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THE STUDY OF SUBLINGUAL, ORAL AND VAGINAL ADMINISTRATION OF MISOPROSTOL IN REGRESSION OF SYMPTOMS OF MISSED ABORTION

Gynaecology

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ABSTRACT

Background: Misoprostol is a widely popularly used drug in treatment of missed abortions. It is very simple to use, easily available and has an average efficiency greater than 90%. A drug this popular and versatile needs better study to improve its efficiency and minimize all possible adverse unwanted effects. Hence the idea to make a comparative study between the different modes of administration of Misoprostol was arrived upon so as to understand it in a much better way. **Aim:** A comparison of the efficacy of Misoprostol used in sublingual, oral and vaginal routes for missed abortion. **Material and methods:** The study was conducted at the Department of Obstetrics and Gynaecology in Nilratan Sircar Medical College and Hospital, Kolkata after approval by the ethical committee. The sample size was 100 women being treated for missed abortions where prospective sampling was carried out to determine the candidates to be selected for the study. Single centred, institution based, randomized controlled trial. Cases included in this study were divided into 3 groups: Sublingual Group, Oral Group and Vaginal Group. **Result:** It was found that in oral, 4(11.8%) patients had fever. In sublingual, 6(17.6%) patients had fever. In vaginal, 2(5.9%) patients had fever. Association of fever vs. group was not statistically significant (p=0.3220). **Conclusion:** The study demonstrates that both vaginal and sublingual misoprostol have similar and higher success rates in inducing abortion compared to oral route.

KEYWORDS

Missed abortions, Misoprostol, Sublingual, Vaginal

INTRODUCTION

Abortion is defined as spontaneous or induced termination of pregnancy before age of viability. WHO define abortion as pregnancy termination prior to 20 weeks of gestation or with a fetus born weighing less than 500 gms.[1]Safe and legal abortion has played an important role for improving women health and quality of life. A 2014 systematic analysis of worldwide data estimates that approximately 8% of all maternal deaths are attributable to unsafe abortion and related complications. Spontaneous abortion occurs in nearly 20% of confirmed pregnancy.[2] Out of these 80% occurs in first trimester. Second trimester abortions constitute 10-15% of induced abortions. Second trimester abortion contributes to 2/3rd of major abortion related complications. Vacuum aspiration is the conventional method of evacuation of uterus and is associated with 4-10% of complications like bleeding, infection, uterine perforation and decreased fertility.[3] Since 1971, abortion has been legalised in our country. Historically, it has been noticed that there is significant shortage of facilities approved for abortion provision in India, and distribution of these facilities have been uneven across the states. Despite the increase in the number of approved facilities over the years from 1,877 in 1976 to 9,859 in 2002 to 12,510 in 2010 access to safe abortion remains inadequate, especially in rural areas. Provisional government figures estimate that 621,748 abortions were performed in 2011-2012, and the number increased slightly to 636,306 in 2012-2013, indicating an annual rate of about two abortions per 1,000 women aged 15-49 in 2013. In India, elective termination of pregnancy is a commonly performed gynaecological procedure.[4] Medical methods like prostaglandin E1 analoguemisoprostol is commonly used along with Mifepristone up to second trimester abortions. Mifepristone acts by inhibiting the effect of progesterone by binding to the progesterone receptor. Thus, in early pregnancy, mifepristone administration results in regular uterine contractility and increased sensitivity of prostaglandins. Misoprostol acts as a cervical ripening and uterotonic agent.[5] It is widely used for termination of pregnancy and combined with mifepristone for medical abortion. It is inexpensive and stable at room temperature. Surgical procedure is associated with faster results, but it can lead to more complications like cervical incompetence, uterine synechiae and uterine perforations. So, nowadays medical method is the treatment of choice for medical termination of pregnancy. Different doses and routes of administration of misoprostol in both first and second trimester have been investigated and results are compared, but optimal doseand route have not been properly identified. Due to its rapid absorption, sublingual route reaches its peak concentration in a short time and has the highest bioavailability.[6] Vaginal route causes prolonged regular uterine contractions and has fewer side effects after administration. So, the present study is done to compare the efficacy of sublingual and vaginal misoprostol for medical abortion up to 20 weeks of gestation.[7]

OBJECTIVE OF RESEARCH

Thus the aims of the study are as follows:

PRIMARY

1. A comparison of the efficacy of Misoprostol used in sublingual, oral and vaginal routes for missed abortion.

SECONDARY

1. Comparison of dose and time interval of drug administration to onset of action of three different routes.

2.Comparison of complications, if any, encountered during the abortion process of three different routes.

