginal delivery and refused cesarean section. She was induced medically followed by controlled drainage of liquor. It was an unstable lie and trial of labour following Cesarean section. A still born male baby was delivered by assisted breech delivery with induction delivery interval of eighteen hours, baby weighed 1.7kg and placenta 1.9kg with large thrombus at the chorangioma. Third stage was actively managed. Mother recovered well after delivery.

Specific treatment modalities of chorangioma include endoscopic devascularization, chemo ablation with absolute alcohol and interstitial laser coagulation of feeding vessels to the tumor.[3,8] Treatment of fetal anemia includes intrauterine transfusions. Intra uterine therapy has improved fetal salvage rate as evidenced from review of literature.[5]

Conclusion

Despite a rare cause placental chorioangioma should be sought after diagnosis of polyydramnious. Once a diagnosis is made serial USG and Doppler evaluation should be available to follow up for progress of lesion and its effect on fetomaternal hemodynamic changes. Planned early intra uterine interventions can prevent feto maternal complications. Multydiscipinary involvement and timely termination of pregnancy can prevent adverse perinatal outcome.

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Original Article: Gynecology

Correlation of Pap Smear with Colposcopy in Evaluation of Unhealthy Cervix

Deepti Chyaunal,[1] Kirti Anima Kerketta,[2] Rita Hansda[3]

Abstract

Objectives: To correlate PAP smear findings with colposcopic and histopathological findings.

Methods: A prospective, analytical study was undertaken in the department of obstetrics and gynecology, Bokaro General Hospital, in 2015-2016.

Results: Sensitivity of PAP smear was 68.75%, specificity was 90.74%, PPV was 81.48%, NPV was 83.05% and accuracy was 82.56% whereas sensitivity of colposcopy was 100%, specificity was 53.70% and PPV, NPV and accuracy was 56.14%, 100% and 70.93% respectively. The results of combined PAP smear and colposcopy were far better than the invidual procedures in terms of sensitivity, specificity and accuracy which were 100%, 96.15% and 97.91% respectively.

Conclusion: Use of single visit approach in which cytology, colposcopy and guided biopsy all can be done in one setting and treated accordingly in resource poor countries like India.

Key words: unhealthy cervix, colposcopy, colposcopy directed biopsy.

CC- Chronic cervicitis, LSIL- Low grade squamous intraepithelial lesion, HSIL- High grade squamous intraepithelial lesion, ASCUS- Atypical squamous cells of undetermined significance, CIN- Carcinoma in situ, SCC- Squamous cell carcinoma, PPV- Positive predictive value, NPV- Negative predictive value, TP- True positive, TN- True negative, FP- False positive, FN- False negative.

Introduction

Unhealthy cervix is a very common finding in our country due to poor genital hygiene, malnutrition and multiparity.[1] An "unhealthy cervix" or grossly abnormal cervix can harbor premalignant cervical lesions or invasive carcinoma.[2] The easy accessibility of the cervix to inspection, palpation and application of cytological and tissue sampling procedures has led to extensive screening programs for early detection and treatment of the disease, thereby contributing to a remarkable lowering of incidence, and mortality from cervical cancer. This screening can be effectively done

Department of Obstetrics & Gynaecology, Bokaro General Hospital, Bokaro steel city, Jharkhand.
1. MBBS, DNB resident
2. MBBS, MD, Senior consultant
3. MBBS, MD, Joint Diector and Head of the Department
✉ Dr Deepti Chyaunal, E-mail: deepti24@gmail.com

by cytology (Pap smear), colposcopy and colposcopy directed cervical biopsy.

Aims & Objectives

The study was undertaken with the aim to correlate PAP smear findings with colposcopy findings by calculating sensitivity, specificity, positive predictive value, negative predictive value and accuracy of PAP smear and colposcopy.

Materials & Methods

This prospective study was undertaken in the Department of Obstetrics and Gynecology, Bokaro General Hospital, Bokaro steel city, from 1st July 2015 to 30th December 2016. 86 women were selected between the age group of 20-65 yrs with symptoms like vaginal discharge, post coital bleeding, post menopausal bleeding, inter-menstrual bleeding and persistent leucorrhoea not responding to antibiotics. Women who were pregnant or menstruating or who had frank cancer, acute pelvic infections or those who had previously been treated for carcinoma cervix were excluded from the study.

