SURVEY ON THE USE OF MISOPROSTOL FOR INDUCTION OF LABOUR AMONG OBSTETRICIANS IN THE WEST AFRICAN SUBREGION

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ABSTRACT:
Context: Wide spread use of misoprostol is increasingly commoner in our obstetrics and gynaecological practice, most especially for Induction of labour in spite of its serious associated risks of maternal and fetal complications
Objective: To determine the use of Misoprostol for induction of labour among the Obstetricians in the West African sub region.
Methodology and settings: During the October 2007 pre examination workshop of the West African College of Surgeons (FWACS), Faculty of Obstetrics and Gynaecology 42 examiners responded through structured questionnaires on the use of misoprostol for induction of labour (IOL) in their institutions of practice.
Results: About 91 % admit using misoprostol for IOL with only half (50%) having written protocols for labour induction with misoprostol. Almost all (93%) prefer the vaginal route for the administration of misoprostol and about 74% do not use misoprostol for those with Caesarean section scar compared to only 19% who do. Misoprostol is used for cervical ripening and control of post partum haemorrhage among 24.4% and 50% of the Obstetricians respectively. The commonest complications encountered were Fetal distress, uterine rupture and uterine hyper tonus among 54.8%, 52.4% and 45.2% of the respondents.
Conclusions: Misoprostol use was high with yet serious complication occurring among those using it for IOL. Despite the manufacturers and other regulatory agents warning against its use in pregnancy because of serious maternal and fetal complications, misoprostol use for IOL is widespread. A regulated use of this drug especially in pregnancy is advocated.

INTRODUCTION

Misoprostol is a synthetic prostaglandin E1analogue developed and marketed as Cytotec by GD, Searle Co, Chicago, IL for the treatment of gastric and duodenal ulcers as well as the prevention of NSAIDS associated ulcers in 1985[1]. The suggestion by Margulies[2] that Misoprostol might be effective for labour induction generated interest that increased it's used in our Obstetrics and Gynaecological practice. Fifteen years after its introduction the manufacturers of the drug Searle pharmaceutical company warned against its use in pregnancy because of its arbotificient property and formally wrote a letter to the American College of Obstetrician and Gynaecologist (ACOG on august 23rd 2000 stressing on the dangers of this drug in pregnancy and its risks both to the mother and fetus when used for induction of labour (IOL)[3]. In spite of the acceptable clinical evidence of other induction agent (Pitocin), wide spread "off" label use of misoprostol became increasingly common among Obstetricians, in spite of its risks from reports and meta analysis including Cochrane database, ACOG, British Royal college of Obstetrics and Gynaecology and other regulatory agencies when used for IOL[4]. Misoprostol compared to other induction agents is observed to be stable analogue, it can withstand tropical conditions, hence does not need refrigeration[5]. It s also cheap and easily available across the counter, and misoprostol may play an important role in Obstetrics and Gynaecology practice in poor resource settings like ours where maternal mortality is high and other prostaglandins preparations are prohibitively expensive[6]. For now "off" label use of misoprostol will continue

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in our hospitals until such a time when our regulatory agencies will approve/license its use for IOL.

This study was undertaken to determine the protocol and use of misoprostol for IOL and associated feto-maternal complications among the Obstetricians in the West African sub region.

METHODS

During the October 2007 Faculty of Obstetrics and Gynaecology of the West African College of Surgeons (WACS) fellowship examination fourty two examiners spread across 22 training institutions were issued with structured questionnaires to determine the use of misoprostol for IOL in their respective institutions. Information pertaining to unit (written) protocol, type and source of misoprostol, the minimum and maximum dose relating to parity and routes of administration of the drug. Also information pertaining to the used of misoprostol in patient with previous caesarean section, and other indication of misoprostol use in our units were obtained.

The data was analysed using SPSS statistical package version 11.0 and test of significance was determined using Chi square test.

RESULTS

Fourty two Obstetricians and Gynaecologists spread across the 22 WACS accredited training institutions in the West African sub region responded to the structured questionnaires, 30 (71.4%) have written protocol for IOL in their institutions as shown on table I. Majority of the respondents (90.5%) were using Misoprostol for labour induction in their units, but only half (50%) of this have written protocol for IOL with misoprostol. Both Oxytocin and misoprostol were used by 30 (71.5%) of the Obstetricians. but expectedly about 31(73.8) still have reservation to use misoprostol to induce labour in those with Caesarean section scar compared to only 8 (19.0) who have no such reservation.