MATERIALS& METHODS

1. Study design

Single centred, institution based, randomized controlled trial.
Cases included in this study was be divided into 3 groups:

Sublingual Group: 100 mcg of Tab Misoprostol (1/2 tablet) was administered to group 1 cases sublingually and will be repeated every 4 hourly for 4 doses.

Oral Group: 100 mcg of Tab Misoprostol (1/2 tablet) was administered to group 2 orally and that was repeated every 4 hourly for 4 doses.

Vaginal Group: 100 mcg of Tab Misoprostol (1/2 tablet) was administered to this group 3 in the posterior fornix of vagina and was repeated every 4 hourly for 4 doses .

Place of study

The study was conducted at the Department of Obstetrics and Gynaecology in Nilratan Sircar Medical College and Hospital, Kolkata after approval by the ethical committee.

4. Period of study

The study would span over a year (from 01/06/2018 to 31/05/2019)

5. Study population

The study population would comprise of patients being treated for missed abortion in Nilratan Sircar Medical College and Hospital, Kolkata by administration of Misoprostol.

Sample size and design

The sample size was 100 women being treated for missed abortions

where prospective sampling was carried out to determine the candidates to be selected for the study.

7. Inclusion and exclusion criteria

The candidates satisfying the below conditions would be included in the study group:

- Diagnosed case of pregnancy loss either by ultrasound or by subnormally rising quantitative hcglevel(Serum hcg estimation may be deferred in patients with financial constraints who will follow up at a clinical site with ultrasound, if the initial diagnosis was confirmed by ultrasound)
- Woman want to expedite expulsion of product of conception without surgery
- Woman who have no contraindication like infection, haemorrhage, severe anaemia, bleeding diatheses, allergy to Prostaglandins
- Woman having easy accessibility to nearest health facility
- Woman willing to come for desired follow up
- Medical treatment for missed abortion would not be considered in candidates without the following contraindications:
- Known allergy to Misoprostol.
- Previouscaesarean section

RESULT AND ANALYSIS

Our study showed that in oral, 11(32.4%) patients had ≤20 years of age, 18(52.9%) patients had 21-25 years of age, 4(11.8%) patients had 26-30 years of age and 1(2.9%) patient had 31-36 years of age.In sublingual, 6(17.6%) patients had ≤20 years of age, 16(47.1%) patients had 21-25 years of age, 8(23.5%) patients had 26-30 years of age and 4(11.8%) patients had 31-36 years of age.In vaginal, 10(29.4%) patients had ≤20 years of age, 14(41.2%) patients had 21-25 years of age, 7(20.6%) patients had 26-30 years of age and 3(8.8%) patients had 31-36 years of age.Association of age in years vs. group was not statistically significant (p=0.5217). In oral,24(70.6%) patients had 0 parity, 9(26.5%) patients had 1 parity and 1(2.9%) patients had 2 parity.In sublingual,20(58.8%) patients had 0 parity, 12(35.3%) patients had 1 parity and 2(5.9%) patients had 2 parity.In vaginal,26(76.5%) patients had 0 parity, 7(20.6%) patients had 1 parity and 1(2.9%) patient had 2 parity.Association of parity vs. group was not statistically significant (p=0.6167).

We found that in oral, 4(11.8%) patients had fever. In sublingual, 6(17.6%) patients had fever. In vaginal, 2(5.9%) patients had fever. Association of fever vs. group was not statistically significant (p=0.3220). In oral, 16(47.1%) patients had nausea. In sublingual, 8(23.5%) patients had nausea. In vaginal, 34(100.0%) patients had no nausea. Association of nausea vs. group was statistically significant (p<0.001). In oral, 9(26.5%) patients had vomiting. In sublingual, 4(11.8%) patients had vomiting. In vaginal, 34(100.0%) patients had no vomiting. Association of vomiting vs. group was statistically significant (p=0.0046). In oral, 20(58.8%) patients had abdominal pain. In sublingual, 21(61.8%) patients had abdominal pain. In vaginal, 14(41.2%) patients had abdominal pain. Association of abdominal pain vs. group was not statistically significant (p=0.1833). In oral,27(79.4%) patients had vaginal bleeding.In sublingual, 30(88.2%) patients had vaginal bleeding. In vaginal,29(85.3%) patients had vaginal bleeding.Association of vaginal bleedingvs. group was not statistically significant (p=0.5952). In oral, 7(20.6%) patients had diarrhoea. In sublingual, 6(17.6%) patients had diarrhoea. In vaginal, 2(5.9%) patients had diarrhoea. Association of diarrhoea vs. group was not statistically significant (p=0.1937).

