

# Hospital Resources Used for Ectopic Pregnancy Treatment by Laparoscopy and Methotrexate

Fabrice Lecuru, Professor, Sophie Camatte, MD, Catherine Viens-Bitker, MD,  
Sophie Chasset, MD, Franck Leonard, MD, Roland Taurelle, Professor

## ABSTRACT

**Objective:** To compare resources used in the medical and laparoscopic treatment of unruptured ectopic pregnancy.

**Methods:** We prospectively recorded all the medical resources required in the treatment of unruptured ectopic pregnancy. The study period ranged from January 1, 1995 to June 30, 1998. Single-dose intramuscular methotrexate injections were administered in 55 women (group I). This therapeutic option was provided on an outpatient basis in small EP ( $\beta$ -HCG level < 5000 IU/L and hematosalpinx diameter < 3 cm). Serial clinical controls and biologic tests were performed until bHCG became negative. Forty women underwent a laparoscopic salpingostomy because they refused the methotrexate regimen or had "social" contra-indications (ie, predictable difficulties in the follow-up) (group II). Twenty-one patients underwent conservative laparoscopic treatment because of "medical" contraindications to methotrexate (group III). We recorded the resources used with the outpatient and inpatient treatment in each group (methotrexate consumption, operating room acts, length of hospital stay, clinical examinations, biological tests, and sonograms during the follow-up).

**Results:** We observed similar cure rates in each group, but it took significantly longer for  $\beta$ -HCG to become negative in group 1. However, hospitalization was significantly less often required, and the length of hospital stay was shorter in this group. But length of follow-up, number of office visits, biological tests, sonograms, and subsequent readmissions were significantly more frequent after methotrexate. Despite more severe clinical presen-

tations for patients in group III, we didn't find any significant differences in the hospital resources used in this group in comparison with those used in group II.

**Conclusions:** The outpatient methotrexate option may result in low consumption of resources for a hospital because most of the follow-up can be performed by city practitioners and laboratories. For the laparoscopic option, efforts should be made to reduce the postoperative hospital stay.

**Key Words:** Ectopic pregnancy, Laparoscopy, Methotrexate, Prospective study, Resource use.

## INTRODUCTION

Today medical treatment of unruptured ectopic pregnancy (unruptured EP) constitutes an accepted alternative to laparoscopic salpingostomy.<sup>1</sup> Randomized trials have demonstrated similar efficacy for laparoscopy and methotrexate either via intramuscular (IM),<sup>2</sup> or intratubal injection.<sup>3-5</sup> Subsequent fertility also appears comparable to that observed after conservative laparoscopy.<sup>5</sup>

Some works have considered the resources used and the cost of EP treatments through simulations and retrospective studies.<sup>6-11</sup> Methotrexate (MTX) appeared of interest because it decreased the costs of EP management by up to 48% when compared with laparoscopy.<sup>6,11</sup> However, the severity of EP treated by MTX or laparoscopy may be quite different, and this difference could influence cost calculations.

It seemed interesting to us to prospectively assess the medical resources used by different approaches for conservative treatment of EP.

## MATERIALS AND METHODS

The aim of this study was to compare the resources used for the treatment of unruptured EP either by single-dose IM MTX injections or conservative laparoscopy. We also wanted to assess medical needs according to the initial presentation of unruptured EP. The study period ranged from January 1, 1995 to June 30, 1998.

Service de Gynécologie-Obstétrique, Hôpital Boucicaut, Paris, France (Professors Lecuru, Taurelle and Drs Camatte, Chasset, Leonard).

Faculté de Médecine Necker-Enfants Malade, Paris, France (Professors Lecuru, Taurelle).

Direction de la Stratégie, Assistance Publique - Hôpitaux de Paris, Paris, France (Dr Viens-Bitker).

Address reprint request to: Pr F. Lecuru, Service de Gynécologie-Obstétrique, Hôpital Boucicaut, 78 rue de la Convention, 75015 Paris, France. Telephone: 01 53 78 81 37, Fax: 01 53 78 82 09, E-mail: fabrice.lecuru@bcc.ap-hop-paris.fr

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**Table 1.**  
Selection of ectopic pregnancies for methotrexate therapy.