A detailed medical, surgical, obstetric and menstrual history was taken. Informed consent was taken from each woman. All women were examined in post menstrual period. Detailed general examination for pallor, oedema, pulse rate and detailed systemic examination was done. After doing per speculum and per vaginal examination, PAP smear and colposcopy was done. Guided biopsy was taken and sent for histopathological examination.

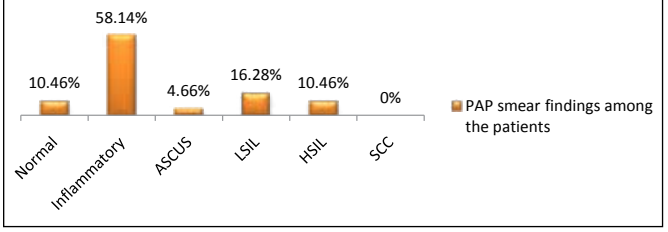
Results

A total of 86 patients were taken. Majority of the patients were of age group 31-40 years. Mean age was 41.23 years. Majority of the patients were mutipara and belonged to low socio-economic class. Most of the patients had active married life of >10 years which shows that duration of marriage and duration of exposure to sexual intercourse has a distinct role in genesis of cervical dysplasia.

Most common presenting complaint among the patients was white discharge per vagina (56.98%) followed by irregular bleeding p/v (26.74%). 24.42% patients presented with pain lower abdomen, 13.95% with post menopausal bleeding and only 4.65% presented with post-coital bleeding.

Pap smear was normal in 10.46%, inflammatory in 58.14%, ASCUS was reported in 4.66%, LSIL in 16.28% and HSIL in 10.46%. No case of SCC was reported in Pap smear. (Chart 1).

Chart 1 : PAP smear findings among the patients



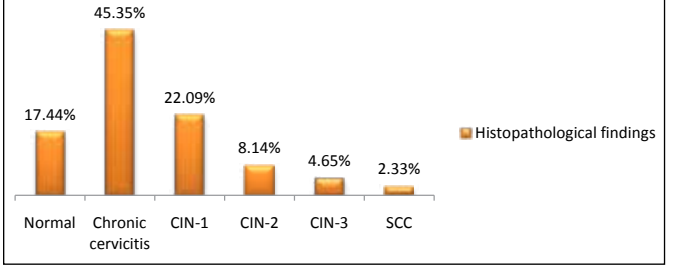
In colposcopy 57 patients (66.27%) showed aceto-white area, 26 patients (30.23%) had punctuations and 14 patients (16.27%) showed mosaic pattern. (Table 1)

Table 1 : Colposcopic findings among patients

Colposcopic Findings	No. of Population (86)	%
Normal	29	33.72%
Aceto-white	26	30.23%
Aceto-white + Punctation	17	19.77%
Aceto-white + Mosaic	5	5.81%
Aceto-white + Punctation + Mosaic	9	10.47%

On Histopathological examination, 17.44% patients were normal, 45.35% had chronic cervicitis, 22.09% had CIN-1, 8.14% had CIN-2, 4.65% had CIN-3 and 2.33% had SCC. (Chart 2).

Chart 2 : Histopathological findings



In table 6, out of 86 patients, findings of 48 patient correlated perfectly in terms of cytology, colposcopy and histopathology. Out of these 48 patients, 22 patients were those who had both cytology and colposcopy positive in their results (i.e., LSIL and HSIL for PAP smear and Aceto-white, mosaic, punctuation for colposcopy) and they also showed histopathology positive (i.e., CIN-1, CIN-2, CIN-3 or SCC).

TABLE 2 : Correlation between PAP smear and Colposcopy

		COLPOSCOPY					TOTAL
		Normal	Aceto-white	Aceto-white + Punctation	Aceto-white + Mosaic	Aceto-white + Mosaic + Punctation	
PAP Smear	Normal	5	3	1	-	-	9
	Inflammatory	20	20	8	1	1	20
	ASCUS	3	1	-	-	-	41
	LSIL	1	2	7	3	1	14
	HSIL	-	-	1	1	7	9
	SCC	-	-	-	-	-	-
TOTAL		29	26	17	5	9	86

TABLE 3 : Correlation between PAP smear and Histopathological findings

		HISTOPATHOLOGY						TOTAL
		Normal	CC	CIN-1	CIN-2	CIN-3	SCC	
PAP Smear	Normal	5	4	-	-	-	-	9
	Inflammatory	8	32	8	2	-	-	50
	ASCUS	2	1	1	-	-	-	4
	LSIL	-	2	8	4	-	-	14
	HSIL	-	-	2	1	4	2	9
	SCC	-	-	-	-	-	-	-
TOTAL		15	39	19	7	4	2	86