The route of administration and dosing regiment relating to parity is illustrated in table II

Almost all the Obstetricians 39(92.9) use the vaginal route for the administration of misoprostol IOL only 2.4% uses the rectal or oral route. About 66.7% of the Obstetricians prefer to use 50ug as a minimum dose to commence IOL for Primigravidae compared to only 19% who use a lower dose of 25ug, while for Multipara 50% prefer to use 50ug as against 42.9% who commenced them with lower dose of 25ug. Cumulative dose of up to 400ug were used for primigravidae as against 200ug as maximum cumulative dose for Multipara with as many as half (49.9%) of the Multipara receiving dose not exceeding 100ug compared to 31.9% of primigravidae.

Twenty two (54.4%) had written protocol for cervical ripening, while 19 (45.2) do not have. 59.5 take the decision for both cervical ripening and IOL at the consultant level as against only 2.4% who said its taken at the level of the resident, 38.1 of the respondents said the decision to use misoprostol could be decided at the level of both the residents and the consultant. This was shown on table III. The use of misoprostol or Foley's catheter and misoprostol and sweeping of the membrane are the popular methods for cervical ripening as practice by 33.3% and 33.1% of the Obstetricians

The commonest complications were Fetal distress and uterine rupture experienced by 54.8% and 52.4% of the Obstetricians in their practice respectively, while uterine hyper tonus, maternal pyrexia and still birth was reported to have occurred among 45.2%, 31% and 28.6% respectively.

TABLE I:
Protocol for IOL and misoprostol used Written protocol for IOL

Response	number	%
Yes	30	71.4
No	12	28.6
Written protocol for IOL with misoprostol		
Yes	21	50
No	21	50
Misoprostol used for IOL		
Yes	38	90.5
No	3	7.1
N/R	1	2.4
What do you use for IOL in your institution?		
Misoprostol	8	19.0
Oxytocin	4	9.5
Both	30	71.5
Misoprostol used with previous caesarean section		
Yes	8	19.0
No	31	73.8
N/R	3	7.2

TABLE II:
Route of administration and Dosage for misoprostol

Route	number	%
Oral	1	2.4
Vaginal	39	92.9
Rectal	1	2.4
N/R	1	2.4
42	**100**	

Dosage regime in relation to parity

Dosage (ug)	Parity			
Minimum	**Primigravidae (%)**		**Multipara %)**	
5	8	19.0	18	42.9
50	28	66.7	21	50
100	3	7.1	0	0
N/R	3	7.1	3	7.1
100	**42**	**100**		**42**
	X^2= 48.142 P = .007		**X^2= 35.783 P = .023**	

Maximum	**Primigravidae (%)**		**Multipara (%)**	
25	1	2.4	3	7.1
50	4	9.5	9	21.4
75	3	7.1	0	0
*100	5	11.9	9	21.4
*150	3	7.1	3	7.1
*200	12	28.6	8	19.0
*250	1	2.4	0	0
*300	2	4.8	0	0
*400	3	7.1	0	0
N/R	8	19.0	10	23.8
	42	**10**	**42**	**100**
	X^2= 32.714 P = .018		**X^2= 24.781 P = .037**	

***Cumulative dose of misoprostol given in multiple of 50ug 6hourly**

TABLE III:
Protocol for cervical ripening and other indications of misoprostol used Written protocol for cervical ripening

Response	Number	%
Yes	22	52.4
No	19	45.2
N/R	1	2.4
42	100	

Decision for cervical ripening and IOL

Person	Number	%
Consultant	25	59.5
Resident	2	4.8
Both	14	33.3
N/R	1	2.4
	42	100

Method of cervical ripening

Method	Number	%
Misoprostol	9	24.4
Foley's catheter	4	9.5
Misoprostol & fol.catheter	14	33.3
Misoprostol & membrane sweeping	13	31.0
	42	100

Other indications for misoprostol used

Indication	Number	%
PPH	21	50
Medication abortion	4	9.5
Incomplete abortion	1	2.4
IUFD	2	4.8
PPH & med. Abortion	2	4.8
PPH & incomp abortion	1	2.4
N/R	11	26.2
	100	