Inclusion criteria	Exclusion criteria
$\beta$ -hCG level < 5000 IU * L <sup>-1</sup>	Spontaneous pelvic pain
Hematosalpinx diameter < 3 cm on TVS	Hemodynamic unstable
Small amount of peritoneal fluid on TVS	Fetal cardiac activity
Acceptance of strict clinical and laboratory follow-up	Evidence of hepatic or renal disease
Dwelling place close to the hospital	

$\beta$ -hCG= $\beta$ -human chorionic gonadotropin; TVS=transvaginal sonography.

MTX was proposed for small unruptured EP in cooperative patients living near our department (inclusion and exclusion criteria are given in **Table 1**) (group I). This was given on an outpatient basis via single IM injections (1 mg/Kg) (Methotrexate, Ledertrexate, Léderlé, Paris, France, 50 mg/ampoule)  $\beta$ -hCG assays were scheduled on posttherapeutic days four and seven, and then once weekly. Biologic tests were mostly performed in our hospital laboratory. Sonograms were performed at the practitioner's request. A second injection was indicated when  $\beta$ -hCG level did not decrease between two consecutive assays.

Laparoscopic salpingostomy was performed in patients who refused the protocol or who had the "medical" inclusion criteria for MTX (group III). Salpingectomies were not included in this study. We used the classic three-port access with the patient under general anesthesia. Patients were discharged on postoperative day two, as is usual in France.  $\beta$ -hCG titre and CBC were assessed on day two. Subsequently,  $\beta$ -hCG level was quantified weekly until normalization. A second MTX injection (1 mg/kg) was indicated for patients with stagnating  $\beta$ -hCG levels.

All the resources needed in each case have been prospectively recorded. We took into account major physicians or laboratory acts required by outpatient, ambulatory, or inpatient management from presentation to completion of follow-up (negative  $\beta$ -hCG assay in clinically normal patients). This included MTX consumption, blood transfusion, surgeon anesthetic acts, duration of hospital stay, and posttherapeutic office visits, biological tests ( $\beta$ -hCG assay, liver tests, CBC), and sonograms during follow-up. The management of failures was included in the calculation as well. Data relevant to clinical and

biologic results and the final evolution were prospectively recorded by the patient's referring physician in the department.

Statistical analysis used the ANOVA test, chi-square test, or Pearson correlation coefficient and was carried out with a statistical software program (SPSS 6.1, SPSS-France, Boulogne, France).

## RESULTS

One hundred twenty-two patients were treated conservatively for unruptured EP during the study period. Fifty-five women received IM MTX (group I), 40 had social contraindications to MTX or refused the protocol (group II), and 21 had medical contraindications to MTX (group III). Six patients received MTX even though they did not strictly fulfil the inclusion criteria. MTX was preferred in these cases, with patients' consent, because of severe surgical or anesthetic risk factors. Patients stayed in the department until the  $\beta$ -hCG level showed a significant fall and were not included in this study. The three groups were comparable for demographic features and gestational age at presentation. Conversely, the initial  $\beta$ -hCG level and mean hematosalpinx diameter were significantly higher in group III in contrast with those in group I or II (**Table 2**) (groups I and II were comparable for those criteria,  $P = 0.4$ ). In group I, 48 women were cured with a single injection (87%), four required a second injection, and two subsequent injections were given in one case (total cure rate = 96%). Two patients underwent laparoscopy during follow-up indicated by serious pelvic pain in one case and a stagnant  $\beta$ -hCG level in the other. We recorded one case of stomatitis as a complication and no biological adverse effect in this group. In group II, 34

**Table 2.**  
Characteristics of groups I, II and III.\*

	Group I n = 55	Group II n = 40	Group III n = 21	P
Age (year)	30.8 +/- 5.5	29.3 +/- 5.2	28.4 +/- 5.7	0.2
0 or 1 Para	87.2%	74.3%	85.7%	0.1
History of EP	20%	12.5%	23.8%	0.3
hCG level at diagnosis (IU / L)	1286 +/- 1152	1513 +/- 1429	3363 +/- 2356	< 0.001
Hematosalpinx diameter (mm)	21 +/- 8.8	19.1 +/- 7.4	42.3 +/- 14.4	< 0.001
Gestational age at diagnosis (days)	41.3 +/- 11.7	43.9 +/- 13.3	36 +/- 14.3	0.3

\*Results are expressed as mean +/- standard deviation or %.  
EP=ectopic pregnancy.

