Original Article

Interruption of Pregnancy with Previous Two to Three Caesarean Sections with Misoprostol

Faiqa Chughtai[1] , Uzma Rahman Kallue[2], Saema Tehseen[3], Abeera Choudry[4]

[1,2,4]Classified Gynaecologist, Pak Emirates Military Hospital, Rawalpindi
[3]Pakistan Aeronautical Complex Hospital, Kamra

Correspondence: *Col Dr. Faiqa Chughtai*
Classified Gynaecologist, Pak Emirates Military Hospital, Rawalpindi
faiqachughtai@yahoo.com

Abstract

Objective: To establish the success rate and safety of vaginal birth with misoprostol for 16 to 30 weeks of pregnancy in women with previous two to three caesarean sections.

Methodology: The prospective observational study was carried out at Obstetrics and Gynaecology department of Pak Emirates Military Hospital Rawalpindi, from 1st Oct 2017 to 30th Sept 2018. 304 patients with a pregnancy between 16 to 30 weeks, with two to three caesarean sections. Indications for interruption/termination of pregnancy included major foetal abnormalities, early severe growth restriction of the foetus, foetal demise, foetal β-thalassemia, preterm pre-labour rupture of membranes, early severe pre-eclampsia and other maternal diseases. The patients with contraindications to vaginal birth like low lying placentae, transverse lie, huge foetal tumours, and hydrops fetalis were excluded from the study. First trimester pregnancy terminations were also excluded. Labour was induced with oral misoprostol 200µg 6 hourly in pregnancies between 16 to 20 weeks and 200µg 12 hourly from 20 to 30 weeks, followed by cervical catheter in selected cases.

Results: Misoprostol induction of labour with two to three previous caesarean sections resulted in vaginal delivery in 94.07% of the cases and repeat scar was avoided in further 2.3%. Uterine scar rupture was encountered in 0.6% of the patients and minor complications were observed in 6.8% in total.

Conclusion: The efficacy and safety of properly chosen dose of misoprostol via oral route in patients with previous caesarean sections was established. Its use should be encouraged in tertiary care consultant led hospitals.

Key words: Misoprostol, pregnancy, caesarean section, pregnancy complications, fetal death.

Cite this article as: Chughtai F, Kallue UR, Tehseen S, Choudry A. Interruption of Pregnancy with Previous Two to Three Caesarean Sections with Misoprostol J Soc Obstet Gynaecol Pak 2019; Vol 9(2):77-82.

Introduction

The rate of caesarean sections (CS) has grown like an epidemic, from 6.7% in 1990 to 19.1% in 2014 worldwide with an average of 4.4% per annum.[1] This is posing numerous implications for the women and their families, their obstetricians, the hospitals and for the state. These include repeated surgeries with technical difficulties, increased incidence of placenta praevia with morbid adherence, need of blood transfusion and economic burden on the state. The gravest of all is to give repeat scar to woman requiring termination of pregnancy (TOP) for foetal or maternal indications. It causes physical and mental trauma to the woman and a sense of failure for her clinician.

Obstetricians usually opt for a repeat CS or hysterotomy because of reasons namely old

Authorship Contribution: [1]Substantial contributions to the conception or design of the work, drafting the work and revising it critically for important intellectual content [2,3]Acquisition, analysis and interpretation of data for the work,[4]Final approval of the version to be published.

Funding Source: none

Conflict of Interest: none

Received: May 09, 2019

Accepted: July 30, 2019

teaching, the anxiety of complications, lack of experience, low resource setup of working and above all to avoid the responsibility of conducting a so-called hazardous procedure.

WHO has suggested 15% of deliveries by CS as a threshold.[2] The largest contributor to increasing CS rate is previous caesarean delivery.[3] The simplest way to achieve this threshold is to avoid repeat scar in a patient with previous CS in cases of preterm and/or non-viable pregnancies.

Misoprostol has emerged as a potent agent for labour induction in last two decades. Initially, it was licensed as a gastric protective agent in 1985.[4] Off-label obstetric use was started in the late 1990s and its action for cervical ripening in patients with previous CS has been studied years back and proven to be safe.[5] However, it had not been licensed even in a few developed countries for labour induction till the recent past.[6] In literature, the repeated CS was appraised as an obstetrics catastrophe and a big gap in research regarding this issue was noticed. Thus, this study was designed to encourage our colleagues to attempt vaginal interruptions with two to three CS, when there is no concern about foetal outcome, and misoprostol was chosen for its prompt action; low cost and easy availability.

