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Studies on the mechanisms of hepatocarcinogenesis by peroxisome proliferators

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ABSTRACT— Early pregnancy losses occur in 10-20% of all pregnancies. Surgical evacuation has always been the mainstay of management of miscarriages. The main aim of this study was to understand the success rate of expectant management of miscarriage with regards to gestational sac size and period of gestation. The secondary outcome was to measure the satisfaction level and the rate of pregnancy after 6 month of expectant management. Patients diagnosed with missed miscarriages were requested to choose between expectant or surgical management. Those decided for expectant management on "wait and watch" approach were assessed weekly up to 5 completed weeks until complete miscarriage was achieved spontaneously. Surgical evacuation was performed if medically indicated or requested by the patients at any time or at the end of fifth week if complete miscarriage was not achieved. Out of 212 cases, 75 (35.4%) opted for expectant management. Complete miscarriage was achieved in 85.3% of subjects by the end of fifth weeks respectively. Mean of Gestational sac size and period of gestation was not found to influence the success rate of complete spontaneous miscarriage in the expectant management. No morbidity was recorded during the five weeks of the study period. Mean satisfaction score was 9.7±8.3. Pregnancy occurred in 47% of patients within 6 months follow up. The Receiver operation characteristic (ROC) curve analysis suggested the end of second week as the cut off for surgical intervention. This study revealed that expectant management of missed miscarriage is a reliable management of missed miscarriage within the first two weeks.

KEYWORDS: Expectant missed miscarriage, Safety, Management

1. INTRODUCTION

Miscarriage is a common complication of early pregnancy and occurs in about 10% to 20% of all pregnancies [1], [2]. In fact the majority of women do not even realize that they were pregnant apart from noticing a slight delay and heavier menstrual flow. Why then when pregnancy is confirmed and found non-viable, there is the compulsion to empty it? [3]. This practice might have been considered to be correct in the first half of the 20th century, when poor hygiene along with illegal abortion, led to high rate of infection with morbidity from septicaemia and heavy bleeding [3], [4]. Undoubtedly, antibiotics and newer surgical techniques have made surgical evacuation a much safer procedure. However, although rare, complications such as perforation of the uterus, leading to haemorrhage, injury to bowel, endometritis and Asherman's syndrome still occur [5], [6]. Studies in the past 30-40 years have proven the viability and efficacy of expectant management as an alternative to surgical evacuation to a variable success [7- 9] Expectant management avoids surgical procedure and costs, minimizing disruption of routine activities and is more acceptable to most women [10], [11]. The MIST trial concluded that the rates of gynaecological infection were reassuringly low irrespective of following surgical, expectant or medical management (2–3%) [12]. There were not many studies looking at the natural history of missed miscarriages [10], [11], [13], [14] and this study was conducted to observe the outcome of missed miscarriage on "wait and watch" approach, to comprehend the safety duration for expectant management before embarking to surgical evacuation, its potential complication, the satisfaction level and the rate of pregnancy at 6 months of follow up.

2. PATIENTS AND METHODS

The study was prospective observational study and conducted from January 2003 until June 2005 in University of Malaya Medical Centre, Kuala Lumpur. Patients presented to the UMMC gynaecology clinic or emergency department with miscarriage at less than or equal to fourteen completed weeks of gestation based on last menstrual period (LMP) early pregnancy. Ethics approval was obtained from the Human Research Ethics Committee prior to commencement of the study. Written consent was taken from every patient. The diagnosis of miscarriage was ultrasound-based and defined according to the guidelines published by the UK's Royal College of Obstetricians and Gynaecologists. The diagnosis of missed miscarriages were made clinically by the following criteria; showing mean gestational sac diameter of at least 15 mm without an embryonic pole or with fetal pole but without heart activity OR gestational sac diameter of less than 15 mm which remain static in size after repeating transvaginal sonography (TVS) at 7 days intervals. The study aimed to see the natural history of missed miscarriage and also to see if expectant management was a good alternative to surgical management. We also wanted to see the return of menses and if possible, any pregnancy during the subsequent six months follows up. The inclusion criteria of the study were age at least 18 years old (to give consent for the study), in good health, haemodynamically stable and able to continue working as usual and gestational age less than or equal to fourteen completed weeks of gestation. The exclusion criteria were severe bleeding or pain, pyrexia above 37.5°C, severe asthma, haemolytic disease or blood dyscrasias, on anticoagulation or systemic corticosteroid treatment, twin or higher order pregnancy, evidence of cervical dilatation or presence of product of conception on the external os, incomplete, inevitable or complete miscarriage, molar pregnancy, and uncertain gestational age. These missed miscarriage women who fulfilled the inclusion criterias were given the options for expectant management or surgical intervention. Those who chose for surgical intervention underwent suction and curettage within 3 days after the diagnosis was made.

Expectant management involved a 'wait-and-watch' approach. Patients were assessed weekly until complete miscarriage was achieved spontaneously. Complete spontaneous miscarriage, was defined as the resolution of symptoms (vaginal bleeding) and the absence of RPOC (retained product of conception) or endometrial thickness less than 15 mm on follow up TVS. Women who had persistent RPOC on TVS or endometrial thickness more than 15 mm on follow up TVS at the end of 5th week or had unplanned surgical curettage were considered to have failure of expectant management. Women undergoing expectant management could change their mind at any time and opt for surgery. If, at any time during expectant management follow-up, the woman developed fever, severe haemorrhage, chills or malodorous vaginal discharge, then expectant management was terminated, antibiotic will be started and surgery arranged on the same day. Surgery involved D&E under general anesthesia. Active follow-up by telephone was continued for period of 6 months to mark the return of normal menses and identify the numbers of subsequent pregnancies. The main outcome measures included the percentage of complete spontaneous miscarriage during each completed week, therefore the safety duration to wait for complete spontaneous miscarriage can be suggested; the percentage of patients who has failure of expectant management at the end of fifth week; the success rate of expectant management compared with mean gestational sac and mean period of gestation. The secondary outcomes were to obtain the satisfaction level and the fertility rates after expectant management of missed miscarriage. Satisfaction rate was calculated based on the subjects' response to the question "How do you rate your satisfaction from expectant management of your miscarriage from the scale of 1 to 10, when 1 indicates no satisfaction and 10 indicating high level of satisfaction?". The mean score for satisfaction was used in the study while the scores were divided into low level of satisfaction (scores below 5) and high level of satisfaction (scores above 6). Fertility rate was defined as having documented pregnancy within 6 months from miscarriage.

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3. RESULTS

A total of 352 subjects with confirmed missed miscarriage were identified, 212 (60%) met all the inclusion criteria of the study. However, only 75 (35.37%) of them chose expectant management and willing to be on weekly follow up. Demographic characteristics of study subjects are shown in Table 1. Mean gestational age of the subjects was 10.4 ± 1.7 weeks.

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