It was found that, in oral,34(100.0%) patients had no taste. In sublingual,22(64.7%) patients had unpleasant taste. In vaginal,34(100.0%) patients had no taste. Association of taste vs. group was statistically significant (p<0.001). In oral, 4(11.8%) patients had fever. In sublingual, 6(17.6%) patients had fever. In vaginal, 2(5.9%) patients had fever. Association of fever vs. group was not statistically significant (p=0.3220). In oral, 16(47.1%) patients had nausea. In sublingual, 8(23.5%) patients had nausea. In vaginal, 34(100.0%) patients had no nausea. Association of nausea vs. group was statistically significant (p<0.001). In oral, 9(26.5%) patients had vomiting. In sublingual, 4(11.8%) patients had vomiting. In vaginal, 34(100.0%) patients had no vomiting. Association of vomiting vs. group was statistically significant (p=0.0046).

We also found that in oral, 20(58.8%) patients had abdominal pain. In sublingual, 21(61.8%) patients had abdominal pain. In vaginal, 14(41.2%) patients had abdominal pain. Association of abdominal pain vs. group was not statistically significant (p=0.1833). In oral,27(79.4%) patients had vaginal bleeding.In sublingual,30(88.2%) patients had vaginal bleeding.In vaginal,29(85.3%) patients had vaginal bleeding.Association of vaginal bleedingvs. group was not statistically significant (p=0.5952). In oral, 7(20.6%) patients had diarrhoea. In sublingual, 6(17.6%) patients had diarrhoea. In vaginal, 2(5.9%) patients had diarrhoea. Association of diarrhoea vs. group was not statistically significant (p=0.1937).

In oral, 6(17.6%) patients had tachycardia. In sublingual, 8(23.5%) patients had tachycardia. In vaginal, 10(29.4%) patients had tachycardia. Association of tachycardia vs. group was not statistically significant (p=0.5200). In oral, 8(23.5%) patients had incomplete abortion.In sublingual, 5(14.7%) patients had incomplete abortion.In vaginal, 6(17.6%) patients had incomplete abortion.Association of incomplete abortion vs. group was not statistically significant (p=0.6359). In oral, 1(2.9%) patient had failure.In sublingual, 34(100.0%) patients had no failure.In vaginal, 34(100.0%) patients had no failure.Association of failure vs. group was not statistically significant (p=0.3643). In oral,the mean age (mean±s.d.) of patients was 22.1471 ± 3.4565 years. In sublingual,the mean age (mean±s.d.) of patients was 24.5294 ± 4.3291 years. In vaginal,the mean age (mean±s.d.) of patients was 23.9118 ± 4.6799 years. Distribution of mean age vs. group was not statistically significant (p=0.0562).

It was observed that, in oral,27(79.4%) patients had 0 living issue, 6(17.6%) patients had 1 living issue and 1(2.9%) patient had 2 living issues. In sublingual,20(58.8%) patients had 0 living issue, 13(38.2%) patients had 1 living issue and 1(2.9%) patient had 2 living issues. In vaginal,26(76.5%) patients had 0 living issue, 7(20.6%) patients had 1 living issue and 1(2.9%) patient had 2 living issues. Association of living issue vs. group was not statistically significant (p=0.3442). In oral,34(100.0%) patients had no taste. In sublingual,22(64.7%) patients had unpleasant taste. In vaginal,34(100.0%) patients had no taste. Association of taste vs. group was statistically significant (p<0.001).

Our study showed that, in oral, 4(11.8%) patients had fever. In sublingual, 6(17.6%) patients had fever. In vaginal, 2(5.9%) patients had fever. Association of fever vs. group was not statistically significant (p=0.3220). In oral, 16(47.1%) patients had nausea. In sublingual, 8(23.5%) patients had nausea. In vaginal, 34(100.0%) patients had no nausea. Association of nausea vs. group was statistically significant (p<0.001). In oral, 9(26.5%) patients had vomiting. In sublingual, 4(11.8%) patients had vomiting. In vaginal, 34(100.0%) patients had no vomiting. Association of vomiting vs. group was statistically significant (p=0.0046). In oral, 20(58.8%) patients had abdominal pain. In sublingual, 21(61.8%) patients had abdominal pain. In vaginal, 14(41.2%) patients had abdominal pain. Association of abdominal pain vs. group was not statistically significant (p=0.1833).

