

# Second-dose methotrexate in ectopic pregnancies: the role of beta human chorionic gonadotropin

Aviad Cohen, M.D., Guy Bibi, M.D., Benny Almog, M.D., Ziv Tsafrir, M.D., and Ishai Levin, M.D.

Department of Gynecology, Tel Aviv Sourasky Medical Center, Affiliated to the Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel

**Objective:** To evaluate the role of  $\beta$ -hCG levels on days 1, 4, and 7 after methotrexate as predictors for second-dose requirement and success.

**Design:** Retrospective cohort study.

**Setting:** Tertiary university-affiliated hospital.

**Patient(s):** A total of 1,703 patients were admitted because of ectopic pregnancy. Four hundred nine received methotrexate, of whom 73 women required a second dose.

**Intervention(s):** The "single-dose" methotrexate protocol with 50 mg/m<sup>2</sup> was administered to patients with progressing ectopic pregnancy. Surgical intervention was performed in cases of methotrexate second-dose treatment failure.

**Main Outcome Measure(s):** Methotrexate second-dose requirement and success according to  $\beta$ -hCG levels on days 1, 4 and 7.

**Result(s):** Second-dose methotrexate was successful in 58 patients (79.4%, success group), whereas 15 patients (20.6%) failed treatment and required surgical intervention (failure group). The medians of  $\beta$ -hCG levels on days 1, 4, and 7 were significantly higher in the "failure group" (1,601 vs. 2,844, 2,164 vs. 3,225, and 1,915 vs. 3,745 mIU/mL, respectively). Logistic regression analysis demonstrated that day-1  $\beta$ -hCG levels were the only significant independent variable for second-dose treatment outcome. The receiver operating characteristic curve for  $\beta$ -hCG levels on day 1 was 0.727, and at a cutoff value of 2,234 mIU/mL the sensitivity and specificity reached the optimum for treatment success (77.5% and 73.3%, respectively).

**Conclusion(s):** Day-1  $\beta$ -hCG levels were the only predictors for methotrexate second-dose requirement and treatment success. The cutoff value of  $\beta$ -hCG on day 1 with the optimal treatment results was found to be 2,234 mIU/mL. (Fertil Steril® 2014;102:1646–9. ©2014 by American Society for Reproductive Medicine.)

**Key Words:** Ectopic pregnancy, beta human chorionic gonadotropin, methotrexate

**Discuss:** You can discuss this article with its authors and with other ASRM members at <http://fertilityforum.com/cohena-methotrexate-ectopic-pregnancies-beta-hcg/>



Use your smartphone to scan this QR code and connect to the discussion forum for this article now.\*

\* Download a free QR code scanner by searching for "QR scanner" in your smartphone's app store or app marketplace.

Extrauterine pregnancies (EUPs) account for 1%–2% of all pregnancies in the United States (1, 2). Improvement in transvaginal sonography and  $\beta$ -hCG assays allows early diagnosis of EUP, resulting in a significant decline in maternal mortality (3). Medical treatment of ectopic pregnancies with methotrexate was shown to be a reasonable alternative to surgery, especially in cases of early diagnosis (4). The

"single-dose" regimen of methotrexate introduced by Stovall et al. in 1991 involves administration of methotrexate at a dose of 50 mg/m<sup>2</sup> (5). The term "single-dose" is actually misleading, because patients receive an additional dose in case of suboptimal response, which is required in approximately 15% of patients (6). Follow-up of patients treated with the single-dose protocol includes assessment of  $\beta$ -hCG levels

on days 1, 4, and 7. A 15% decrease in  $\beta$ -hCG level from day 4 to day 7 is expected and was shown to predict successful treatment in 93% of patients (7). Initial  $\beta$ -hCG level was shown to be the single most important predictor of treatment success in cases of ectopic pregnancies (8), with a reported success rate between 73% and 96% (9, 10).

The aim of our study was to investigate the correlation between  $\beta$ -hCG levels on days 1, 4, and 7 as a predictor of second-dose requirement and treatment success.

## MATERIALS AND METHODS

This was a retrospective study conducted in a tertiary university-affiliated hospital. Institutional review board

Received May 20, 2014; revised July 15, 2014; accepted August 11, 2014; published online September 17, 2014.

A.C. has nothing to disclose. G.B. has nothing to disclose. B.A. has nothing to disclose. Z.T. has nothing to disclose. I.L. has nothing to disclose.

