Comparison Of The Effect of Oral Misoprostol Tablet With Intravenous Oxytocin for Pregnancy Termination In Gynecology Wards Of Academic Hospitals in Mashhad (2003-2004)

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مقایسه اثر قرص میزوپروستول با آمپول اکسی توسین جهت ختم حاملگی (۸۴– ۱۳۸۳)

خلاصه

مقدمه: با توجه به اینکه بسیاری از موارد ختم حاملگی به وسیله اکسی توسین انجام می شود که نیاز به هزینه، مدت زمان زیاد بستری و کنترل دقیق پزشک دارد و همچنین عوارضی مثل مسمومیت با آب در اینداکشنهای طولانی مدت مشاهده می شود جهت جایگزینی برای اکسی توسین از میزوپروستول استفاده شده است. هدف از این مطالعه مقایسه اثرات میزوپروستول و اکسی توسین در ختم حاملگی در سه ماهه دوم باردار می باشد.

روش کار: این مطالعه کارآزمایی در سال ۸٤-۱۳۸۳ در زنان باردار بستری در بخش زنان بیمارستانهای دانشگاه علوم پزشکی مشهد انجام شده است. ۱۲۵ زن باردار که در سه ماهه دوم حاملگی و کاندید ختم حاملگی بودند به صورت تصادفی به دو گروه٤۳ نفر گروه مورد و ۸۲ نفر گروه شاهد تقسیم شدند. جهت ختم حاملگی در گروه مورد ۳ عدد قرص خوراکی میزو پروستول $100\ g^{3}$ و یک عدد قرص واژینال استفاده شد. در صورت عدم انقباض هر ۳ ساعت یک قرص خوراکی و هر ٦-٤ ساعت یک قرص واژینال تجویز شد و این کار تا ٤۸ ساعت ادامه یافت.

در گروه شاهد ختم حاملگی با اکسی توسین تزریقی انجام شد به اینصورت که $50\ I/U^{CC}$ اکسی توسین در ۵۰۰ رینگرلاکتات در عرض۳ ساعت پرفیوز شد و سپس ۱ ساعت استراحت داده شد و بعد به مرور هر ۳ ساعت ۵۰ واحد اکسی توسین در 500^{CC} رینگر لاکتات اضافه شد تا حداکثر به $300^{I/U}$ در۵۰۰ برسد و یا انقباضات بیمار شروع شود. در هردو گروه مورد مطالعه در صورت عدم انقباض پس از ٤۸ ساعت روش دیگری جهت ختم زایمان در نظر گرفته شد. مشخصات فردی، نتایج درمان در پرسشنامه جمع آوری گردید. اطلاعات به دست آمده با استفاده از آمار توصیفی و جداول توزیع فراوانی پردازش شد.

نتایج: در گروه میزو پروستول انقباضات زایمانی و ختم حاملگی در مدت زمان کوتاهتری نسبت به اکسی توسین انجام شد ($P = ۰/۰۰۱$) .احتباس جفت و هزینه مصرفی در گروه مورد کمتر بود . تب ، خونریزی و عوارض گوارشی و پارگی رحم در دو گروه تفاوتی نداشت ($P> ۰/۰۵$).

نتیجه گیری: میزو پروستول زمانی که جهت ختم حاملگی در سه ماهه دوم استفاده می شود نسبت به اکسی توسین در زمان کوتاهتری سبب زایمان خواهد شد و همچنین میزان هزینه ، عوارض جانبی و نیاز به مراقبت های شدید درمصرف میزو پروستول کمتر است، بنابراین جهت ختم حاملگی در سه ماهه دوم میتواند جایگزین مناسبی برای اکسی توسین باشد.

کلمات کلیدی: میزو پروستول، سه ماهه دوم حاملگی، اکسی توسین، ختم حاملگی

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Introduction

Termination of pregnancy in the second trimester maybe caused by several factors such as pre-eclampsia, early rupture of membrane, fetal death. And some maternal diseases and etc.

Termination of pregnancy is the stimulation of uterine contractions before the beginning of normal delivery process.

Pregnancy may be terminated by different methods, including:

Medical, Mechanical and surgical methods.