It was found that, In oral,27(79.4%) patients had vaginal bleeding.In sublingual,30(88.2%) patients had vaginal bleeding.In vaginal,29(85.3%) patients had vaginal bleeding. Association of vaginal bleedingvs. group was not statistically significant (p=0.5952). In oral, 7(20.6%) patients had diarrhoea. In sublingual, 6(17.6%) patients had diarrhoea. In vaginal, 2(5.9%) patients had diarrhoea. Association of diarrhoea vs. group was not statistically significant (p=0.1937). In oral, 6(17.6%) patients had tachycardia. In sublingual, 8(23.5%) patients had tachycardia. In vaginal, 10(29.4%) patients had tachycardia. Association of tachycardia vs. group was not statistically significant (p=0.5200).

Our study showed that, In oral,the mean age (mean±s.d.) of patients was 22.1471 ± 3.4565 years. In sublingual,the mean age (mean±s.d.) of patients was 24.5294 ± 4.3291 years. In vaginal,the mean age (mean±s.d.) of patients was 23.9118 ± 4.6799 years. Distribution of mean age vs. group was not statistically significant (p=0.0562). In oral,the mean gestation (mean±s.d.) of patients was 10.3735 ± 2.3527 weeks. In sublingual,the mean gestation (mean±s.d.) of patients was 9.4912 ± 1.9215 weeks. In vaginal,the mean gestation (mean±s.d.) of patients was 9.6059 ± 1.9506 weeks. Distribution of mean gestation vs. group was not statistically significant (p=0.1704). In oral,the mean BMI (mean±s.d.) of patients was 22.1176 ± 2.0213kg/m2. In sublingual,the mean BMI (mean±s.d.) of patients was 22.0324 ± 2.4242kg/m2. In vaginal,the mean BMI (mean±s.d.) of patients was

21.9035 ± 2.4070 kg/m2. Distribution of mean BMI vs. group was not statistically significant (p=0.9276).

We found that in oral, the mean Body surface area in metre 2 (mean±s.d.) of patients was 1.6838 ± .0335.In sublingual, the mean Body surface area in metre 2 (mean±s.d.) of patients was 1.6844 ± .0341.In vaginal, the mean Body surface area in metre 2 (mean±s.d.) of patients was 1.6871 ± .0279.Distribution of mean Body surface area in metre 2 vs. group was not statistically significant (p=0.9060). In oral, the mean amenorrhoea (mean±s.d.) of the patients was 66.7059 ± 13.2631 days.In sublingual, the mean amenorrhoea (mean±s.d.) of patients was 67.3235 ± 12.3085 days.In vaginal, the mean amenorrhoea (mean±s.d.) of patients was 64.4412 ± 12.7545 days.Distribution of mean amenorrhoea vs. group was not statistically significant (p=0.6206). In oral, the mean regression of symptoms of pregnancy (mean±s.d.) of the patients was 10.8529 ± 1.5980 days.In sublingual, the mean regression of symptoms of pregnancy (mean±s.d.) of patients was 7.0294 ± .9996 days.In vaginal, the mean regression of symptoms of pregnancy (mean±s.d.) of patients was 8.8529 ± 1.2585 days. Distribution of mean regression of symptoms of pregnancy vs. group was statistically significant (p<0.001).

DISCUSSION

Ayswarya Shanmugam et al[8] (2016) found that the maternal age distribution, parity and gestational age in the two groups were found to be comparable. Requirement of mean dose of misoprostol in sublingual and vaginal were 1300 mcg, 1253 mcg respectively.

We found that in oral, 11(32.4%) patients had ≤20 years of age, 18(52.9%) patients had 21-25 years of age, 4(11.8%) patients had 26-30 years of age and 1(2.9%) patient had 31-36 years of age. In sublingual, 6(17.6%) patients had ≤20 years of age, 16(47.1%) patients had 21-25 years of age, 8(23.5%) patients had 26-30 years of age and 4(11.8%) patients had 31-36 years of age.In vaginal, 10(29.4%) patients had ≤20 years of age, 14(41.2%) patients had 21-25 years of age, 7(20.6%) patients had 26-30 years of age and 3(8.8%) patients had 31-36 years of age. Association of age in years vs. group was not statistically significant (p=0.5217). Association of parity vs. group was not statistically significant (p=0.6167).