Methodology

The study was conducted on 304 patients, in Obstetrics and Gynaecology (Ob/Gyn) Department of Pak Emirates Military Hospital (PEMH) from 1st Oct 2017 to 30th Sept 2018, with a singleton pregnancy, from 16 to 30 weeks either by dates or by fundal height, requiring termination.

The sample size was calculated using the WHO sample size calculator, including parameters: 95% Confidence Level, 18.6% Population proportion[1] and Level of significant 5%, from the above parameters sample size came out 233 but as we recruited patients for one year so we took a sample of 304.

Out of 304, 199 (65.5%) were with previous two and 105 (34.5%) were with previous three CS whereas54 (17.7%) had undergone a vaginal delivery in past. The indications for interruption are shown in Table I. The patients with low lying placentae, huge foetal tumours like sacrococcygeal teratomas, hydrops fetalis and first trimester pregnancy terminations were excluded from the study. The patients with confirmed classical CS, last CS in less than a year time, and those who refused were not included. Ethical approval was taken from concerned committee.

Table I: Distribution of indications for termination of pregnancy

Indications	Total number of patients	Previous 2 CS	Previous 3 CS
	n (%)		
Intrauterine foetal demise	162(53.3)	97 (31.9)	65 (21.3)
Early severe intrauterine growth restriction	21(6.9)	6 (2)	15 (5)
Foetal structural anomalies	68 (22.3)	39 (12.8)	29 (9.5)
Foetus with β thalassemia major	8 (2.6)	1 (0.3)	7 (2.3)
Foetus with Down syndrome	2 (0.6)	0	2 (0.7)
Preterm Pre-labour Rupture of Membranes	20 (6.6)	18 (5.9)	2 (0.7)
Early severe preeclampsia	17 (5.6)	11 (3.6)	6 (2)
Acute fatty liver of pregnancy	2 (0.7)	2 (0.7)	0
Chronic kidney disease	2 (0.7)	2 (0.7)	0
Malignancy	2 (0.7)	1 (0.3)	1 (0.3)
Total	304 (100)	177 (58.2)	127 (41.8)

Informed written consent was taken from all the patients. The couples were counselled about the procedure, its benefits, risks and approximate time of delivery. The convincing and empathetic attitude was the mainstay of counselling. Blood cross match was sent for all the patients. Oral misoprostol 200µg was given six hourly from 16 to 20 weeks and 12 hourly from 20 to 30 weeks of pregnancy. Cervical Foley catheter was introduced in 67 (22%) selected cases when the cervix was 1.5cm dilated with intact membranes. Out of these 67, 11 (16.4%) of the cases were less than 20 weeks while the rest i.e.,56 (83.58%) were from 20 to 30 weeks of pregnancy. Injection Cefixime 1g intravenous 12 hourly was started in patients with cervical Foley, preterm pre-labour rupture of membranes (PPROM) and those requiring surgical intervention. Injection Nelbuphine was given intramuscularly for analgesia and an antiemetic was added when required. Sympathetic

attitude and careful maternal monitoring was continued. Foetal monitoring was not required. Failed termination was defined as no improvement in cervical findings 48hours after the initiation of procedure. After expulsion, each patient underwent ultrasonographic examination to confirm the completion of the procedure. The patients were discharged from the hospital after 24 hours and were called for postnatal visit seven days afterward. Statistical analysis was performed using statistical software SPSS 23. Frequency and percentages were calculated for qualitative variable i.e. age, gender etc. Chi-square test was used for the comparison between two qualitative variables. p value ≤ 0.05 was taken statistically significant.

Results

Distribution of patients by history and demography is shown in Table II. Mean age of patients was 29.08 ± 5.8 years. Among 304, 151 (49.7%) patients were para 3 and 146 (48.0%) were of normal body mass index (BMI). There were 31 obese patients but none was morbidly obese i.e., BMI 40 kg/m^2 or more.

Spontaneous vaginal birth was achieved in 286 (94.07%) patients. In addition, in 7 (2.3%) of the patients, foetal mutilation and evacuation of the uterus was performed vaginally under anaesthesia when the cervical dilatation did not improve beyond 1.5 cm after 48 hours. Therefore, in total, 293 (96.3%) patients were saved from a repeat scar. Time from induction to delivery varied from 8 hours 30 minutes to 84 hours with weighted average of 41.89 hours. Out of 304, 9(2.9%) patients needed evacuation of retained products of conception. Blood transfusion was required in 13 (4.3%); out of these, 6 patients were transfused to correct their pre-existing anaemia (Hb < 10.0g/dl). Blood loss secondary to procedure requiring transfusion was encountered in 7 (2.3%) patients.