In our country, prostaglandin usage (alone or accompanied with foley catheter) for the purpose of decreasing oxytocin dosage or promoting delivery induction is not common.

Most of delivery inductions in the second trimester at the academic hospitals in Mashhad are done with oxytocin and also catheter traction or saline infusion via extraamnionic catheter. But these approaches are invasive and accompany side effects such as disseminated intravascular coagulopathy or cardiopulmonary failure. Besides, induction with oxytocin may take a long time and administration of large amounts of drugs causes some risks for the patients such as water toxification. Furthermore, a pre-eclampsia case might be kept in the stressful atmosphere of a maternity ward for hours and even days. Several studies have been done regarding different methods of pregnancy termination in different trimesters. Many of these researches have shown that prostaglandins are able to make the cervix ready for delivery and leads to pregnancy termination with contractions like a normal labor.

Winkler (2001) has shown that PG vaginal suppository and oxytocine induce delivery in 93% and 91% of cases, respectively. Mean delivery duration is 13.1 hours in Prostaglandin group and 8.2 hours in oxytocin group [2]. Diskinson (2001) has reported better therapeutic results and fewer side effects for PG in comparison to oxytocin. He has shown that 400 µgr vaginal PG suppository can induce delivery in 6 hours in pregnancy age of 20 weeks. [3]

Pajak (2001) also showed a rapid pregnancy induction with PG tablet in comparison to Oxytocin and reported less pain in those who get Misoprostol. [4]

According to the studies mentioned above and other contradictory reports we tried to suggest a safe and less expensive method for Pregnancy termination in the second trimester and to compare it with the common method of using oxytocin usage.

Materials and Methods

This is an interventional Case – Control, prospective Study on 16 – 37 year-old, nulipar or multipar pregnant women who were found to need for pregnancy termination and delivery induction in the second trimester of pregnancy.

Our study was done in academic hospitals of Mashhad during 2003 – 2004. There weren't any contraindications for oxytocin or misoprostol usage in these patients, such as previous uterine surgery, genital Herpes infection.

Inclusion criteria were: necessity of pregnancy termination in the second trimester, absence of contraindications for delivery induction, absence of uterine contractions and dilatation or effacement.

Exclusion criteria were: previous uterine scar, uterine contractions, dilatation or effacement, placenta previa, cardiopulmonary diseases and renal dysfunction.

125 cases were divided into 2 groups of case and control. The case group contained 43 patients and control group was consisting of 82 cases. All cases were randomly divided into 2 groups which were almost similar in age, parity, pregnancy age and Bishop Score.

The case group used three l00$^{\mu g}$ oral tablet of misopratol together and one vaginal l00$^{\mu g}$ tablet of misoporstol. If there weren't any uterine contraction, we administered an oral tablet every 3 hours and a vaginal tablet every 4 – 6 hours up to 48 hours or until the uterine contractions began.

We decided to discharge the vaginal tablet if the uterine contractions became hypertonic but we didn't meet such a case in our study. If contractions didn't begin

after 48 hours, we considered them as Misoprostol tolerant cases.

Pregnancy termination was induced by Novac method in 82 patients as the control group. $50^{I/U}$ of oxytocin was diluted with 500^{CC} Ringer and infused in 3 hours, then the patients were given a resting period of l hour. After that we infused $100^{I/U}$ Oxytocin diluted with 500^{CC} Ringer and over a 3 hour period and then provided a resting period of 1 hour. The dosage of oxytocin then was increased gradually in 3 hours to maximum 300 $^{I/U}$ in 500^{CC} Ringer or until the contractions began. Our plan was 3 hours of induction followed by an hour of resting until the beginning of contractions or termination of procedure if there was response in 48 hours.

Data was gathered by questionnaires. the time of active phase contractions initiation was measured duration from the beginning of active phase to the termination of pregnancy, complications such as hemorrhage, fever, diarrhea, hypertonic contractions, drug resistance and no responding uterine were taken into consideration.

Variables were analyzed statistically by SPSS software after description of studies; we analyzed our data by chi square test, T – test and Pearson and spearman correlation coefficient were used to analyze the data.

Results

Our candidates for pregnancy termination in second trimester were between 16 to 37 years old and 66% of them were primigravid or gravid 2, 28% were multigravid 3-4 and others were multigravids with 5 or more previous pregnancies (maximally 7).

