Comparison of Different Medical Treatment of Missed Abortion

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Abstract

Missed abortion constitutes a significant problem in gynecology patient, as it represents an unfortunate outcome of early pregnancy. Despites its frequency however, there is still scope for improvement in patient care as it remains responsible for considerable emotional and psychological trauma to the patients. **Aim of The Study:-** This study is designed to evaluate for using misoprostol therapy in compare to other medical therapy for Iraqi female. **Patients and Method:-** The current study represent a prospective clinical trial that was done on patients with missed abortion. The total number of cases that involving in the study were included 104 cases & 52 of them use mifepristone in a standard regimen and 52 use misoprostol in standard regimen, and those who failed to response from the two groups were selected to use a combination of these two drugs. Of these drugs misoprostol alone regimen was shown to be the most effective method for inducing complete abortion in 77.8% of the patient using this drug alone within a shorter duration (<12 hours), and equal rate of complication with other groups while mifepristone shows (55%) rate of complete abortion while the rate for combination of drugs was (43.6%). Other factors such as the gestational age of the patient, types of delivery, Parity and the patient age were not show to be significantly correlated with the end results. **Conclusion:-** The current study found a significant correlation between the duration from the last delivery and the end result, that complete miscarriage occurs more in patient delivered since more than 11 months.

مقارنة العلاجات الطبية الدوائية المستخدمة في علاج الأسقاط النسبي

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الخلاصة

يشكل الاسقاط المنسي معضلة كبيرة لدى المرضى الزائرين لعيادات النسائية من حيث انها تمثل نتيجة مؤسفة لشهور الحمل الاولى وما تسببه من صدمة عاطفية ونفسية للمرضى. الغرض من هذه الدراسة مقارنة انواع وطرق مختلفة من العلاج الدوائي في حالات الاسقاط المنسي في الثلث الاول والثاني من الحمل لتحديد الدواء والطريقة الانسب والاسرع والاكثر امانا في اتمام الاجهاض تحت الاشراف الطبي. أجمالي المرضى المشاركين في الدراسة هو 104 حالة، 52 منهم استخدموا المفيبرستون بجرعة قياسية و 52 منهم استخدموا الميزوبرستول. تبين من خلال الدراسة ان استخدام الميزوبرستول لوحده هي الطريقة الاكثر فعالية لاحداث الاجهاض الكامل في 77.8% من المرضى.

Introduction

Missed abortion is a term used to describe the condition when the fetus or embryo died but is retained in the uterus[(1)]. Missed abortion is a condition where the pregnancy is still visible within the uterus[(2,3)]. With ultrasound finding of crown rump length >6mm, no fetal heart movement or empty gestational sac with mean diameter > 20mm. Medical abortion with mifepristone and misoprostol is increasingly used by women worldwide. Women report high level of acceptance and satisfaction with these methods, citing privacy, noninvasiveness and case of use as some of medical abortion. Improvements in the regimen and in service delivery have resulted in several nightly effective options for women that offer new routes of administration of misoprostol, fewer visits to the clinic and shorter procedure times. These methods are often favored as they appear more physiological, like a miscarriage, and avoid the need for uterine instrumentation . These methods are required to provide safe and acceptable technique for both patient and staff, in order to reduce the risk for future health and enhance fertility and pregnancy outcome[(3)].

Antiprogesterones: An anti progesterone effect can be obtained by inhibiting the synthesis of progesterone or by blocking its action. Epostane and trilstane, inhibitors of the 3 beta-hydroxy steroid dehydrogenase, the enzyme responsible for the conversion of pregnenolone to progesterone, reduce the synthesis of progesterone by the corpus luteum, placenta and adrenal glands[(4)]

Mifepristone is an orally active progesterone antagonist at the receptor level. Mifepristone (or RU-486) that was discovered in 1980 by chemists at Roussel – UCI-AF; (france) is a synthetic steroid compound with both antiprogesterone and antiglucocorticoid properties[(4-6)] Misopristol is a prostaglandin El analogue that has approves by the food and Drug Administration (FDA) to be taken orally. Misoprostol, which was discovered in 1973. Is a synthetic 15 deoxy – 16 hydrixy-16 methyl analog of naturally occurring prostaglandin El. The 16 hydrozy group is important in reducing side effects typical of prostaglandins and the 16-methyl group increases the activity and duration of action and enables oral administration[(7-11)].

