

Methotrexate Treatment of Ectopic Pregnancy: Prognosis at Senlis Hospital

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Abstract

Introduction: Ectopic pregnancy is dreadful and can lead to the death of the patient if it is ignored. Diagnosed early, it offers the possibility of medical treatment with methotrexate. **Objective:** To describe the prognosis of ectopic pregnancies treated methotrexate. **Patients and Methods:** Retrospective study of the management of ectopic pregnancy by Methotrexate at Senlis hospital from June 2020 to May 2021 were included in the study, patients with a Fernandez score of less than 13, and having received Methotrexate as first-line treatment. Data were collected using gynecological emergency admission registers, and telephone interviews. **Results:** 35 cases were identified. The average age of the patients was 32 years old. Forty-nine percent were smokers. The mean gestational age was 5 weeks + 2 days. The diagnosis was made in all of our patients with the combination of the kinetics of β -hcg and vaginal ultrasound. The size of adnexal mass was less than 4 cm with an average size of 20 mm. The average value of β -hcg was 1405 IU/L. All patients had received a single dose of methotrexate 1 mg/kg intramuscularly. A second dose was administered to 17.1% of patients for stagnation or re-ascension of the β -hcg level. The success rate was 91.4%. Thirty percent were obtained spontaneous intra uterine pregnancy, the first year following methotrexate treatment. **Conclusion:** The success rate of medical treatment for ectopic pregnancy is high in terms of meeting the eligibility criteria for treatment. The subsequent prognosis of fertility is generally preserved.

Keywords

Ectopic Pregnancy, Methotrexate, Prognosis

1. Introduction

An ectopic pregnancy happens when a fertilized egg implants outside of the uterus, most commonly in the fallopian tube. It is a common cause of morbidity and occasionally of mortality in women of reproductive age by rupture and dangerous internal bleeding if not diagnosed and treated early. In developing countries, its incidence ranges from 2.41% to 3.45% [1] [2], and it is most often diagnosed at a late stage and is life-threatening. Thus, the management is most often surgical by laparoscopy which is not available in all hospitals, or especially by laparotomy as reported by Gabkika B. M. in Tchad where the management was mainly radical in 90.4% of cases by laparotomy [1]. Fortunately, diagnosed early, ectopic pregnancy offers the possibility of simple and inexpensive medical treatment, protecting patients from surgery complications. Thus, medical treatment with methotrexate could concern 30% to 40% of ectopic pregnancy and makes it possible to avoid first-line surgery in a large number of cases [3] [4] with a success rate ranging from 68% to 90.7% [5].

We report the experience of medical management of ectopic pregnancy at Senlis Hospital to describe the prognosis. This will allow us to inspire ourselves to better take care of our patients from our disadvantaged neighborhoods where the morbidity and mortality of ectopic pregnancies remain high.

2. Material and Methods

This was a retrospective study of cases of ectopic pregnancy treated with methotrexate at Senlis hospital from June 2020 to May 2021. We included in our study all patients admitted with biological and ultrasound confirmed ectopic pregnancy and treated with methotrexate during the study period. Were included in the study, hemodynamically stable patients with Fernandez score less than 13 (Table 1). The methotrexate was administered by intramuscular injection at a dose of 1 mg/kg, followed by a second injection one week later if the first injection fails. Data studied were Socio-demographic characteristics, diagnosis, and prognosis. Data were collected using gynecological emergency admission registers, telephone interviews, and was analyzed with epi inf 7.2.

Table 1. Fernandez score.

	1	2	3
Gestational age (amenorrhea weeks)	>7	>6 to <7	<6
β-hcg titre (mIU/mL)	<1.000	1.000 to 5.000	>5.000
Progesterone (ng/ml)	<5	5 to 10	>10
Abdominal pain	Absent	Caused	Spontaneous
Hematosalpinx (cm)	<1	1 to 3	>3
Hemoperitoneum (ml)	0	1 to 100	>100

3. Resultants

During the study, 35 patients were included.

Socio-demographic characteristics

	n	%
Age (year)		
<20	5	14.28
20 - 35	22	62.86
>35	8	22.86
Parity		
Nullipara	10	28.57
Primipara	20	57.14
Multipara	5	14.29
Tabagism		
Yes	17	48.57
No	18	51.43

The mean gestational age was 05 weeks 02 days.

Diagnosis

The diagnosis was made in all our patients by the clinic and vaginal ultrasound couple with level of β -hcg. **Table 2** shows the distribution of patients according to the diagnostic parameters.

The size of adnexal mass was less than 4 cm with an average size of 20 mm. The average value of β -hcg was 1405 IU/L.

Prognosis

All patients received a single dose of methotrexate 1 mg/kg intramuscularly. For 17.1%, a second dose was administered for stagnation or re-ascension of β -hcg levels. A transient elevation of bhcg was reported in 60% of cases within 4 days following methotrexate administration. The overall success rate was 91.4%. About the other 8.6% patients, treatment was failed and laparoscopy was performed.