TABLE 4 : Correlation between PAP smear and Histopathological findings

		HISTOPATHOLOGY		TOTAL
		POSITIVE	NEGATIVE	
PAP Smear	POSITIVE	22	5	27
	NEGATIVE	10	49	59
TOTAL		32	54	86

TABLE 5 : Correlation between Colposcopy and Histopathology findings

		HISTOPATHOLOGY		TOTAL
		POSITIVE	NEGATIVE	
COLPOSCOPY	POSITIVE	32	25	57
	NEGATIVE	0	29	29
TOTAL		32	54	86

TABLE 6 : Correlation of combined cytology and colposcopy with histopathology

		HISTOPATHOLOGY		TOTAL
		POSITIVE	NEGATIVE	
CYTOLOGY +	POSITIVE	22	1	23
COLPOSCOPY	NEGATIVE	0	25	25
TOTAL		22	26	48

Only 1 out of 48 patients showed normal histopathology report despite having abnormal cytology and colposcopy.

Similarly, with normal cytology and colposcopy findings, none of the patients showed abnormal histopathology.

Discussion

As in the present study, inflammatory Pap smear was the commonest finding in Suguna M et al[3] (76%) and Joshi C et al[4] (64%). Also, the results of inflammatory PAP smear finding of present study (58.14%) was comparable with that of Kaveri S B et al[5] (55%).

TABLE 7 : Sensitivity and Specificity of PAP smear, Colposcopy and combined cytology + colposcopy

	Formula	PAP smear	Colposcopy	Combined PAP + Colposcopy
Sensitivity	TP/TP+FN	68.75%	100%	100%
Specificity	TN/TN+FP	90.74%	53.7%	96.15%
PPV	TP/TP+FP	81.48%	56.14%	96.65%
NPV	TN/TN+FN	83.05%	100%	100%
Accuracy	TP+TN/TP+TN+FP+FN	82.56%	70.93%	97.91%

Present study shows that 66.27% of the patients were found to be aceto-white on colposcopy, 30.23% were punctation, 16.27% were mosaic which was comparable with the study of Ramesh G et al6 i.e., 64%, 40% and 16% respectively.

Statistics reveal that the histopathology was normal in 17.44%, showed chronic cervicitis in 45.35%, CIN-1 in 22.09%, CIN-2 in 8.14%, CIN-3 in 4.65% and SCC in 2.33% which was comparable with the study of Joshi C et al4 (chronic cervicitis = 48%, CIN-1 = 28%, CIN-2 = 11%, CIN-3 = 4%).

Sensitivity, specificity, PPV, NPV and accuracy of PAP smear was calculated in the present study which came out to be 68.75%, 90.74%, 81.48%, 83.05% and 82.56% respectively. It was similar to that found in the study of Joshi C et al[4] (sensitivity= 65.38%, specificity= 95.83%, PPV= 94.44%, NPV= 80% and accuracy= 80%) and Kaveri S B et al.[5]

The results of colposcopy were also calculated. A similar study by Kohli B et al[7] showed sensitivity 100%, specificity 57.14%, PPV 50%, NPV 100% and accuracy 70% which was comparable with our study. Another study by Suguna M et al[3] also showed similar results.

Sensitivity, specificity, PPV, NPV and Accuracy of combined cytology and colposcopy was calculated in the present study which was found to be 100%, 96.15%, 96.65%, 100% and 97.91% respectively and that it was more than individual cytology and colposcopy suggesting that both cytology and coploscopy are complementary to each other. Shashwat V et al[8] study also concluded the same and emphasized on combined use of cytology and colposcopy.

Conclusion

Colposcopy and cytology are not competitive method, but complementary to each other. Best result in early detection of pre-invasive carcinomas could be obtained by combined use of cytology, colposcopy and colposcopic directed biopsy.

So, use of 'single visit approach' in which cytology, colposcopy and guided biopsy all are done in one setting and treated accordingly in resource poor countries like ours will enable maximum utilization of scarce medical resources.

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Case Report: Gynecology

Suture Granuloma

Dr. K. Satyavaty,[1] Dr. K. Swarajyalakshmi,[2] Dr. Nori Madhavi[3]

Abstract

Suture granulomas are localised inflammatory reactions in response to retained suture material. Non absorbale suture material thread is used in this case to suture uterine wound which resulted in suture granuloma and produced diagnostic dilemma.