There were 2 (0.6%) cases of uterine scar rupture. Both of these patients had two previous CS and BMI of 18kg/m^2 and 24.4kg/m^2. They underwent laparotomy and successful uterine repair. Out of 304,4 (1.3%) patients refused further procedure within 24 hours after induction; one of these was under 20 weeks of pregnancy while three were between 20 to 30 weeks of pregnancy. These four patients were delivered by abdominal route. Out of 304, 5 (1.6%) patients did not show any improvement of cervical score at 48 hours leading to

Table II: Distribution of patients by history and demography.

Age	18 – 30 Years	31 – 40 Years	≥ 40 Years	
	121 (39.8%)	152 (50.0%)	31 (10.2%)	
Education	**Under Matriculate**	**Matriculate**	**Graduate**	**Post Graduate**
	115 (37.8%)	157 (51.7%)	28 (9.2%)	4 (1.3%)
BMI	**< 18.5 kg/m^2**	**18.5 – 24.9 kg/m^2**	**25 – 29.9 kg/m^2**	**>30 kg/m^2**
	17 (5.6%)	146 (48.0%)	112 (36.8%)	29 (9.6%)
Parity	**2**	**3**	**≥ 4**	
	119 (39.1%)	151 (49.7%)	34 (11.2%)	
Previous Vaginal Deliveries	0 (0%)	19 (6.25%)	35 (11.5%)	

Table III: Summary of outcomes of interruption of pregnancy.

Outcomes	Total number of patients	Previous 2 CS	Previous 3 CS	p value
		n (%)		
Spontaneous vaginal birth (taken as Success Rate)	286 (94.1)	189 (62.2)	97 (31.9)	0.832
Foetal mutilation and vaginal evacuation (taken as Success Rate)	7 (23)	5 (1.6)	2 (0.7)	
Need of blood transfusion secondary to haemorrhage	7 (2.3)	4 (1.3)	3 (1)	
Need for surgical evacuation of retained products of conception	9 (3)	4 (1.3)	5 (1.6)	
Uterine scar rupture	2 (0.7)	2 (0.7)	0	
Refusal to continue the procedure	4 (1.3)	1 (0.3)	3 (1)	
No change in cervical score after 48 hours	5 (1.6)	2 (0.7)	3 (1)	
Scar Rupture (taken as Safety)	2(0.6)	1(0.3)	1(0.3)	

failed induction which culminated in abdominal delivery. The indications were breast carcinoma, PPROM and chronic kidney disease in one each and foetal demise in rest two. The results are summarized in Table III.

Discussion

CS rates of army medical corps hospitals has risen as dramatically as worldwide. Total number of maternities in period of study was 13740 at PEMH out of which 6046 (44%) were CS. The indications, in addition to those described earlier, includes the fear of litigation, free of cost treatment and desire of the parturient and the attendants for safe, *easy and rapid* delivery. PEMH, a tertiary care setup, also entertains all the high risk pregnancy form the periphery. Keeping in view that vaginal birth after two CS is not absolutely contraindicated, the study was conducted to access one of the measures to avoid a repeat caesarean for interruption of pregnancy in a consultant led obstetric unit.[7]

The drug used for labour induction was misoprostol, which is being used for this purpose for the last twenty years in non-scarred uterus. International Federation of Obstetrics and Gynaecology has published its regimens in 2017 for use of misoprostol for TOP in non-scarred uterus and recommends to generate individual schedules for patients with previous scars.[8,9] The dose administered under this study was far less than that already been used by Bhattacharjee *et al.* in 2007 i.e., 400µg 6 hourly.[10] It was also less than the dose used by Ouerdiane *et al.* in 2015 i.e., 200µg 3 hourly. It was greater than that used in the study by Chamsi *et al.* i.e., 50µg 6 hourly for TOP between 18 to 26 weeks.[12] The routes for administration of misoprostol include oral, vaginal, rectal, sublingual and, recently introduced, buccal.[9] In our study oral route of misoprostol administration was selected to avoid repeated vaginal examinations in cases of foetal demise or PPROM. Oral route also carries less effect of uterine hyper-stimulation; it has been proven to be safe and requires less patient monitoring in undermanned hospitals.[13]

The successful termination was achieved with misoprostol in 94.07% of the patients ($p<0.001$) which is slightly better than 90.3% achieved by Fawzy *et al.* and 90% achieved by Naguib *et al.*[14,15]

As the aim of the study was to avoid a repeat CS scar, 7 (2.3%) patients were evacuated vaginally after mutilation of fetuses under anaesthesia. Out of these, one patient was with PPROM, two were carrying anencephalic fetuses, three were with foetal demise and one had ovarian malignancy. All these patients were carrying pregnancies of 16 to 20 weeks and a special consent was taken for this procedure. This is at variance with relevant literature where success rate of complete abortion with previous scars is 68%.[16] The study by Chamsi *et al.* revealed successful termination in 67.8% of the patients with a scarred uterus.[12] They attributed this apparently low success rate to the higher order CS in their study in Saudi Arabia.