TABLE IV:
Complications encountered with the used of misoprostol

Complications	Number (n=42)	%
*Stillbirth	12	28.6
*Fetal distress	23	54.8
*Uterine hypertonus	19	45.2
*Ruptured uterus	22	52.4
*Maternal pyrexi	13	31
N/R	3	7.1

*** Multiple responses.**

DISCUSSION

The use of misoprostol for induction of labour among Obstetricians in West African sub- region is appreciably high reaching up to 90.5% prevalence, which is much higher than reported in a randomised study of 46% prevalence among Obstetricians and Gynaecologist in Brazil, Jamaica and United States of America[7], this appreciable use might have been encourage by institutional studies in the sub-region which lay credence to its efficacy and other physical advantages over other induction agents[5, 6, 8, 9-11]. Despite this widespread use, institutional protocol for its use in IOL is only found in about 50%. One third of the obstetricians still use both Oxytocin and misoprostol for IOL in their respective units

The general reservations for its use in those with previous caesarean section scar of 73.8% is not unconnected with the fear of uterine rupture observed and cautioned by other regulatory bodies in other part of the world[3, 12-16].

The generally preferred route of administration of misoprostol for IOL among the Obstetricians was the vaginal route with 92.9% compared to oral, rectal and sublingual routes of only 2.4% prevalence. Toppozado[17] reports that the vaginal route has success rate in a shorter interval as compared to oral route, while Bartusevicius[18], in a randomised controlled trial observed that sublingual 25ug and vaginal route 50ug has similar efficacy.

Significant number of our obstetrician 66.8% prefer to commence IOL for primigravidae with 50ug compared to 19% who commenced with 25ug, but there was no much significant difference between those that use 25ug (42.9%) and 50ug(50%) for IOL in Multipara. Though there was no clear safety advantage, Sanchez had earlier reported that 50ug is more efficacious than 25ug tablet[19]. It is worth noting that misoprostol (synthetic prostaglandin E1 analogue) is available in 200ug tablets and smaller doses are obtained by breaking into pieces which may not be accurate. The study also reports that the decision for the use of misoprostol for IOL was taken at the consultant level (59.5%) as against 2.4% at the level of the resident, while in about 38% the decision could be taken at either level. Misoprostol is equally used for other indications

like cervical ripening, medication abortion, missed abortion and control of postpartum haemorrhage as widely use elsewhere.

Complication rate of between 28.6% - 54.8% of Fetal distress, uterine hyper tonus, uterine rupture, maternal pyrexia and stillbirth either alone or in combination were encountered during the course of their practiced, this finding is the general observed adverse outcome of misoprostol use as reported from many studies[4, 20, 21]. Use of misoprostol for IOL may not be better substitute for Oxytocin infusion neither is it better than membrane sweeping or Foleys catheter for ripening of cervix if this complications are put into perspective [22, 23]. Use of misoprostol as single agent for cervical ripening is also common, 24.4% compared to 33.3% for misoprostol with Foleys catheter, 31% misoprostol with membrane sweeping, while Foleys catheter alone is only used by less than 10% of the respondents. Digital stretching of fetal membrane for cervical ripening is a common practice although largely unreported[22].

The ease of administration, availability low cost, and its efficacy despite disastrous consequences may be the main motivation for its widespread use. Fifty percent of the respondents also use this drug for the control of postpartum haemorrhage, while about 26% use it for PPH and incomplete abortion. However use of misoprostol in abortion related condition is very low, this is a surprise finding. It is a well known fact that pregnancy termination in most countries is illegal except where the mother's life is in danger or the fetus not viable or has major congenital abnormality. The observed low incidence for pregnancy termination may therefore be an under reporting. Further most recent survey by IPAS (Nigeria) of major pharmaceuticals outlets indicate that some of the drugs are probably dispensed without prescription[24].

All the respondents recorded some major complications associated with misoprostol use as highlighted by the manufacturers. This is a major source of concern. Maternal and fetal death and ruptured uterus are particularly worrisome. Since this drug is not available in smaller dosage preparation, it's usually broken into pieces to approximate the doses. This is also another set back for its use in ripening of the cervix and IOL especially that incidences of complications increases with dosage.

It is absolutely necessary that this drugs are available in smaller doses and its use strictly regulated including close monitoring of patient after administration when use for ripening of the cervix and induction of labour.

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