Introduction

Suture granulomas are localized inflammatory reactions in response to retained suture material. Suture granulomas are a mass or cluster of immune cells that develop at the site of surgical sutures, or stitches. These granulomas are most commonly associated with embedded suture material, or material inadvertently left under the skin following the removal of surgical sutures or staples. Commonly seen with non absorbable suture material though occasionally also seen with absorbable suture material.

Case Report

This case is presented for its diagnostic dilemma.

25 year old P2L2 came with a history of continuous bleeding since the time of delivery 18 months back, she is not able to differentiate between periods and bleeding.

Past obstetric history: She is P2L2.

1. FT ND live birth 5 yrs back. She had no antepartum and intra partum complications.
2. FT LSCS done at a private hospital. Surgery lasted for 4-5 hours. She received multiple blood transfusions. Post operarive period was hectic. She had high fever and was referred to a tertiary centre on 8th post op day. Patient was treated and discharged after one week.

Since then patient is having continuous bleeding. She visited many hospitals and was treated with styptics, hormones, and oc pills with partial relief. She also underwent D&C without any relief.

On exam

General condition: Mild palor+, pulse 80/mt, BP 120/80 mm of Hg. Heart and lungs normal.

Local exam:

PA: Suprapubic cesarean scar with suprapubic tenderness.

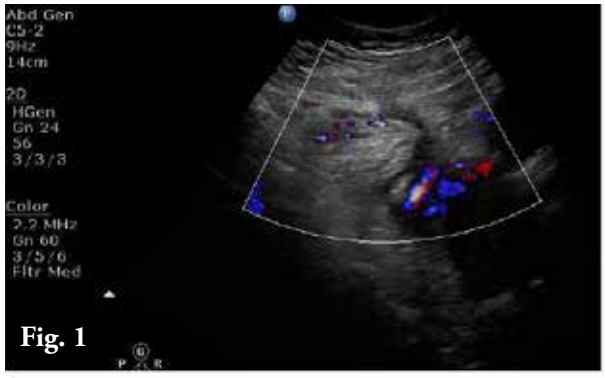
PS: Cervix healthy. Bleeding from within the cervical canal present.

PV: Uterus bulky. Movements are tender, tender mass felt over the anterior wall.

Hb 9.5 gm%. Serum ß HCG normal. X-ray chest; normal. LFT & RFT normal.

1. M.D., Former Professor and HOD of OB&GYNE, Osmania Medical College, Hyderabad
2. M.D., D.G.O., Former Professor of OB&GYNE, Osmania Medical College, Hyderabad
3. M.D., Consultant Radiologist, Maxcure Mediciti Hospital, Hyderabad

✉ Dr. K Swarajyalakshmi
E-mail: swarajyalakshmi6@gmail.com



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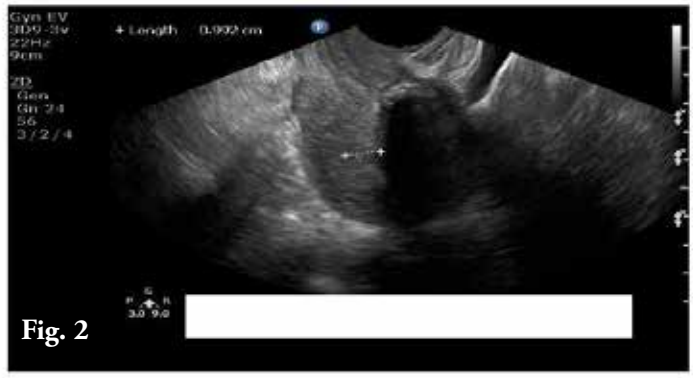

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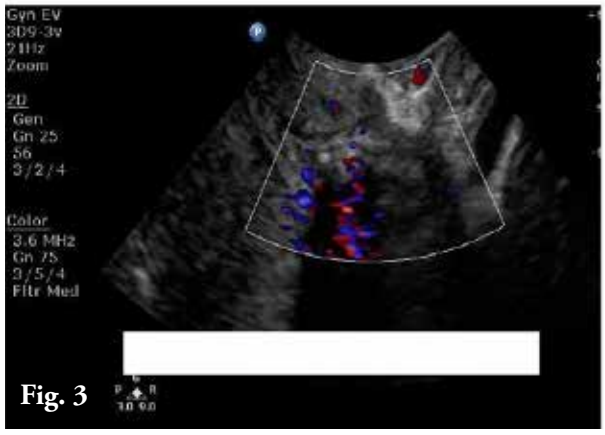

