Comparison of oral misoprostol and intramuscular oxytocin for treating of primary post partum haemorrhage caused by uterine atony

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Abstract
To compare oral misoprostol with intramuscular oxytocin in the treatment of atonic uterus that cause primary post partum haemorrhage after vaginal home deliveries .A prospective study , 38 women were categories in two group; as follow: twenty-five women received intramuscular oxytocin and thirteen received oral misoprostol. Measurement of the blood loss after medication was recorded as a main outcome measure. The result showed that 72% of the patient received intramuscular oxytocin injection had blood loss less that 500 ml while 46% of the patients received oral misoprostol had blood loss less than 500ml. Intramuscular oxytocin injection is effective in treatment of primary post partum hemorrhage caused by uterine atony.

مقارنة فعالية عقار الميزوبروستول عن طريق الفم وعقار الاوكستوسين او معجل الولادة بالحقن العضلي لمعالجة حالات النزف المهبلي بعد الولادة والذي تسبب نتيجة وجود استرخاء في الرحم

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المستخلص
أجريت هذه الدراسة في مستشفى تكريت التعليمي خلال عام ٢٠٠٦-٢٠٠٨ لمقارنة عشوائية لفعالية هاذين العقارين. شملت الدراسة (٣٨) امرأة أنجبت أطفال أحياء خارج المستشفى وتم إدخالهم إلى المستشفى بسبب وجود استرخاء في الرحم بعد الولادة أعطيت (٢٥) منهم عقار الاوكستوسين بالحقن العضلي و (١٣) منهم تم عطائهم الميزوبروستول عن طريق الفم وتم حساب النزف الدموي المهبلي بعد إعطاء العقار.لوحظ إن عقار الاوكستوسين قادر على إيقاف النزف المهبلي بنسبة (٧٢%) من السيدات وعقار الميزوبروستول بنسبة (٤٦%) بعد خمسة عشر دقيقة من إعطاء العقار. إن عقار الاوكستوسين عن طريق الحقن العضلي ذو فعالية لإيقاف النزف المهبلي أكثر من عقار الميزوبروستول عن طريق الفم.

Introduction

Post partum haemorrhage (PPH) is a major cause of maternal deaths around the world (1) . Evidence from several controlled trials suggest that uterine atony accounts for 75-90% of primary (acute) post partum haemorrhage. It has traditionally been defined a blood loss of greater than 500 ml . Which occurs in the first 24 hours after child birth(2) Nature has provided excellent preparation for such haemorrhage after delivery of placenta by contraction of the uterine muscle and occlusion of placental sinuses. Atonic uterus occurs when the uterus fails to contract and then distended with blood, forming a soft boggy uterus on abdominal palpation, which can occur after delivery of the placenta or the placenta is still attached to the uterus. Over distention of the uterus (polyhydramnios, multiple pregnancy, Fetal macrosomia), prolonged labour, distended bladder, abruption placenta, history of previous Post partum haemorrhage and presences of leiomyomas are thought to be factors associated with uterine atony(2,3).

- The injection of uterotonic drugs immediately after delivery of the newborn is one of the most important interventions used to prevent post partum haemorrhage(4) .
- The most commonly used uterotonic drug, oxytocin, has proven to be very effective in reducing the incidence of PPH. Oxytocin (Pitocin) stimulated contraction of uterine smooth muscle by increasing the sodium permeability of uterine myometrial tissue. The drug increase the amplitude and frequency of uterine contractions and it also exhibits vasopressor and antidiuretic effects. Onset of action is immediate ; half life is 3 - 9 minutes with duration lasting approximately 1 hour after intramuscular oxytocin injection. It must be continuously refrigerated to maintain its potency(5,6).

Recently, Oral Misoprostol has been used to treat post partum haemorahage although several clinical studies have suggested that rectal administrated misoprostol can be used effectively in treatment of post partum hemorrhage but it is not available in our hospital.