Bishop score was zero in 78.4% and 1 in 4% and 2 in 18.4%.

Both case and control groups were almost similar in age, parity, gestational age and cervical status.

In the case group, uterine contractions were detected in 28 patients (66.7%) during the first 5 hours after induction while only 8 patients (21.9%) had uterine contractions in the control group. [Table 1]

Table 1: comparison of induction duration after medication usage in case and control groups in academic hospitals of Mashhad in 2003 – 2004.

Induction duration	< 5 h	5 – 15 h	15 – 24 h	24 – 48 h	Sum
Oxitocin	18cases(21.95%)	50cases(60.97%)	13cases(15.8%)	1case(1.2%)	82cases(100%)
Misoprostol	28cases(65.1%)	13cases(30.23%)	2cases(4.9%)	0	43cases(100%)

Fetus expulsion in the first 5 hours occurred in 14 Misoprostol users (32.55) while only in 7 Oxytocin users (8.53%) [Table 2].

Table 2: Comparison of delivery time after drug usage in case and control groups in academic hospitals of Mashhad in 2003 – 2004

Delivery time	< 5 h	5 – 15 h	15 – 24 h	24 – 48 h	Sum
Oxytocin	7cases(8.53%)	41cases (50%)	27cases (32.92%)	1cases (1.2%)	76cases (92%)
Misoprostol	14cases(32.55%)	20cases (46.51%)	6cases (13.95%)	1cases (2.32%)	41 cases(95.33%)

Table 1 show that uterine contractions began in all 34 cases (100%) during the first day of induction in case group and delivery occurred in 41 cases (95.33%). In the same time contractions began in 81 patients in the control group (98.8%) and in 76 patients (92.68%) labor was induced during the firs 48 hours [table 1 – 2].

Time onset mean of contractions was 4.46 hours in case group and 9.9 hours in control group. Delivery time mean in case group was 9.6 hours and in control group was 14.8 hours.

Maternal complications such as uterine rupture and significant vaginal bleeding which needed blood transfusion were not

reported in any group. More than one minute long contractions with less than one minute intervals (hyper tonic contractions) were reported in one patient in the control group which was relieved by decreasing the oxytocin dosage.

Complications such as nausea, vomiting and diarrhea were not reported after Misoprostol usage in control group but two patients became febrile (37.8^{oc}) which were relieved by fetus expulsion and without any medical intervention.

Placenta retention and need for curettage in misoprostol users was less than oxytocin users (58% against 92 %) ($P < 0.05$).

Mean Costs in the case group who responded to treatment in the first 48 hours was 36729 Rials but it was 75896 Rials in the control group. Medication cost in misoprostol group is lower than oxytocine group whether induction was successful or not ($p<0.05$).

Two Patients in the case group and 6 patients in the control groups underwent hysterectomy because they didn't respond to the medical interventions.

Discussion

High risk patients often are referred to academic centers and some of them might need pregnancy termination in the second trimester because of fetal death, premature rupture of membrane, pregnancy induced hypertension and fetus anomalies.

In such centers in some countries, delivery is induced by oxytocin alone or with catheter traction which needs a long time of induction and is also costly. In other countries prostaglandin usage is common because they have less side effects and more success.

It is almost accepted when the cervix is not prepared for the labor; misoprostol can prepare the cervix and induce uterine contractions and delivery more rapidly.

Effects of misoprostol in pregnancy termination in the second trimester have been studied from 1993 and many articles have mentioned its effects in pregnancy termination. Misoprostol is a PG E_1 which can prepare the cervix for labor and may prevent post delivery bleeding. It may be used oral, transvaginal or transrectal.

The following reports confirm these facts: College of obstetric and gynecology studied more than 1900 cases in term pregnancy by using misoprostol tablets (25 $^{\mu g}$)vaginaly. They showed that misoprostol in term pregnancy reduced oxytocin dose, and time interval between induction of labor, and increased the probability of vaginal delivery.