Aim of The Study

The aim of this study is to compare the efficacy of mifepristone and misoprostol in achieving abortion in patient with missed miscarriage, with the two drugs taken separately or in combination. Taking into account side effects of drugs complication of abortion, time, hospital stay and cost.

Patients and Methods

A clinical longitudinal study was performed in obstetrics and gynecology department of Tikrit teaching hospital in Tikrit from 1st of November 2013 to the 1st of June 2014. A detailed history of full medical and obstetrical examination was carried out. The demographic characteristics of each patient were assessed including age (years), gravidity, parity, history of previous medical abortion, previous uterine scare, any complication with the current pregnancy were recorded, and gestational age was determined by last menstrual periods (LMP) and sonography. The Royal College of Obsetetritics & Gynecology **(RCOG)** and the World Health Organization **(WHO)** in their guidelines for care of women requesting abortion recommend mifepristone 200 mg vaginally followed 36 – 48 in later by 800 mg misoprostol by the vaginal route. From a total of 104 patients, half of them (52 patients) and selected randomly to be treated

primarily with mifepristone and the other half had treated primarily with misoprostol. Of these 52 using mifepristone only 20 patients show response. While the other 32 whose not respond referred to be treated with combinations of drugs. The same strategy used with misoprostol group. The end effects of drugs used were observed in terms of expulsion of conception products, time till response to occur and complication that occur after drug usage.

Result

In this study table (1) shows the characteristic of the patient enrolled .The mean age of the patient was (27.2) years, the examination of the patient revealed that the mean gestational age calculated by ultrasound examination was (9.47) weeks, and the mean response time was (52.13) hours. Of these 52 patients using mifepristone only 20 patients showed response. While the other 32 were not respond and referred to be treated with combinations of drugs. The same strategy used with misoprostol group and the result was that 45 out of 52 patients showed primary response with misoprostol only and the remaining 7 patients were referred to combination of drugs, so the total number of cases in the combination group was 39 patients. Table (2) showed that the group of patients with time for the response to occur of <12 hours were significantly higher in the group of patients who treated by misopristol alone (44.4%) compared to the group who treated by mifepristone (10%). These difference were statistically significant chi –square =23.8, P- value = 0 .002. Table (3)showed that the group of patients with their time of response to occur less than 12 hours was higher among the groups of patients with their gestational age of less than 5 weeks compared to other periods of gestational age however this difference was not statically significant, chi – square =19,79,P-value=0.071. Table (4) showed that most of patient get bleeding complication among all periods of gestational age mainly the 12 -24 weeks with the highest rate (70.4%). Table (5) showed that the group of patients with their time for response to occur of less than 12 hours and 12-48 hours were equally distributed with prevous vaginal delivery (33.3%) for each one.

Table (1):- Demographic profile of patients.

Variables	Mean	Standard Deviation
Age (year)	27.2	5.34
Gestational Age (Week)	9.47	3.78
Response (Hours)	52.13	14.65

Table (2):- Percentage of time for response therapy in different groups of patients

	Type of Treatment			**Total**
Time for the response to Occure	**Mifepristone**	**Misoprostol**	**Combination**	
< 12h	2	20	4	26
	10.0%	44.4%	10.3%	25.0%
12 – 48h	12	12	16	40

	55.0%	20.0%	41.0%	34.6%
3-5 days	3	8	8	19
	15.0%	13.3%	20.5%	16.3%
>6 days	3	3	4	10
	15.0%	2.2%	10.3%	16.3%
No response	0	2	7	9
	0%	4.4%	17.9%	7.7%

