Use Of Mifepristone To Reduce The Induction Abortion Time In Patients With First and Second Trimester Terminations: An Observational Study

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Abstract: In the developing countries unsafe abortions form a major factor for increased maternal morbidity and mortality. The use of medications like prostaglandin derivatives one of them beingmisoprostol can help in reducing these catastrophic events. The addition of mifepristone prior to misoprostol has been seen to be effective for reduction in induction abortion time. We conducted a studyto investigate the effect of mifepristone before administration of the prostaglandin derivative on induction abortion time. Method:This study was conducted in 1016 patients from April 2012 till March 2016. The patients were randomised into two groups with combination or study group "A" comprising of 512 patients and control group using misoprostol alone having 504 patients. Results: The age of the patients ranged from 21 to 46 years. Majority of the patients were in age group 21 to 30 (n=660, 64.9%). Most of the patients were primigravida (n= 459, 45.17%). The combination grouphad a shorter interval time between the induction and expulsion of the products to the tune of 14.95± 10.95 hours. On the other hand the patients in misoprostol only group (n=504) had an induction expulsion time of 24.4±20.6 hours. This difference in the expulsion time was statistically significant with p value of <.001. There was no mortality or major morbidity in the two groups.Conclusions: We were able to document that mifepristone followed by misoprostol 24 hours later led to the most rapid abortions as compared to use of a single drug. The safety profile of the drug combination was same as the single drug. We strongly recommend combination of mifepristone and misoprostol to reduce the abortion time which can help quicker discharge of the patient from the hospital and reduce the congestion in our wards. [Anjum M NJIRM 2017; 8(1): 17-20]

Key Words: mifepristone, misoprostol, induction-expulsion time

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Introduction: One the most important events in a woman's life is the course of childbearing. It is the desire of almost every female to be a mother. Unfortunately nature does not allow all pregnancies to bear a fruitful end, i.e birth of a normal and healthy baby. As per the statistics, it is estimated that every female who enters the fertile period will have one abortion till she attains menopause[1].

Women may have to undergo a termination of pregnancy in first or second trimester due to various reasons. The causes can be an anembryonic pregnancy, a missed abortion, an abnormality in the development of the fetus or a termination may be required in the interest of maternal wellbeing.

Surgical evacuation and medical methods have long been the treatment of choice for termination of such pregnancies. In the underdeveloped nations untrained "dias" perform abortions leading to an increased rate of complications[2],. As per the World Health Organisation report 13% of all maternal deaths are related to abortions[1]. The medical management for performing terminations using drugs has been the answer for these situations.

Management of cases requiring termination by prostaglandin formulations like misoprostol, gemeprost and dinoprostone, have been credited with excellent results. However it requires a considerable time for these medications to produce the desired results ranging sometimes even more than 24 hours. This induction expulsion time can be reduced by adding an antiprogestrone derivative mifepristone, before the prostaglandin. Mifepristone because of its anti-progestogenic effect as a competitive inhibitor of the progesterone receptors, causes reduction in the uterine contraction threshold and promotes cervical ripening. The combination of mifepristone and misoprostol gives excellent results even in advanced weeks of pregnancy.

In this situation a study was conducted by our department to assess the effect on induction expulsion time in patients using a combination of mifepristone and misoprostol requiring termination of pregnancy due to any reason.

Methods: This observational study was conducted in the department of obstetrics and gynaecology, SKIMS Medical College, Srinagar. The admitted patients who required termination of pregnancy due to any reason

in first and second trimester (8 weeks to 24 weeks) formed the basis of this study. The patients who had known allergy/intolerance to these drugs, anaemia, patients in process of expulsion, suspected ectopic pregnancy, and patients with complete or partial placenta praevia, coagulopathy and cardiac disease were excluded from the study. Only those patients who agreed to be a part of study after proper informed consent were included in the study.

This study was conducted from April 2012 till March 2016 on 1016 patients. The patients were properly examined and required investigations were conducted as per the protocol of the department. The patients were divided into two groups using a randomisation table.

In the study group "A" the patients were advised to take a single dose of mifepristone 200 mg orally at home. The patient was advised to report to hospital next day. This was followed 24 hours later by misoprostol 600 mg soaked in saline instilled per vaginumevery four hours in the posterior fornix depending upon the progress of the patient.

In the control group "B" the patients were given misoprostol 600 mg per vaginum every four hours as per the response, in the ward.