Misoprostol (cytotec) is a synthetic analog of prostaglandin E, Like other uterotonics, misoprostol causes the uterus to contract, and thus can reduce postpartum bleeding. It has arrange of potential benefit including ease of administration, low cost, long half-life and does not require any special storage conditions(7,8).

- Oral administrated Misoprostol has rise in plasma concentration quickly, peak between 12-60 min after administration and falls steeply by 120 min and remains low thereafter (9) .
- This study aims to compare between the oral misoprostol and intramuscular oxytocin in the treatment of established post partum haemorahage, caused by atonic uterus following vaginal home delivers attend by midwifes.

Materials and Methods

This prospective study was carried out in the Department of obstetrics and Gynecology in Tikrit Teaching Hospital , Tikrit, Iraq between October 2006 and December 2008 . Forty two with atonic uterus were recruited in this study only thirty eight of them were included in the study . Four of those forty two had hypovolemic shock at the time of admission . So they were excluded. The women were included in this study had delivery of a life single baby outside the hospital by a mid wife. But they complain of vaginal bleeding post delivery. All patients in this study were admitted to the Department of obstetrics and Gynecology, the patients informed about the study. History (Include maternal age, parity, the time between

delivery and arrival to the hospital) , general and genital tract examination were carried out. This patient received a life saving method , continuous monitoring of the vital signs and urine output .Exclusion criteria included all patient that has other cause of post partum haemorrhage like genital tract trauma, abnormalities in the delivery of placenta and coagulation disorders, that discovered immediately or during 24 hour from the admission . All gauze and pads were collected from the patients at the time of arrival .weigh of the pad as one gram equal to one ml of blood. The women received one of the following two treatment(1) intra muscular administration of 1 ml of oxytocin (l0 iu) (2) three orally administered tablets of misoprostol (600mg). as a single dose. A clinical examination of the uterus and the amount of vaginal blood loss was measured after 15 minutes. A new pads was placed. The difference in its weight before 15 minutes after the medication was calculated an increase of one gram in the pad weight considered to be equivalent to one ml of blood. If blood loss more than 500 ml after 15 minutes other options of treatment was concerned. The primary out come measures were the decrease in the amount of blood loss after medications.

Statistical analysis

The t test of significance was used to compare numerical value and the Chi square test was used to compare percentages, a P- value less than or equal to 0.05 were considered as statistically significant.

Results

Thirty eight women included in this study, twenty five of them received in tramusular injection of oxytocin and thirteen were received oral misoprostol. Table (1) describes the age distribution of the patients. Table (2) describes the parity of the women , seventeen of the patients were multigrvida. There were no significant differences between the groups with respect to their demographic characteristics. Table (3) shows that the time of arrival to the hospital after labour Twelve of the patients received oral misoprostol they arrive in less than one hour, while twenty-four of the patient received intramuscular injection of oxytocin in less than one hour. Table (4) shows the outcome measure among two groups. Seventy- two percents of patients received intramuscular oxytocin had blood loss less than 500ml, twenty-four percent had blood loss between 500-1000ml and four percent blood loss more than 1000ml in the first 15 minutes after medication. Forty-six percent of patients received oral misoprostol had blood loss less than 500ml , thirty-eight had blood loss between 500-1000ml and fifteen percent had blood loss more than 1000ml in the first 15 minutes after taken the tablets. Table (5) shows the side effects of drugs in both group. Nausea occurs more frequently in group received oral misoprostol while abdominal pain occurred more frequently in group received intramuscular injection of oxytocin. Other side effects like vomiting, headache and diarrhea occur in patient received oral misoprostol than the patient received intramuscular injection of oxytocin. Table (6) shows that both group need another uterotonic agent and two of the patients received oral misoprostol they need other intensive intervention while one of the group received intramuscular oxytocin need intensive interventions.