Nigma (2004) has compared the effects of oxytocin and vaginal misoprostol in pregnancy termination and showed that misoprostol can induce delivery faster than oxytocin [5]. However Culver (2005), etal showed that oxytocin and foley catheter induced labor faster than misoprostol (18 hours compared to 24 hours) [6]. The reason might have been the effects of folely catheter in preparing cervix by stimulating PG release. Oboro (2003) has reported better results for oral and vaginal PG rather than Oxytocin used for pregnancy termination. [7]

Wing, etal (2004) has indicated that $100^{\mu g}$ misoprostol in the patients with ripe cervix (Bishop score of 6 or more) in contrast to oxytocine might cause uterine hyper stimulation which leads to uterine rupture in multiparous [8] but they haven't mentioned pregnancy age of the cases.

In our research, labor in second trimester was induced by PG in 100% of the patients during the first 24 hours and delivery occurred in 95% of them but the rates in the control group (oxytocin users) were 98.8% and 92% respectively.

Mozurkewich (2003) has used oral misoprostol to induce labor in PROM cases and he didn't report any need for cesarean section [15] .In our study also only 2 cases in misoprostol group and 6 cases in the oxytocin group underwent surgery [9].

Pajika (2001) has showed that misoprostol can induce labor faster than oxytocin and has less side effects and pain in misoprostol users [4]. In our study, contractions and fetus expulsion happened sooner in misoprostol users and no side effects were reported in these cases. Also there was less need for revision and surgery in this group [table 3].

Conclusion

According to Previous studies and our study it seems that Misoprostol is a useful medication to prepare the cervix and induce labor in a Bishop score of less than 3 especially in the second trimester of pregnancy when oxytocin receptors are few and Bishop score is low. In this situation, misoprostol acts like a normal labor procedure and prepares the cervix for delivery.

Misoprostol is easy to use, safe, and acts quickly which results in short hospitalization and its success rate in delivery induction is high. Therefore, there won't be much need for surgical intervention.

Finally, its low cost which makes it more acceptable for patients. All of the above make it more suitable for labor induction in second trimester of pregnancy especially in maternity wards which accept high risk patients.

Labor contractions in the first 5 hours were detected in misoprostol group more than oxytocin users and labor was initiated in the first 24 hours in 100% of misaprostol users and 98.8% of oxytocin users ($p < 0.05$)

Fetus expulsion happened earlier in misoprostol users compare to oxytocin users ($P < 0.05$)

Abstract

Introduction: Since most of cases of pregnancy termination are induced by oxytocin of which needs special care, much time, costs, and it has side effects such as water toxicity especially in prolonged inductions trying to find suitable replacement for oxytocin is necessary. The aim of this research is compared on oxytocin with misoprostol in the second trimester of pregnancy gynecology ward of academic hospitals in Mashhad. (Imam Reza – Ghaem – Hazrat Zeinab)

Materials and Methods: In this prospective case – control study, we divided 125 pregnant women in the second trimester to two groups.

Pregnancy termination in the case group was induced by administration 3 $100^{\mu g}$ oral tablets of misoprostol and one vaginal misoprostol tablet.

If there wasn't any uterine contraction we used one oral tablet every 3 hours and a vaginal tablet every 4 –6 hours for 48 hours.

In the control group pregnancy termination was induced by oxytocin. $50^{I/U}$ of oxytocin was diluted with 500^{CC} Ringer and infused in 3 hours then there was a resting period for l hour and then we increase $50^{I/U}$ oxytocin in 500^{CC} Ringer untile maximum $300^{I/U}$ in 500 ^{CC} Ringer. Our plan was 3 hours of induction and an hour resting until beginning of contraction or no responding after 48 hours induction.

Another method of delivery induction was replaced, if no contraction was observed after 48 hours in both groups.

Results: Labor contraction and pregnancy termination happened sooner in the misoprostol group than oxytocin group. ($p = 0.001$)

Placental retention and costs were less in the case group ($p<0.05$). Fever, bleeding, gastrointestinal tract complications and uterine rupture had no difference in both groups. ($p>0.05$)

Conclusion: Misoprastol alone induced delivery sooner when was compared to oxytocin, in the second trimester and it also had less cost and less side effects. Besides it dose not need intensive nurse care. So we recommend misoprostol for pregnancy termination in the second trimester.

Key words: Misoprostol, Second trimester of pregnancy, Oxytocin, Termination of pregnancy !

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