Table (3):- The group of patients with their time of response to occur in relation to gestational age

	Time for response to occurs					**Total**
Gestational Age	**<12h**	**12-48h**	**3-5 day**	**>6 day**	**No response**	
<5 weeks	11	7	3	1	0	22
	50.0%	31.8%	13.6%	4.5%	0%	100.0%
5-9 weeks	6	14	6	3	12	41
	14.6%	34.1%	14.6%	7.3%	29.3%	100.0%
9-12 weeks	5	5	4	2	4	20
	25.0%	25.0%	20.0%	10.0%	20.0%	100.0%
12-24 weeks	4	10	4	2	1	21
	19.0%	47.6%	19.0%	9.5%	4.8%	100.0%

Table (4):- Relationship between complication and gesational age of the current abortion

Complications	**Gestational Age of the current pregnancy**				**Total**
	< 5 weeks	**5-9weeks**	**9+-12weeks**	**12-24 weeks**	
Infection	0	0	0	1	1
	0%	0%	0%	3.7%	1.0%
Bleeding	5	26	17	19	67
	71.4%	59.1%	65.4%	70.4%	64.4%
Failure of method	0	2	1	0	3
	0%	4.5%	3.8%	0%	2.9%
Other	0	2	1	0	3
	0%	4.5%	3.8%	0%	2.9%
None	2	14	7	7	30
	28.6%	31.6%	26.9%	25.9%	28.8%

Chi square=6.469. P-value=0.891

Table (5):- Relationship between type of previous delivery type and time for response to occur

	Type for response to occurs					Total
Type of Delivery	**<12h**	**12-48h**	**3-5 day**	**>6 day**	**No response**	
Vaginal delivery	18	18	9	1	8	54
	33.3	33.3	16.7	1.9	14.8	100.0
Caesarean section	6	9	5	2	5	27
	22.2	33.3	18.5	7.4	18.5	100.0
BOTH	1	2	1	2	0	6
	16.7	33.3	16.7	33.3	0	100.0
None	1	7	2	3	4	17
	5.9	41.2	11.8	17.6	23.5	100.0

Chi-square= 16.17. P-value = 0.183

Discussion

Medical abortion induced with a combination of mifepriston and misoprostol was licensed and taken into routine use between 1989 and 1992 in several European countries .The current study was studied a regimen of mifepriston alone which results in complete miscarriage in only 60% of women. It's efficiency is highest in very early pregnancy ,and it is about 85% within 10 days of missed period. Misopristol of 400 microgram vaginally every 3 hours was proved by SinghK,Fong YF ,and Dong F. which resulted in complete miscarriage in 85% of women at 2 weeks and 96% at 6 weeks[12]. According to data of the study, misopristol alone was shown to be statistically significant and associated with complete abortion with higher percent of women showed a response in less than 12 hours (after 3 doses) and with equal rate of complication (especially vaginal bleeding and abdominal pain at a rate of 62% -66%) among all groups. The improvement in the efficiency of the end results after vaginal administration of misoprostol could be explained by different contractility patterns, vaginal administration case long lasting and contractility while non regular contractility after oral administration which is agreed with SinghK[12]. Second outcome mifepriston alone regimen in performing complete miscarriage with the majority of the patients showed the highest response to be after 24-48 hours of starting treatment, but it was associated with the highest rate of incomplete miscarriage and no difference in response rate when extending the time interval for giving misopristol for up to 6 days which agreed with Couzinet B,Lestrat N, Ulmann A, and Baulieu EE. While in contrast to Baird DT who showed that combination of drugs have the highest effect among other groups of drugs, current study showed that it was the least effective in performing complete miscarriage, with highest rate of vaginal bleeding, failure of the method and need for surgical evacuation[13]. Interestingly a women who had previous history of uterine scar did not show a significant difference from those who had pure vaginal delivery or combined vaginal and cesarean delivery regarding rate of complication ,time till response to occur and patient end results. These finding are consistent with result obtained by Beatrice A, and Kurt Barenhart[14].

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