Hassan FI et al [9] (2007) found that the low incidence of side-effects especially vomiting diarrhoea and bleeding misoprostol whether by oral or rectal route seems to be an effective as a non invasive method for evacuation of the uterus in women with retained products of conception.

Diop A et al [10] (2009) found that 400 mcg sublingual misoprostol and 600mcg oral misoprostol. Mean pain scores were2.95 and 3.04, respectively, for the oral and sublingual groups. Side effects included abdominal pain, bleeding, headaches and dizziness/weakness with no differences reported between the two groups. Acceptability and satisfaction were high for both routes and women indicateda preference for medical versus surgical treatment if ever needed in the future.

It was found that in oral, 4(11.8%) patients had fever. In sublingual, 6(17.6%) patients had fever. In vaginal, 2(5.9%) patients had fever. Association of fever vs. group was not statistically significant (p=0.3220). We found that in oral, 27(79.4%) patients had vaginal bleeding. In sublingual, 30(88.2%) patients had vaginal bleeding. In vaginal, 29(85.3%) patients had vaginal bleeding. Association of vaginal bleeding vs. group was not statistically significant (p=0.5952).

Parveen S et al [11] (2011) found that the intra-operative pain score of the S/L group was significantly lower (1.9±1.1, *P*<0.05) as compared to the vaginal (2.6±1.7) or oral route (3.3±1.7). Loose motions and nausea/vomiting were more with the S/L and oral routes while blood loss was more in the vaginal route. Administration of misoprostol by the sublingual route is better than the oral and vaginal routes for cervical ripening.

We found that in oral, 16(47.1%) patients had nausea. In sublingual, 8(23.5%) patients had nausea. In vaginal, 34(100.0%) patients had no nausea. Association of nausea vs. group was statistically significant (p<0.001). In oral, 9(26.5%) patients had vomiting. In sublingual, 4(11.8%) patients had vomiting. In vaginal, 34(100.0%) patients had no vomiting. Association of vomiting vs. group was statistically significant (p=0.0046).

CONCLUSION

In Sublingual misoprostol unpleasant taste was more common. Side effects, such as Fever, Abdominal Pain, Vaginal Bleeding , Diarrhoea , Tachycardia as not statistically significant in three groups but vomiting was significantly higher in oral compared to others. Incomplete abortion was higher in oral, followed by Vaginal and Sublingual misoprostol. Success rate was higher in Sublingual compared to Vaginal and Oral.

Oral and sublingual routes of administration have shown to be more acceptable compared to vaginal route of administration. But the efficacy of oral administration is less. Therefore, sublingual misoprostol has the advantage that it can avoid the uncomfortable vaginal administration. Also absorption of the drug may be affected when the patient starts bleeding.

The study demonstrates that both vaginal and sublingual misoprostol have similar and higher success rates in inducing abortion compared to oral route.

Table: Distribution of mean Age, Gestation (wk), BMI, Amenorrhoea in days, Regression of symptoms of pregnancy in Days vs Group

		Number	Mean	SD	Minimum	Maximum	Median	p-value
Age (yrs)	Oral	34	22.1471	3.4565	18.0000	32.0000	21.0000	0.0562
	Sublingual	34	24.5294	4.3291	18.0000	34.0000	24.0000	
	Vaginal	34	23.9118	4.6799	18.0000	36.0000	24.0000	
Gestation (wk)	Oral	34	10.3735	2.3527	6.0000	14.2000	10.2000	0.1704
	Sublingual	34	9.4912	1.9215	6.3000	16.0000	9.1000	
	Vaginal	34	9.6059	1.9506	6.3000	15.0000	9.1500	
BMI (Kg/m2)	Oral	34	22.1176	2.0213	18.3000	26.5000	22.0500	0.9276
	Sublingual	34	22.0324	2.4242	17.2000	28.3000	21.9500	
	Vaginal	34	21.9035	2.4070	17.7000	29.0000	21.7000	
Amenorrhoea in days	Oral	34	66.7059	13.2631	42.0000	84.0000	66.5000	0.6206
	Sublingual	34	67.3235	12.3085	49.0000	84.0000	70.0000	
	Vaginal	34	64.4412	12.7545	42.0000	84.0000	63.0000	
Regression of symptoms of pregnancy in Days	Oral	34	10.8529	1.5980	8.0000	13.0000	11.0000	<0.001
	Sublingual	34	7.0294	.9996	5.0000	8.0000	7.0000	
	Vaginal	34	8.8529	1.2585	5.0000	10.0000	9.0000	

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