ORIGINAL RESEARCH

Effect of parity on blood loss during the third stage of labour: Comparison between misoprost and syntocinon groups

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ABSTRACT
Misoprostol is a prostaglandin E1 analogue that has been approved by the Food and Drug Administration (FDA) initially to be taken orally for the prevention & treatment of gastric ulcers. Now the drug is being used successfully in prevention and treatment of postpartum haemorrhage. Two hundredpregnant women at term with spontaneous onset of labour were included in the study and were randomly divided into 2 groups of 100 women each group A and group B were given per rectal misoprostol (600µg) and intramuscularsyntocinon(10U)respectively at that delivery of anterior shoulder of foetus. In misoprostol group, G1 had average blood loss of 250ml, G2 and 228ml of average blood loss, G3 had 210.3ml of blood loss and G4 had average loss of 266.7ml. In Syntocinon group, G1 had average blood loss of 162.7ml, G2 lost154.3ml,G3 lost 171.1ml whereas maximum loss seen in G4 patients which were 200ml. So average blood loss was maximum in 4th gravidaThe p value is >0.05 showing no relation of the effect of parity on blood loss duringthird stage with Misoprost and Syntocinon.

Key words: Third stage of labour, parity, misoprost and syntocinon

INTRODUCTION

Oxytocin is an octapeptide. In 1950, De Vigneaud and co-workers did the Nobel Prize winning work on the structure of oxytocin. It is synthesised in the supraoptic and paraventricular nuclei of the hypothalamus. By carrier protein it is transported from the hypothalamus to the posterior pituitary where it is eventually released. [1]

Oxytocin is thought to bind to the oestrogen dependent receptor on myometrial cell membranes. Bound intracellular calcium near the cell membrane is eventually metabolised from the sarcoplasmic reticulum to activate the contractile protein. Oxytocin is also thought to release prostaglandins from the decidua. The uterine contractions are similar to the physiological pattern i.e. causing fundal contraction and relaxation of the cervix. [2]

Misoprostol is a prostaglandin E1 analogue that has been approved by the Food and Drug Administration (FDA) initially to be taken orally for the prevention & treatment of gastric ulcers. Now the drug is being used successfully in prevention and treatment of postpartum haemorrhage.

Characteristic of Misoprostol: [3]

- It is inexpensive.
- Easily stored (Shelf life: 3 years) at room temperature.
- In comparison with other prostaglandins, it has minimal effects on cardiovascular and bronchial tree smooth muscle and can be safely used in hypertensive patients and asthmatics.
- It is not affected by ambient temperature and needs no refrigeration, needles or syringes for its storage and administration respectively.
- Mode of administration - oral, vaginal, intracervical intrauterine, sublingual, buccal, rectal.

After oral administration this drug is absorbed quickly and then de-esterified to be converted into its active pharmacological form misoprostol acid, less than 90 percent of which remains bound to serum protein. Misoprostol acid is responsible for different chemical activities. [4]

Concentration of this metabolite reaches its peak in plasma approximately by next 30 minutes and declines rapidly thereafter (half life 21 minutes).
Maximum plasma concentration of misoprostol acid is diminished when the drug is taken with food and total availability of the active metabolite is reduced by concomitant antacid. Primary site of metabolism of this drug is in liver and less than 1% of this metabolite is excreted in urine. [5]
Dose of drug needs adjustment when used in patients with liver disease whereas it is not required in patient with renal insufficiency who do not require dialysis.
This drug has no known drug interaction and does not induce the hepatic cytochrome P-450 enzyme system.
The effect of misoprostol on reproductive tract are increased and gastrointestinal adverse effects are decreased if the oral preparation of misoprostol is administered vaginally or rectally.
The most common adverse effects of misoprostol are nausea, vomiting, diarrhoea, abdominal pain, chills, shivering and fever. [6]

Methodology
The present randomized study is to compare the efficacy of per rectal misoprostol andintramuscularsyntocinon in the management of third stage of labourto prevent Post partum hemorrhage.
Two hundredpregnant women at term with spontaneous onset of labour were included in the study and were randomly divided into 2 groups of 100 women each group A and group B were given per rectal misoprostol (600µg) and intramuscularsyntocinon(10U)respectively at that delivery of anterior shoulder of foetus.
200 cases admitted to the above hospitals who fulfilled the selection criteria were included for the study.

Inclusion criteria
All patientsin the age group of 19-<35 years, period of gestation ranging from 37-40 weeks and gravidity – both primi and multigravida, at term with spontaneous onset of labour were included in the study and subjected to vaginal delivery.

Exclusion criteria
- Multiple pregnancy, intrauterine foetal death, previous caesarean section, pregnancy induced hypertension, antepartum haemorrhage, heart disease, bronchial asthma, renal disease, liver disease, allergy to drug, and haematological disorders.

The selected cases with inclusion criteria was divided into 2 groups

Group A: Misoprostol 600µg was inserted per rectally immediately following birth of baby (100).

Group B: Injectionsyntocinon(10U) intramuscular was given at the delivery of anterior shoulder (100).
Each of the patients will be allotted to one of the groups by coloured coins method (self selection — random sampling method).
An informed consent was taken from the patients who met the inclusion criteria. These women underwent a thorough general and systemic examination like cardiovascular system, respiratory system, per abdomen and per vaginal examination.
The women were given either syntocinon(10U) intramuscular or per rectal misoprostol (600µg) at the delivery of anterior shoulder of foetus.