Table (1):- Age distribution between two groups

Age (yrs)	Oral misoprostol	I.M Oxytocin
15-25	3	8
26-35	9	14
> 36	1	3
Total	13	25

P > 0.05 (Not significant)

Table (2):- Parity of the patients in two groups

Parity	Oral misoprostol	I.M Oxytocin
Primgravida	3	8
Multigravida	10	17
Total	13	25

P > 0.05 (Not significant)

Table (3):- Time of arrival to the hospital after labour

Arrived Time (hours)	Oral misoprostol	I.M Oxytocin
< 1 hr	12	24
> 1hr	1	1

P > 0.05 (Not significant)

Table (4):- comparison of blood loss between two groups in first 15minutes after treatment

Amount of Blood loss (ml)	Oral Misoprostol		I.M Oxytocin	
	No.	%	No.	%
< 500 ml	6	46%	18	72%
500 – 1000 ml	5	38.5%	6	24%
> 1000 ml	2	15.5%	1	4%
Total	13		25	

Table (5):- comparison of side effects of treatment between two groups

Side effect	Oral Misoprostol		I.M Oxytocin	
	13	%	25	%
Nausea	3	23	0	0
Vomiting	2	15	0	0
Headache	5	38	3	12

Fever	3	23	1	4
Abdominal pain	10	76	18	72
Diarrhea	2	15	0	0
shivering	0	0	0	0

Table (6):- subsequent management of patient in two groups

Subsequent treatment	Oral Misoprostol		I.M Oxytocin	
	13	%	25	%
Additional uterotonic drugs	12	92	11	44
Other intervention	2	15	1	4

Discussion

- Post partum hemorrhage is a grave condition that cause at least one third of global maternal mortality. Administration of uterotonics drugs help to control bleeding (Goldberg 2001).
- The most commonly used uterotonics drugs is oxytocin. In this study using intramuscular injection of oxytocin provide superior to misoprostol for treatment of established primary post partum hemorrhage that cause from atonic uterus. This observation agrees with the world health organization (WHO) multi-center that found the oral misoprostol was not effective as oxytocin in reducing maternal bleeding. A similar findings have been present in the study done by (Soriano etl 1996). These results agree with Gulmezoglu 2001 whom concluded that 2.5% of women received intramuscular oxytocin had post partum hemorrhage, while 3.6% had post partum hemorrhage if orally misoprostol was used. The need for another uterotonic was greater in the oral misoprostol groups than in the oxytocin groups (15% and 11% respectively)(Suellein 2004)
- A similar study done by Eray 2003 reported that misoprostol has significantly less effective than the traditional intramuscular injection of oxytocin. Cooks 1999 explain that delayed absorption of misoprostol make misoprostol ineffective in treatment of post partum hemorrhage especially atonic uterus, it's need at lest 12 minutes after administration. (9) Oxytocin still should be considered as useful option in the treatment of established primary post partum hemorrhage.
- Another study concluded that oral administered misoprostol can reduce the incidence of PPH (Goldberg 2000 , Fouzia et 2004) by producing a rapid sustained uterine contraction that decrease post partum hemorrhage. Bugalb repot that misoprostol was effective as first line treatment and the bleeding was arrested in less than 5 minutes with no immediate side effects observed. The side effects observed in oral misoprostol was higher than intramuscular oxytocin group especially nausea and vomiting, which were comparable with other studies (6,12). Bugalb found that misoprostol was accepted by families, had low cost and stable at high temperature while

oxytocin require especial temperature and light storage condition to remain effective(13,14). One of the limitation of this study was the inability to standardize the quantity of vaginal bleeding . According to American college of obstetrics and Gynecology has suggested the more relevant definition of post partum hemorrhage based on change in laboratory finding in the post partum period. A drop of haemotocrit of 10% but all the patients involved in this study had no pre-delivery reading of haemotocrit, so further trial with larger number of patients are needed to search the difference in two groups especially when the placental pieces was retained in the uterus because most of the deliveries handled by unskilled provider outside the hospital. In conclusion traditional oxytocin is effective in treatment of primary post partum hemorrhage and it is accepted in our area.

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