The study was designed for termination with higher order CS with respect to safety, therefore no upper time limit was defined as a long patient was making progress. The patients were counselled for probable maximum time of four days. The time was noted as a by-product of the study and it was found to be longer when compared with the study by Bhattacharjee *et al.* i.e., 41.89 hours versus 16.4 hours.[10] This longer time was due to low dosage schedule. This disadvantage of longer induction time was counterbalanced by higher rates of successful terminations. In a low resource setup like ours, there is less margin for error. Therefore, while some units may run a 2nd cycle in case of the unresponsive cervix at 48 hours, our policy was to offer a CS at this point in this high risk population.

Evacuation of the uterus was needed in 9 (2.9%) of the patients. This is similar to that achieved by Belachew*et al*.[17] Only 7 (2.3%) patients required blood transfusion for their procedure related loss. This further highlights the safety of procedure.

Misoprostol is being used for inducing labour in term pregnancies as well as in preterm terminations. For the former case, small doses of drug were administered as 25µg 6 hourly by Nwachuko *et al.* and by Alfirivic *et al.* without any documented uterine scar rupture.[18,19] The latest data from Sweden reveals that the incidence of uterine rupture with misoprostol with previous one caesarean in term pregnancy is 2%.[20] In patients with mid-trimester terminations, high doses of misoprostol were used without any absolute increase in uterine scar

rupture.[15] In our study scar ruptured in 2 patients i.e., 0.6% which is less 0.8% reported in meta-analysis by Andrikopoulou *et al*.[21] It is same as that reported by Berghella *et al*.[22] Both of these patients were having two CS. One of these was at 24th week of pregnancy with hydrocephalic foetus. Scar ruptured 26 hours after induction of labour. The second patient was with PPROM at 28th week of pregnancy and rupture took place 18 hours after induction. Both uteri were repaired successfully. Our success rate was tarnished by refusals of 4(1.3%) patients after 24 hours of induction. After suitable counselling, all of them were delivered by abdominal route.

In the study, 5 (1.6%) patients were found to be nonresponsive after 48 hours, two patients had two CS while three had previous three CS. Incidentally, none of these patients had ever delivered vaginally and had to be evacuated by CS.

Conclusion

This study proved the efficacy and safety of properly chosen dose of misoprostol and the oral route of administration. It has proved to be valuable for use in a society with large family size, poor economy and high rate of CS, as vaginal birth was accomplished in 96.3% of the patients and scar rupture took place only in 0.6% of the patients. However, there are some grey areas in its use, the most important of which is the unavailability of the exact dose regimens with previous CS. In the authors' opinion, misoprostol with previous CS should be administered via oral route with lower and less frequent dosing. This would translate into less complication coupled with a higher success rate.