In the first year after treatment, 30% of patients were obtained spontaneous intra uterine pregnancy. Any complications were not notified among the patients.

4. Discussion

The incidence of ectopic pregnancy varies widely. The highest rates are observed in developing countries, particularly in Africa, with rates varying from 2.41% to 3.45% [1] [2]. In our study, the incidence of ectopic pregnancy is 2.1% reflecting the overall incidence in France which is approximately 2% [6].

Table 2. Distribution of patients according to diagnostic parameters.

	n	%
Functional signs		
Amenorrhea	28	80
Pelvic pain	25	71.4
Metrorrhagia	22	63
Ultrasound diagnosis		
Empty uterus	32	91.4
Adnexal mass	30	85.7
Hemoperitoneum	5	14.3
HCG titre		
Less than 1000 IU/L	20	57.1
1000 - 5000 IU/L	12	34.3
More than 5000 IU/L	3	8.6

The clinical signs suggestive of ectopic pregnancy are not always typical. It's the combination of β -hcg kinetic and vaginal ultrasound that makes it possible the early diagnosis of ectopic pregnancy, offering medical management with methotrexate [7] [8]. In our study, amenorrhea was the most clinical sign (80%), followed by pelvic pain (71.4%) and bleeding (63%). All our patients had had vaginal ultrasound coupled with the kinetics of β -hcg. The average value of β -hcg was 1405 IU/L. The medical treatment of ectopic pregnancy has become a therapeutic entity if the diagnosis is made early, without recourse to laparoscopy. It has been shown to be effective, both in terms of resolving ectopic pregnancy itself and subsequent fertility. This technique is reproducible, easy to use by anyone when the criteria for medical treatment, methotrexate dose to be administered and the monitoring procedures are respected [9]. A pre-therapeutic assessment (haematological, hepatic and renal) is always requested before methotrexate administration. An initial single dose of 1 mg/kg was sufficient for 82.8% patients and 17.1% required a second additional dose of 1 mg/kg of methotrexate. The overall success rate was 91.4%, comparable to that of BOTTIN P. *et al.* [3] who also reported a success rate of 89%.

Three patients with initial β -hcg rate over than 5000 IU/L had secondary laparoscopy for failure of medical treatment by rupture of the ectopic pregnancy.

The kinetics of β -hcg before and after methotrexate injection appears to have greater predictive value in the success or failure of methotrexate treatment. Thus, a decrease β -hcg rate of 15% between 4th and 7th day would be the guarantee of success, with regular weekly monitoring of β -hcg rate decrease [10] [11]. According to authors, a greater increase of β -hcg rate before administration of methotrexate, and the presence of an extrauterine gestational sac with yolk sac may be a predictor of treatment failure [12] [13]. The initial β -hcg rate

is therefore a major prognostic factor for the success of treatment with methotrexate. However, the existence of a threshold value beyond which this treatment is ineffective has not been validated, due to the drop and the negativity of β -hcg rate for 50% of patients with an initial rate more than 5000 IU/L. It is legal to offer methotrexate to patients with pre-therapeutic β -hcg rate of 5000 IU/L or less, without cardiac activity or visible gestational sac [5] [14]. In addition, the patient should be informed of the risk of significant failure if the rate is greater than 2000 IU/L with the potential need for surgical management. Regarding monitoring, we used the standard protocol of Stovall [10] with monitoring β -hcg rate at 1st, 4th and 7th, then weekly until negative after injection of a single dose of methotrexate. The decision for a second dose is taken when β -hcg rate decrease of less than 15% between 4th and 7th day and or, an increase or stagnation of this rate between two weekly dosages. After methotrexate injection, a transient increase between 1st and 4th day or a plateau is reported in 86% of cases [10]. The same observations were reported in our study where a transient increase of β -hcg rate was observed in 60% of cases.

The prognosis of fertility is more related to the patient herself than the choice of treatment. Regarding the subsequent prognosis, the size of the adnexal mass, the location, the notion of tubal rupture or the initial volume of the hemoperitoneum do not appear to affect the prognosis of fertility. On the other part, the personal history of ectopic pregnancy, salpingitis, single tubes, tubal surgery, or the existence of adhesions or alteration of the contralateral tube would profoundly modify the subsequent prognosis [4]. For patients without history, the rate of intrauterine pregnancies is around 90%, while it is only 30% to 40% in the case of a pathological history [4]. In our study, 30% of patients had obtained spontaneous intra uterine pregnancy.