Both the groups were observed in the ward for the progress of expulsion of products of conception. The patients were allowed oral sips only and if suffering from nausea/vomiting an IV infusion of 5 % dextrose was started. The patients were clinically assessed by way of pulse and blood pressure. Excessive vaginal bleeding or any other untoward effect was noted and managed accordingly. Pain due to uterine contractions was managed by antispasmodics. The expulsion of products of pregnancy including placenta was assessed by per vaginal examination initially. An Ultrasound scan was performed 8 to 10 hours later for confirmation of complete expulsion. The induction expulsion time in each of the patients was noted in both groups.

The patient's haemoglobin was rechecked and if less, iron infusion or blood transfusion was started depending on the severity of anaemia. Injection anti D was given to Rh negative patients. The patients were discharged from the hospital and asked to report back if they experienced excessive pain, bleeding or fever. A follow up examination of these patients was performed in the outpatient department after one week.

Results: This observational study was conducted in Sheri Kashmir Institute of medical sciences Medical College, Bemina, Srinagar, Deptt of obstetrics and gynaecology from April 2012 t0 March 2016. A total of 1016 patientswho required termination of pregnancy due to any reason in first and second trimester (8 weeks to 24 weeks) formed the basis of this study.
The age of the patients ranged from 21 to 46 years. Majority of the patients were in age group 21 to 30(n=660, 64.9%). 310 (30.51%) patients were in the age group 31 to 40 years and 46 (4.56.%) were beyond 41 years. Majority of the patients were primigravida (n= 459, 45.17%) with second gravida 222 (21.8%) and third gravida and more accounting for 335 patients.

It was noted that patients in the combination group 512 had a shorter interval time between the induction and expulsion of the products to the tune of 14.95 hours with range of 10.95 hours on either side. On the other hand the patients in misoprostolgroup(n=504) had an induction expulsion time of 24.4±20.6 hours.This difference in the expulsion time was statistically significant with pvalue of <.001.There was no mortality or major morbidity in the two groups.

Discussion: In the modern era of obstetric sciences, there is always an endeavour to manage patients on fast track basis. However this management should always be done with special emphasis on the safety of the patient.

This study was conducted in our department with an aim to see whether addition of oral mifepristone taken at home before the misoprostol can reduce the overall induction expulsion time in patients requiring medical termination of pregnancy.

Most of our patients were in the age group of 21-30 years. This is evident from the fact that majority of our population is married early especially from the rural areas of our state. The primi-gravidas formed the major chunk of our study population.

On statistical analysis between the two groups we found out that the combination group had a reduced induction expulsion time by around 10 hours as

compared to misoprostol group. This was statistically quite significant. Mifepristone because of its anti-progestogenic effect as a competitive inhibitor of the progesterone receptorscauses, reduction in the uterine contraction threshold and promotes cervical ripening. This results in earlier expulsion of the products of pregnancy. The early expulsion helped us to discharge the patient usually within 24 hours. The direct effect of this was transmitted to the decongestion of the hospital beds and better patient satisfaction. There was no difference noted in the postoperative events in the two groups.

This reduction in induction expulsion time has been noted by other authors in published medical literature. Jannet D et al. showed that induction times were significantly shorter in multipara when using a drug regimen similar to our study in 106 terminations[4]. Hoopmann M et al. in their study concluded that the combination of mifepristone and misoprostol significantly decreased the induction expulsion time by over 10 hours[5].

The combination of mifepristone and misoprostol has been licensed in France since 1988[6]. The superiority of this combination over regimens which use dinoprostone or gemeprost had been confirmed in several studies, some of them randomised[7,8]. In a Cochrane analysis, even though the use of misoprostol as a single abortifacient agent was confirmed to be an effective method; however its combination with mifepristone appeared to significantly increase its effectiveness[9]. The vaginal administration of misoprostol at four-hourly intervals appears to be the most effective option with an acceptable side effect profile. The most frequently described side effect in this study was transient diarrhoea. Regarding the time interval between administration of mifepristone and misoprostol, a recent meta-analysis showed only moderate differences: the induction interval between the initial dose of misoprostol and delivery was only 1–2 hours shorter when mifepristone was used 12–24 hours before compared to a 36–48 hours interval[10]. Therefore, in a clinical setting the prior use of mifepristone preceding the prostaglandin administration appears to be most favourable, as the total duration of the abortion is effectively reduced and the variance of the possible abortion duration is limited to the greatest extent[11,12].

Conclusions: In this study, we were able to document that mifepristone followed by misoprostol 24 hours later led to the most rapid abortions as compared to use of a single drug. The safety profile of the drug combination was same as the single drug. We strongly recommend combination of mifepristone and misoprostol to reduce the abortion time which can help quicker discharge of the patient and reduce the congestion in our wards. This can reduce the mortality associated with unsafe abortions especially in underdeveloped and developing nations.

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