EARLY PREGNANCY TERMINATION; USING TAMOXIFEN AND MISOPROSTOL

ORIGINAL
PROF-1969

DR. NABILA ATA ULLAH
Assistant Professor
Department of Obstetrics and Gynaecology
Nishtar Medical College, Multan

DR. HANIA ATA ULLAH
WMO, Family Planning Centre,
Civil Hospital, Multan.

ABSTRACT… Objective: To determine the effectiveness and safety of elective termination of pregnancies from 56 days gestational age 2nd trimester in which ingestion of 20 mg tamoxifen for 4 days was followed by oral administration of 1 or 2 days of 800 µg misoprostol. **Design:** A clinical trial. **Setting:** Department of Obstetrics and Gynaecology, Nishtar Hospital, and Private setup, Multan. **Period:** January 2009 to January 2010. **Material and methods:** A total of 50 patients were included in the trial on outdoor basis. **Results:** Of the 17 subjects with a gestational age between 50 and 56 days, 15 (88.2%) aborted their pregnancies. The mean duration of uterine bleeding in the group of women who aborted their pregnancies was 8.1 days with a range of 1-34 days. **Conclusions:** In conclusion, the regimen of oral tamoxifen followed by oral administration of misoprostol was found to be an effective and rapid method to electively terminate early gestation of 8 weeks duration or less with no serious side effects.

Key words: Gestational age, Tamoxifen, Misprostol.

INTRODUCTION

All of the estimated pregnancies, 25%, 30% pregnancies are electively terminated[1]. More than 60% of these electively terminated during first trimester of gestation by the technique of vacuum aspiration[2]. Although the percentage of women desiring a medical method of abortion varies in different geographical areas, more than half the women who desire early pregnancy termination choose to have the abortion performed medically instead of by surgical evacuation[3]. Mifepristone is not available for use as an abortifacient in any countries and Pakistan is one of them.

Second trimester abortions are done in which chemotherapeutic agent methotrexate is injected followed by administration of misoprostol was originally described by Creinin and Darney and has since been studies in several clinics[4,5,6]. In a multicentre study in which these types of medical abortifacient therapy was used by woman with pregnancy less than 8 weeks gestational age, about 88% of pregnancy aborted[7]. However, only about 65% of the abortions occurred within one day after the first or second dose of misoprostol had been administered. The remaining 35% of the women, who aborted, did so after a mean delay of 24 days after misoprostol was given. The mean number of days of uterine bleeding with this drug combination was 14 and 11 days in the women with immediate and delayed abortion, respectively. If the method fails concerns exist about possible teratogenicity associated with the use of methotrexate.

In an effort to develop a medical method of abortion with a rate of effectiveness and short duration of action similar to that of the mifepristone plus prostaglandin combination, it was decided to study the use of currently available estrogen receptor agonist, tamoxifen, followed by administration of the same prostaglandin, misoprostol, which is also used following methotrexate. The rationale for use this treatment protocol was based upon the finding that administration of tamoxifen for several days to pregnant hamsters and guinea pigs lowered endogenous estradiol levels and interrupted their pregnancies[8,9]. Therefore, a clinical trial was initiated to determine the effectiveness and safety of elective termination of pregnancies of 56 days gestational age in which ingestion of 20 mg tamoxifen for 4 days was followed by oral administration of 1 or 2 days of 800 µg misoprostol.

MATERIAL AND METHODS

This clinical trial was carried out in the Department of Obstetrics and Gynaecology, Nishtar Hospital and Private setup, Multan from January 2009 to January 2010. A total of 50 patients were included in the trial on outdoor basis.

The patients having any evidence of cervical dilatation uterine infection, anemia (Hb <10 g/dl), uterine bleeding

during the current gestation or cardiovascular or cerebrovascular disease were excluded from the study. In addition, potential subjects were excluded if they possessed a known allergy or contraindication to misoprostol or tamoxifen as listed in the product labeling, excluding the contraindication of pregnancy.

At the time the presence of symptoms was recorded, serum âHCG and hemoglobin levels were measured again and pelvic sonography performed. If the gestational sac was still present in the uterine cavity, a clinician placed four 200 g tablets of misoprostol in the posterior vaginal fornix with the use of speculum.

RESULTS

A total of 50 women participated in this trial. The mean age was 26.6 years (range 16-45) with a mean gravidity of 2.7 (1.7) and a mean parity of 1.1 (0-5). Forty seven (94%) of the subjects were nuliparous. Complete abortion occurred in 46 (92%, 95% CI 86.9%, 97.3%) of the 50 subjects. Of the 33 subjects with a gestational duration of 49 or fewer days at the time of enrollment, 31 (94%) aborted their pregnancies. Of the 17 subjects with a gestational age between 50 and 56 days, 15 (88.2%) aborted their pregnancies (Table-I).

Table-I. Abortion rate by gestational age

	Days gestational age	
	<49	50-56
Total	33	17
Success	31	15
Continuing pregnancy	01	01
Incomplete abortion	01	01

Of the 46 women who aborted, 4 did so after ingesting tamoxifen alone and did not receive misoprostol. The gestational age of their pregnancies ranged between 41 and 48 days. Forty two who received misoprostol had a complete abortion within 24 hours after a single dose of misoprostol. Thus, 44 (88%) women had a complete abortion before receiving misoprostol or within 24 hours after misoprostol were administered.