References

1. Betrán AP, Ye J, Moller AB, Zhang J, Gülmezoglu AM, Torloni MR. The increasing trend in caesarean section rates: global, regional and national estimates: 1990-2014. PloSOne. 2016 ;11(2):e0148343.
2. Cavallaro FL, Cresswell JA, França GV, Victora CG, Barros AJ, Ronsmans C. Trends in caesarean delivery by country and wealth quintile: cross-sectional surveys in southern Asia and sub-Saharan Africa. Bulletin of the World Health Organization. 2013;91:914-22D.
3. Timofeev J, Reddy UM, Huang CC, Driggers RW, Landy HJ, Laughon SK. Obstetric complications, neonatal morbidity, and indications for cesarean delivery by maternal age. Obstetrics and Gynecology. 2013 ;122(6):1184.
4. Vogel JP, West HM, Dowswell T. Titrated oral misoprostol for augmenting labour to improve maternal and neonatal outcomes. Cochrane Database of Systematic Reviews. 2013(9).Available fromdoi/10.1002/14651858.CD010648.
5. Nwachuku V, Sison A, Quashie C, Chau A, Yeh SY. Safety of misoprostol as a cervical ripening agent in vaginal birth after cesarean delivery. Obstetrics &Gynecology. 2001;97(4):S67.
6. Voigt F, Goecke TW, Najjari L, Pecks U, Maass N, Rath W. Off-label use of misoprostol for labor induction in Germany: a national survey. European Journal of Obstetrics &Gynecology and Reproductive Biology. 2015 Apr 1;187:85-89.
7. Royal College of Obstetricians & Gynaecologists. Birth after previous caesarean birth. Green-top Guideline No. 45. 2015.
8. Misoprostol-Only Recommended Regimens 2017 [Internet]. FIGO. 2017. https://www.figo.org/sites/default/files/uploads/project-publications/Miso/FIGO_Dosage_Chart EN_0.pdf
9. Morris JL, Winikoff B, Dabash R, Weeks A, Faundes A, Gemzell-Danielsson K, et al. FIGO's updated recommendations for misoprostol used alone in gynecology and obstetrics. International Journal of Gynecology& Obstetrics. 2017 ;138(3):363-366.
10. Bhattacharjee N, Ganguly RP, Saha SP. Misoprostol for termination of mid-trimester post-Caesarean pregnancy. Australian and New Zealand Journal of Obstetrics and Gynaecology. 2007;47(1):23-25.
11. Ouerdiane N, Othmani K, Daaloul W, Ben SH, Bouguerra B. Efficacy of misoprostol for medical termination of pregnancy in second trimester: prospective study. La TunisieMedicale. 2015 ;93(4):212-216.
12. Chamsi AT, Morsy E, Rifaei RE, Bahyan RA. The Safety of Misoprostol for Medical Termination of Pregnancy in First and Second Trimester in Women with Previous Uterine Scar [Internet]. Insights in Reproductive Medicine. iMedPub; 2018 http://www.imedpub.com/articles/the-safety-of-misoprostol-for-medical-termination-of-pregnancy-in-first-and-second-trimester-in-women-with-previous-uterine-scar.php?aid=21837
13. Alfirevic Z, Weeks A. Oral misoprostol for induction of labour. Cochrane Database of Systematic Reviews. 2006(2). Available from doi/10.1002/14651858.CD001338.
14. Fawzy M, Abdel-Hady ES. Midtrimester abortion using vaginal misoprostol for women with three or more prior cesarean deliveries. International Journal of Gynecology& Obstetrics. 2010;110(1):50-52.
15. Naguib AH, Morsi HM, Borg TF, Fayed ST, Hemeda HM. Vaginal misoprostol for second-trimester pregnancy termination after one previous cesarean delivery. International Journal of Gynecology& Obstetrics. 2010;108(1):48-51.
16. Naz S, Sultana N. Role of misoprostol for therapeutic termination of pregnancy from 10-28 weeks of gestation. J Pak Med Assoc. 2007 ;57(3):129-131.
17. Belachew J, Eurenius K, Mulic-Lutvica A, Axelsson O. Placental location, postpartum hemorrhage and retained placenta in women with a previous cesarean section delivery: a prospective cohort study. Ups J Med Sci.. 2017;122(3):18515-18519.
18. Nwachuku V, Sison A, Quashie C, Chau A, Yeh SY. Safety of misoprostol as a cervical ripening agent in vaginal birth after cesarean section. Primary Care Update for Ob/Gyns. 2001 ;8(6):244-247.

19. Alfirevic Z, Aflaifel N, Weeks A. Oral misoprostol for induction of labour [Internet]. Oral misoprostol for induction of labour. 2014. https://www.cochrane.org/CD001338/PREG_oral-misoprostol-induction-labour
20. Wallstrom T, Bjorklund J, Frykman J, Jarnbert-Pettersson H, Akerud H, Darj E, et al. Induction of labor after one previous Cesarean section in women with an unfavorable cervix: A retrospective cohort study. PloSOne. 2018;13(7):e0200024.
21. Andrikopoulou M, Lavery JA, Ananth CV, Vintzileos AM. Cervical ripening agents in the second trimester of pregnancy in women with a scarred uterus: a systematic review and metaanalysis of observational studies. Am J Obstet Gynecol.. 2016;215(2):177-194.
22. Berghella V, Airoldi J, O'Neill AM, Einhorn K, Hoffman M. Misoprostol for second trimester pregnancy termination in women with prior caesarean: a systematic review. BJOG: An International Journal of Obstetrics & Gynaecology. 2009 Aug 1;116(9):1151-1157.