CONSERVATIVE MANAGEMENT OF CHRONIC ECTOPIC PREGNANCY WITH A NOVEL PROTOCOL OF METHOTREXATE: A CASE REPORT

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ABSTRACT

BACKGROUND: Ectopic pregnancy is the implantation of an embryo at sites outside the uterine cavity. With advances in medicine, non-surgical (medical) therapeutic approaches had been introduced in the management of ectopic pregnancy, and they are gaining wide clinical application. Of such medical therapeutic approaches is the use of methotrexate. The use of combined regimen of methotrexate and leucovorin (folinic acid) and single dose regimen of methotrexate, has been reported. However there is still paucity of research information and reports on the use of divided doses of only methotrexate in management of chronic ectopic pregnancy especially in the tropics where affordability of medication imposes a challenge.

MATERIALS AND METHOD: This is a case report of a patient with chronic ectopic pregnancy, successfully managed with four doses of methotrexate only.

RESULT AND CONCLUSION: Chronic ectopic pregnancy can be treated successfully with divided doses of methotrexate alone with minimal side effects.

KEYWORDS: Chronic, Ectopic, Pregnancy, Methotrexate.

INTRODUCTION

Ectopic pregnancy has varied symptoms and signs depending on whether it has acute or chronic presentation. The chronic form of ectopic pregnancy accounts for approximately 6% of ectopic pregnancies.[1] In chronic ectopic pregnancy, there is gradual disintegration of the tubal wall with slow and/or repeated episodes of haemorrhage leading to the formation of a pelvic mass of haematocele or sealed off inflammatory mass.[2] Its clinical features are often confusing, and laboratory evaluations are often misleading.[3] The classical surgical management of ectopic pregnancy is being replaced in recent times by conservative medical management, such as use of methotrexate. Some guidelines for selection of candidates for this medical management have been reported, candidates with Human Chorionic gonadotropin (HCG) <5000mIU/ml are considered good candidates for methotrexate treatment.[4] Also different methotrexate regimens have been applied. This presentation is a case report of chronic ectopic pregnancy with serum B-HCG of 3850.99mIU/ml, which was successfully treated with an uncommon regimen of four doses of methotrexate alone and only minimal side effects were noticed.

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CASE REPORT

A 23 year-old nulliparous unmarried undergraduate, presented to St Elizabeth Specialist Hospital Owerri on 19th September 2017, on account of positive urine pregnancy test and vaginal spotting. Her LMP was on 20th July 2017. Abdomino-pelvic examination showed normal sized uterus with no palpable adnexal mass and no tenderness. Transvaginal ultrasound scan showed empty uterus, fluid in the pouch of Douglas, and a gestation sac 5cm in diameter posterior to the uterus. Serum β-HCG level was 3850.99mIU/ml. The patient was diagnosed as a case of chronic ectopic pregnancy, based on the triad of amenorrhoea, empty uterus, and elevated βHCG. She was then counselled on the different modalities of treatment, and

she refused surgical treatment for social and financial reasons. As there was no contraindication to methotrexate injection after evaluation, 50mg/m^2 of methotrexate was administered intramuscularly daily for 4 days. After the fourth dose, serum B-HCG dropped to 8.0mIU/ml, and full blood count showed normal hematological findings. However the patient had stomatitis and sore throat, which were successfully treated with ampiclox and dequadin lozenges (dequalinium chloride)

DISCUSSION

Choice of treatment option/modality for chronic ectopic pregnancy can be challenging. The American College of Obstetricians and Gynaecologists recommends patients with β-HCG <5000mIU/ml as good candidates for methotrexate treatment.[4]

Different methotrexate treatment protocols reported include; Multi-dose protocol with leucovorin, single dose protocol, and two dose protocol.[5] Multi-dose protocol requires alternate day doses of methotrexate and leucovorin. Single dose regimen requires giving methotrexate 50mg/m^2 with HCG monitoring on day 0, 4, and 7. In these regimens HCG decline of 15% is considered successful treatment. In a meta-analysis by Barnhart et al, overall success rate of multi-dose regimen is reported as 92.7%, and that of single dose protocol as 88.1%.[5] Therefore, the single dose regimen may be more convenient but the multi-dose protocol appears to be more efficacious.

In an attempt to optimize balance between convenience and efficacy, Barnhart et al introduced a two dose protocol without leucovorin, in which 50mg/m^2 methotrexate were given on days 0 and 4, with HCG monitoring on days 0, 4, and 7.[6] Successful treatment is considered as 15% drop in HCG between days 4-7. With this protocol, 87% of patients were treated successfully. They also observed that in limited number of women, no safety concerns were noted with up to 4 doses of methotrexate in a 2 week period without leucovorin.

All these protocols require serial HCG monitoring. The multi-dose protocol with the highest success rate requires alternate day measurements. Cost affordability of such could be challenging especially in resource poor countries such as are in tropical Africa. Also affordability of leucovorin could be a challenge too, as in this patient. In Nigeria, the cost of Leucovorin is three times that of methotrexate according to National Health Insurance Scheme drug price list.[7]

In the management of this patient, medical treatment with methotrexate was considered as option of choice, as criteria were suitable for the option, in addition to patient's refusal of surgery. Also difficulty in affordability of treatment was considered. In an attempt to optimize balance between efficacy and affordability, a novel protocol of intramuscular injection of methotrexate 50mg/m^2 given daily for 4 days (4 doses) was used. Just two HCG measurements were done, on days 1 and 4 and 99.79% decline in HCG was noted on day 4. Mild side effects [stomatitis and sore throat] were noticed, and all haematological parameters on full blood count remained normal.

CONCLUSION

With satisfactory result obtained in this report, chronic ectopic pregnancy can be treated successfully with 4 doses of methotrexate alone with minimal side effects in patients who cannot afford leucovorin and serial HCG measurements. There is need to further evaluate and study this novel protocol that has satisfactory result with cost effectiveness. This will be of great benefit especially in resource poor countries where affordability of medical care is posing great challenge amongst the citizenry.

REFERENCES:

1. Terry C, Robert C C, Chronic ectopic pregnancy. Obstetr Gynecol 1982;59:63-68.
2. Deepak G. Bedi, Charles J. Fagan, Roger M. Nocera, Chronic ectopic pregnancy. JUltrasound Med 1984;3:347-352.

3. Ugur M, Turan C, Vicdan K, Ekici E, Oguz O, Gokmen O. Chronic ectopic pregnancy: a clinical analysis of 62 cases. Aust N Z J Obstet Gynaecol 1996;36(2)
4. ACOG Practice Bulletin No 94: Medical management of ectopic pregnancy. Obstetrics and Gynaecology 2008;111:1479-85.
5. Barnhart K T, Gosman G, Ashby R, Sammel M. The Medical management of ectopic pregnanacy: a meta-analysis comparing "single dose and multi-dose" regimens. Obstetrics and Gynecology 2003;101:778-84.
6. Barnhart K, Hummel A C, Sammel M D, Menon S, Jain J, Chakhtouria N. Use of "2-dose" regimen of methotrexate to treat ectopic pregnanacy. Fertil Steril 2007;87:250-6.
7. National Health Insurance Scheme Drug Price List. 2nd ed. 2013.