The mean duration of uterine bleeding in the group of women who aborted their pregnancies was 8.1 days with a range of 1-34 days (Table-II).

Table-II. Total days of uterine bleeding in women with complete or incomplete abortion after medication (n=50)

Days	Subjects	%age
<7	28	56.0
8-14	10	20.0
15-21	05	10.0
22-28	04	8.0
29-34	03	6.0

DISCUSSION

The rationale for studying the abortifacient action of tamoxifen was based on studies that reported a high rate of pregnancy termination[8,9]. In addition, Zhou et al reported that when tamoxifen was added to cultures of human placental tissue for 4 days, it decreased the production of âhCG and progesterone[10].

A dose of 20 mg/day tamoxifen was chosen because this is the minimal daily dose recommended for humans according to current product labeling[11]. Koopersmith and Mishell administered multiple dose of 200 to 400 µg of misoprostol intravaginally to 58 women with pregnancies less than 10 weeks gestational age and the rate of complete abortion was about 60%[12].

In contrast to the relatively low effectiveness reported in these studies in which misoprostol was used as a single agent to terminate pregnancies in the first trimester, Carbonell et al recently reported that 93% of 141 women with pregnancies less than 70 days gestational age aborted after receiving 1 to 3 doses of 800 µg of misoprostol intravaginally every 48 hours[13]. However, about half of these abortions were incomplete and required one or two additional doses of misoprostol to expel the remaining intrauterine tissue. Side effects were common. About half the women had nausea or vomiting, more than half had diarrhea and a third had symptoms of fever.

The results of the present study do not indicate whether the high rate of complete abortion in early gestation is due to the combination of tamoxifen followed by misoprostol tablets. In previous reports, vaginally administered misoprostol tablets were not moistened and low rates of success were reported. The high rate of success in this study may be a result of moistening the tablets to cause more rapid and complete abortion of misoprostol. Additionally, Ziemen et al has reported higher systemic bioavailability of vaginally administered misoprostol when compared to oral administration[14]. Further studies are needed using vaginal misoprostol by itself to determine its incidence of effectiveness and acceptability as a method to induce abortion in early gestation.

CONCLUSIONS

In conclusion, the regimen of oral tamoxifen followed by vaginal administration of misoprostol was found to be an effective and rapid method to electively terminate early gestation of 8 weeks duration or less with no serious side effects.

REFERENCES

1. Hinshaw SK, VanVort J. **Abortion services in the United states 1991 and 1992.** Fam Plann Perspec 1994; 26: 100-12.
2. Henshaw S. **Characteristics of US women having abortions 1982-83.** Fam Plann Perspec 1987; 19: 5-9.
3. Cameron ST, Glasier AF, Logani J, Benton L, Baird DT. **Impact of the introduction of new medical methods of therapeutic abortions at the royal Infirmary at Edinburgh.** Br J Obstet Gynaecol 1996; 103: 1222-9.
4. Crenin MD, Darney PD. **Methotrexate and misoprostol for early abortion.** Contraception 1993; 48: 339-48.
5. Creinin MD, Vittinghoff E. **Methotrexate and misoprostol vs misoprostol alone for early abortion.** JAMA 1994; 272: 1190-5.
6. Husknech RU. **Methotrexate and misoprostol to terminate early pregnancy.** N Engl J Med 1995; 333: 537-40.
7. Creinin MD, Vittinghoff E, Kedar L, Darney PD, Tiller G. **Methotrexate and misoprostol for early abortion; a multicentre trial.** Contraception 1996; 53: 321-7.
8. Majumdar N, Data JK. **Contraceptive efficacy of tamoxifen in female hamsters.** Contraception 1990; 41: 93-103.
9. Wisel MS, Data JK, Saxena RN. **Effects of anti-estrogens on early pregnancy.** Int J Fert Menopausal Study 1994; 39: 156-63.
10. Zhou MH, Han GZ, Chu YH. **Effects of antiestrogenic drug tamoxifen on human placental excretion of progesterone and human chorionic gonadotrophin during early gestation.** Acta Phaemaceutica Sinica 1991; 26: 801-4.
11. El-Rafacy H, Rajasckar D, Abdulla M, Calder L, Templeton A. **Induction of abortion with mifepristone and oral or vaginal misoprostol.** N Engl J Med 1995; 332: 983-7.
12. Koopersmith TB, Misshll DR. **The use of misoprotol for termination of early pregnancy.** Contraception 1996; 53: 238-42.
13. Carbinell JLL, Varela L, Velazen A, Fernandez C. **The use of misoprostol for termination of early pregnancy.** Contraception 1997; 55: 165-8.
14. Zieman M, Fong SK, Benowitz NL, Banskter D, Darney PD. **Abortion kinetics of misoprostol with oral or vaginal administration.** Obstet Gynaecol 1997; 90: 88-91.

Article received on: 31/03/2012 Accepted for Publication: 08/09/2012 Received after proof reading: 03/11/2012

Correspondence Address:
Dr. Nabila Ata Ullah
Assistant Professor
Department of Obstetrics and Gynaecology
Nishtar Medical College, Multan

Article Citation:
Ata Ullah H, Ata Ullah N. Early pregnancy termination; using tamoxifen and misoprostol. Professional Med J Dec 2012;19(6): 794-796.