5. Conclusion

From our study and through publications, it appears that the success rate of methotrexate treatment for ectopic pregnancy is high in meeting the eligibility criteria for treatment. The subsequent fertility prognosis, relative to medical treatment, is generally maintained. Thus, in the light of the results of this work, we wish to encourage the early detection of ectopic pregnancies for medical treatment.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

- [1] Gabkika, B.M., Abdelsalam, S., Ilboudo, S.R.W., Adoum, T. and Domga, K. (2015) Ectopic Pregnancy: Epidemiological Aspects and Maternal Prognosis at District Hospital of N'djamena sud (Chad). *Kisangani Médical*, **6**, 111-116.
- [2] Kenfack, B., Noubom, M., Bongoe, A., Tsatedem, F.A., Ngono, M., Tsague, G.N.

- and Mboudou, E. (2012) Extrauterine Pregnancy in a Semi-Rural Region in Africa: Epidemiological, Clinical and Therapeutic Aspects of a Series of 74 Cases Treated at Sangmelima District Hospital in the South. *Pan African Medical Journal*, **13**, 71.
- [3] Bottin, P., Gnisci, A., Crochet, P., Butzbach, P., Cravello, L., Gamarre, M. and Agostini, A. (2014) Prognostic Value of the Early Kinetics of the hCG Level after Injection of Methotrexate for Ectopic Pregnancy. *Gynecology Obstetrics & Fertility*, **42**, 3-7.
- [4] Gervaise, A. and Fernandez, H. (2010) Diagnostic and Therapeutic Management of Ectopic Pregnancies. *Journal of Obstetric Gynecology and Reproductive Biology*, **39S**, F17-F24.
- [5] Garbin, O., Helmlinger, C., Meyer, N., David-Montefiore, E. and Vayssiere, C. (2010) Peut-on traiter 74 % des grossesses extra-utérines par untraitement médical? À propos d'une série de 202 patientes. *Journal de Gynécologie Obstétrique et Biologie de la Reproduction*, **39**, 30-36. <https://doi.org/10.1016/j.jgyn.2009.11.003>
- [6] Bouyer, J. (2003) Epidemiology of Ectopic Pregnancy: Incidence, Risk Factors and Outcomes. *Journal de Gynécologie Obstétrique et Biologie de la Reproduction*, **32**, S8-S17.
- [7] Coste, J., Bouyer, J., Fernandez, H., Pouly, J.L. and Job-Spira, N. (2000) A Population-Based Analytical Approach to Assessing Patterns, Determinants, and Outcomes of Health Care with Application to Ectopic Pregnancy. *Medical Care*, **38**, 739-749. <https://doi.org/10.1097/00005650-200007000-00006>
- [8] Seror, V., Gelfucci, F., Gerbaud, L., Pouly, J.L., Fernandez, H., Job-Spira, N., Bouyer, J. and Coste, J. (2007) Care Pathways for Ectopic Pregnancy: A Population-Based Cost-Effectiveness Analysis. *Fertility and Sterility*, **87**, 737-748. <https://doi.org/10.1016/j.fertnstert.2006.11.005>
- [9] Rosenberg, P., Chevret, S., Camus, E., De Tayrac, R., Garbin, O. and Poncheville, L. (2003) Medical Treatment of Ectopic Pregnancies: A Randomized Clinical Trial Comparing Methotrexate-Mifepristone and Methotrexate-Placebo. *Human Reproduction*, **18**, 1802-1808. <https://doi.org/10.1093/humrep/deg344>
- [10] Stovall, T., Ling, F. and Gray, L. (1991) Single Dose Methotrexate for Treatment of Ectopic Pregnancy. *Obstetrics & Gynecology*, **77**, 754-757.
- [11] Lipscomb, G., Mc Cord, M., Stovall, T., Huff, G., Portera, S. and Ling, F. (1999) Predictors of Success of Methotrexate Treatment in Women with Tubal Ectopic Pregnancies. *New England Journal of Medicine*, **341**, 1974-1978. <https://doi.org/10.1056/NEJM199912233412604>
- [12] Dudley, P., Heard, M., Sangi-Haghpeykar, H., Carson, S. and Buster, J. (2004) Characterizing Ectopic Pregnancies That Rupture Despite Treatment with Methotrexate. *Fertility and Sterility*, **82**, 1374-1378. <https://doi.org/10.1016/j.fertnstert.2004.03.066>
- [13] Lipscomb, G.H., Gomez, I.G., Givens, V.M., Meyer, N.L. and Bran, D.F. (2009) Yolk Sac on Transvaginal Ultrasound as a Prognostic Indicator in the Treatment of Ectopic Pregnancy with Single-Dose Methotrexate. *American Journal of Obstetrics and Gynecology*, **200**, 338.E1-338.E4. <https://doi.org/10.1016/j.ajog.2008.12.006>
- [14] Marret, H., Fauconnier, A., Dubernard, G., *et al.* (2015) Etat des lieux et expertise de l'usage hors AMM du méthotrexate en gynécologie-obstétrique: Travail du CNGOF. *Journal de Gynécologie Obstétrique et Biologie de la Reproduction*, **44**, 230-236. <https://doi.org/10.1016/j.jgyn.2014.12.008>