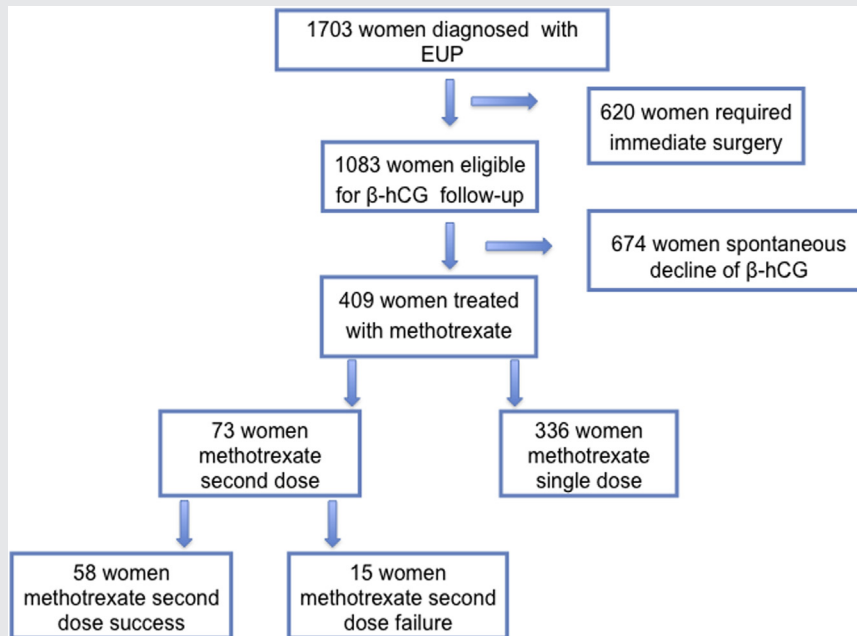
Reprint requests: Aviad Cohen, M.D., Department of Gynecology, Tel Aviv Sourasky Medical Center, 6 Weizmann Street, Tel Aviv 69234, Israel (E-mail: [co.aviad@gmail.com](mailto:co.aviad@gmail.com)).

Fertility and Sterility® Vol. 102, No. 6, December 2014 0015-0282/\$36.00

Copyright ©2014 American Society for Reproductive Medicine, Published by Elsevier Inc.

<http://dx.doi.org/10.1016/j.fertnstert.2014.08.019>

FIGURE 1



Flow chart of patients admitted with ectopic pregnancy.

Cohen. Second-dose MTX in ectopic pregnancies. *Fertil Steril* 2014.

approval was obtained. Medical records of all women who were diagnosed with EUP between January 2001 and June 2013 were reviewed. We included all patients who were diagnosed with EUP and were candidates for medical therapy.

Diagnosis of EUP was made using both  $\beta$ -hCG measurement and imaging with transvaginal ultrasound. Women were excluded from the study and referred for immediate surgery if one of the following conditions occurred: hemodynamic instability,  $\beta$ -hCG  $>10,000$  mIU/mL, EUP with cardiac activity, and signs and symptoms of hemodynamic instability. Women without contraindications for medical therapy were treated according to our “watchful waiting” protocol (9). Briefly, patients with a spontaneous daily decline of  $\beta$ -hCG of more than 15% were discharged with a diagnosis of spontaneously resolving ectopic pregnancy. Women with  $>15\%$  daily increase in  $\beta$ -hCG were considered as having progressing EUP and were treated with methotrexate. In other patients with plateauing  $\beta$ -hCG levels we repeated  $\beta$ -hCG testing daily for a maximal duration of 5 days, after which we administered methotrexate. Criteria for methotrexate administration were according to the accepted guidelines (11). We used the “single-dose” protocol with  $50 \text{ mg/m}^2$  of methotrexate. Day 1 referred to the injection day, and additional  $\beta$ -hCG measurements were taken on days 4 and 7 in our outpatient clinic using the same laboratory. Whenever the  $\beta$ -hCG level failed to decline by 15% between days 4 and 7, an additional injection of methotrexate was given. We considered treatment failure in those patients with suspected tubal rupture (severe abdominal pain, hemodynamic instability) or a continuous rise in  $\beta$ -hCG despite two sequential injections of methotrexate.

To investigate variables associated with the need for a second dose of methotrexate, we compared women who were successfully treated with a single dose with women who required an additional one. Additionally, we sought to determine those predictors that were associated with methotrexate second-dose success. For this analysis we examined the correlation of both  $\beta$ -hCG levels and percent  $\beta$ -hCG change (e.g., [ $\beta$ -hCG day 4 –  $\beta$ -hCG day 1]/ $\beta$ -hCG day 4) among days 1, 4, and 7 as predictors for second-dose treatment failure. A receiver operating characteristic (ROC) curve was designed to determine methotrexate second-dose treatment success as a function of  $\beta$ -hCG level.

We used the Shapiro-Wilk test to evaluate the distribution of the data. Because data were not normally distributed, we used a Mann-Whitney  $U$  test for comparison between continuous variables. Fisher’s exact and  $\chi^2$  tests (2 by k) were used

TABLE 1

Characteristics of women treated with second dose of methotrexate.

Characteristic	Methotrexate second dose success group (n = 58)	Methotrexate second dose failure group (n = 15)	P value
Age, y	31.6 $\pm$ 4	28.8 $\pm$ 5	.07
Parity	0.6 $\pm$ 0.8	0.4 $\pm$ 0.6	.4
Gravidity	2.1 $\pm$ 1.3	1.8 $\pm$ 0.8	.9
Gestational age, wk	6.2 $\pm$ 0.8	6.6 $\pm$ 1.2	.1

Note: Data are presented as mean  $\pm$  SD.

Cohen. Second-dose MTX in ectopic pregnancies. *Fertil Steril* 2014.

Download English Version:

<https://daneshyari.com/en/article/6181937>

Download Persian Version:

<https://daneshyari.com/article/6181937>

[Daneshyari.com](https://daneshyari.com)