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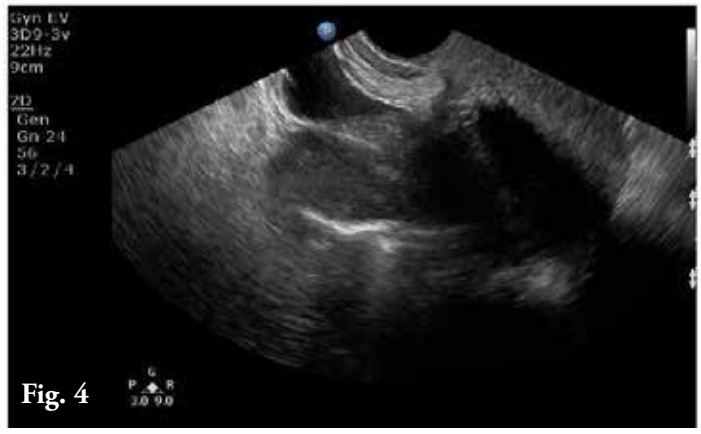


Fig. 4

Ultrasound findings

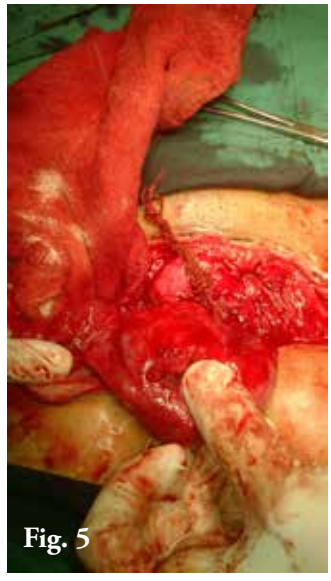
Fig. 1 Transabdominal survey reveals ill definition at vesicouterine space with loss of definition of anterior uterine contour.

Fig. 2 Transvaginal sonogram reveals dense acoustic shadowing at the LSCS scar region.

Fig. 3 Closure evaluation of LSCS scar reveals cluster with distal acoustic shadowing consistent with suture material.

Fig. 4 No free fluid collection.

In view of above findings and continuous bleeding not responding to treatment decided to do laparatomy (Figs 5, 6 & 7).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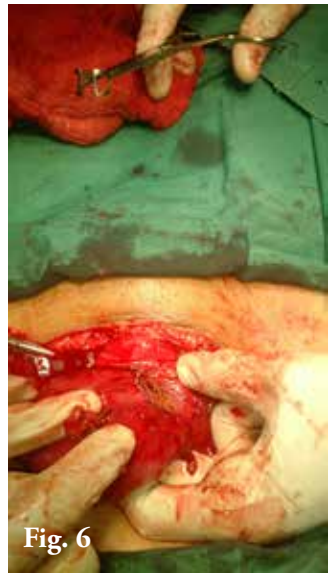
Fig. 6


Fig. 7

Operative findings

Uterus adherent to parietal peritoneum with thick band LSCS scar is high, UV fold and bladder are adherent to scar.

Right tube and an ovary adherent to parietal peritoneum.

Scar gaping of about 11/2 to 2 cms towards Rt angle present. Granulomatous lesions on the side of the

angle. Cluster of Threads are seen protruding as shown in picture. Lot of Threads removed and scar sutured in 2 layers .and abdomen closed. Patient had post op pyrexia controlled with broad spectrum antibiotics. Patient discharged. Since then she is getting periods regularly without any intermenstual bleeding or spotting.

Differential diagnosis

1. Deficient uterine scar after cesarean section is one of the causes of abnormal bleeding.
2. Gestational trophoblastic disease.

Discussion

Foreign body materials include non absorbable sutures; surgical sponges, Teflon, and activated charcoal induce foreign body reactions. In such cases, lesions related to the suture are called suture granulomas. The initial reaction of the tissue is a reflection of the amount of injury inflicted by the passage of the needle and sutures. After the initial reaction subsides, the suture material causes a specific inflammatory reaction. Non absorbable sutures are encapsulated by a rim of connective tissue, whereas histiocytes, giant cells, and lymphocytes are found near the suture line. These findings are most marked with silk and cotton compared with other materials.

Previous studies have reported that non absorption of thread is a more frequent cause of suture granulomas. Moreover, suture granulomas that develop following absorbable suture tend to heal after simple drainage within 1 week, whereas those that develop following non absorbable suture like thread require a longer period of time to heal, necessitating removal of the infected suture materials.

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