Results

Table1: Distribution of patients according to parity

Parity	Misoprostol	Syntocinon
Primi	49	63
G2P1	29	27
G3P2	19	9
G4P3	03	1
Total	100	100

In misoprostol group, 51% of cases were multigravidas and 49% of cases were primigravidas.
In syntocinon group, 37% cases were multigravidas and 63% wereprimigravidas.

Table2: Distribution of Patients according to Period of Gestation

Period ofgestation	Misoprost	Syntocinon
37-38	28	26
38-39	26	31
39-40	46	43
Total	100	100
MeanGA	38.5	38.4
SD	1.3	1.2
Z= 0.17	P0.86(p> 0.05),NS	

In misoprostol group maximum numberi.e 46patients delivered at 39-40 weeks of gestation, 26casesdelivered at 38-39 weeks of gestation& Rest 28 casesdelivered at 37-38 weeks of gestational age. Mean of period of gestation at which delivery occurred was 38.5±1.3 weeks.
In syntocinon group maximum number of patients 43 delivered at 39-40 weeks of gestation. 31 cases delivered at 37-38 weeks of gestation. The rest 26 cases delivered at 38-39 weeks of gestation. Mean of period of gestation at which delivery occurred was 38.4±1.2 weeks.

Table3:Effect of Parity on Blood Loss During Third Stage of Labour

Parity	Average amount of blood loss(ml)	
	Misoprost	Syntocinon
Primi	250.3	162.7
G2P1	228.6	154.3
G3P2	210.3	171.1
G4P3	266.7	200
p value	p>0.05, ns	p>0.05, ns

In misoprostol group, G1 had average blood loss of 250ml, G2 and 228ml of average blood loss, G3 had 210.3ml of blood loss and G4 had average loss of 266.7ml. In Syntocinon group, G1 had average blood loss of 162.7ml, G2 lost154.3ml,G3 lost 171.1ml whereas maximum loss seen in G4 patients which were 200ml. So average blood loss was maximum in 4th gravida. The p value is >0.05 showing no relation of the effect of parity on blood loss duringthird stage with Misoprost and Syntocinon.

Discussion

According to the WHO[5] multicentricrandomised trial using oral Misoprostol with oxytocinthey concluded that oral Misoprostol was associated with significantly high incidence of side effects like shivering and rise in body temperature and hence oxytocin is preferred to 600 µg of oral Misoprostol in management of third stage of labour in hospital settings, but still Misoprostol has been suggested for the management of third stage of labour in developing countries, because it has strong uterotonic effects, can be given orally, inexpensive and does not need refrigeration. [5]

Bernard Spitz *et al*, [6]in their double blind study with methyl ergometrine(0.2mg) and PGE1(400µg)concluded that although protection from post partum hemorrhage using parenteral methyl ergometrine and oral misoprostol is nearly equal, misoprostol is associated with more side effects. But side effects of Misoprostol were self-limiting and produced a sustained contraction of the uterus and hence reduced the total blood loss.[6]

O'Brien *et al*[7]based on their trial on 14 women with post partumhaemorrhage unresponsive to oxytocin and ergometrine concluded that rectally administered Misoprostol appears to be an effective treatment for PPH unresponsive to oxytocin and ergometrine, therefore it might be an alternative to parenteral prostaglandins or at least minimize the number of women this invasive treatment. In this study Misoprostol 1000 µg (five tablets) was administered rectally. This was followed by several studies that examined the use of rectal Misoprostol for third stage of labour.

Ramsey and Ramin*et al* [8] suggested that the failure of Bambigboye*et al* [19] to demonstrate a significant efficacy of Misoprostol for the prevention of PPH represented a pharamacokinetics problem rather than a lack of clinical efficacy and concluded that, when rectally administered, delayed absorption would make Misoprostol ineffective for the prevention of post partumhaemorrhage.

Subsequently, Ramsey and Ramin*et al* [9] stated that sustained uterine contractions observed within 3 minutes after drug administration were secondary to rectal Misoprostol.

Goldberg *et al*[10] stated that there is currently insufficient evidence to support the routine use ofmisoprostol to prevent PPH, when oxytocin or methyl ergometrine is available, but misoprostol may lower the incidence of PPH if these drugs are not readily available. They recommended 400-600 µg misoprostol orally or rectally after delivery of the baby but before delivery of the placenta. For treatment of PPH,1000 µg Misoprostol given rectally, if treatment with oxytocin and methyl ergometrine is unsuccessful and if PGF2α, is not available may be helpful.

Gohil T *et al*, [11] conducted a A study to compare the efficacy ofMisoprostol 400µg per rectally, Inj Oxytocin 10 IU i.m.,Inj Methyl ergometrine 0.2mg i.v. and Inj(Ergometrine 0.5mg+ 5IU Oxytocin) i.m. in reducing blood loss in active management of third stage of labour, and concluded that Methyl ergometrine has best uterotonic drug profile amongst all. Misprostol was foundto cause higher blood loss compared to other drugs with higher requirement of bloodtransfusion andOxytocics. They concluded that misoprostol to be used when the non-availability of other drugs and its role in third stage of labour needs larger studies to be proved. [11]

Walder*et al* [12]suggested that Misoprostol a prostaglandin, might be effective in the prevention of PPH. It can be given orally, does not require refrigeration and has few side effects. If Misoprostol(600µg) is found to be an acceptable alternative to the other oxytocic agents then it may be helpful in reducing worldwide deaths from PPH.

Conclusion

So average blood loss was maximum in 4th gravidaThe p value is >0.05 showing no relation of the effect of parity on blood loss duringthird stage with Misoprost and Syntocinon.

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