**Table 3.**  
Patterns of hospitalization.

**Rate of hospitalization:**

	Group I (n = 55)	Group II (n = 40)	Group III (n = 21)	P
Initial treatment				
ambulatory	80%	0	0	
outpatient	9%	0	0	
inpatient	11%	100%	100%	< 0.001
Subsequent Readmission	11%	2%	0	< 0.05

**Mean length of hospital stay:**

	Group I (n = 55)	Group II (n = 40)	Group III (n = 21)	P
Initial treatment	0.6 +/- 1.7	2.7 +/- 0.7	4.2 +/- 6.6	< 0.05
Subsequent Readmission	2 (1 - 2)	4	-	< 0.05

**Table 4.**  
Resources use.\*

	Group I (n = 55)	Group II (n = 40)	Group III (n = 21)	P
Blood Transfusion	0	0	0	-
Laparoscopy	2	42	21	
Ampoules of MTX	2.2 +/- 0.7 (2-6)	0.2 +/- 0.6 (0-2)	0.2 +/- 0.7 (0-2)	< 0.001
Office visits	2.4 +/- 1.4 (1-7)	1.01 +/- 1 (1-4)	1.4 +/- 1.2	< 0.001
hCG assays	4.6 +/- 2 (1-10)	2.6 +/- 1.7 (1-9)	2.5 +/- 1.5	< 0.001
CBC	2.7 +/- 1.1 (1-8)	1.2 +/- 0.9 (1-6)	0.9 +/- 0.5	< 0.001
Liver tests	2.2 +/- 1.2 (0-6)	0.15 +/- 0.4 (0-2)	0.15 +/- 0.4 (0-2)	< 0.001
Sonograms	1 +/- 1 (0-4)	0.4 +/- 0.6 (0-3)	0.3 +/- 0.6 (0-3)	< 0.01

\*Results are expressed as mean of acts and standard deviation (range)  
MTX=methotrexate; CBC=complete blood cell count.

patients were cured after laparoscopy (85%) and five subsequently required a methotrexate injection (1 mg/Kg) for persistent EP. In addition, one patient underwent a laparoscopic salpingectomy for persistent bleeding. In Group III, 18 patients (86%) were cured with laparoscopy, and three subsequently required one MTX injection. The cure rates for the three approaches were not significantly different ( $P = 0.7$ ).

Resources needed for the three strategies are shown in **Tables 3** and **4**. No blood transfusion was required. Management has naturally been significantly different for the two treatment options, with a high rate of outpatient and ambulatory care in group I, whereas hospitalization was constant in the other two groups (**Table 3**) ( $P < 0.001$ ). Hospital stay was significantly longer in group II and III ( $P < 0.05$ ). Mean hospital stay was longer in group III in comparison with that in group II, but the difference here is not significant. On the other hand, subsequent readmission to the hospital was significantly more frequent in group I (11% vs 2% vs 0,  $P < 0.05$ ). In addition, follow-up was significantly longer in the MTX group (27.3 +/- 10.8 days) in comparison with that in group II (10.2 +/- 8.4) and III (8.7 +/- 8.2) ( $P < 0.05$ ). Finally, office visits,  $\beta$ -hCG assays, CBC, and liver tests were significantly more numerous in this group (**Table 3**).

In terms of observed resources used, MTX resulted in a low number of days in the hospital and in a high number of posttherapeutic laboratory tests and office visits. Laparoscopy had the opposite characteristics.

## DISCUSSION

Health technology assessment is now an important aspect of analysis and planning of medical activities. Besides weighing different surgical options, comparing surgical and medical management is now gaining interest.<sup>12</sup> Analysis of medical goods and service consumption constitutes a part of this assessment that could help in decision making or planning of health structures. In this study, we analyzed the resources used instead of cost because reimbursement systems largely differ among countries.

Unruptured EP treatment is an interesting topic because it remains a frequent pathology in western countries, leading to consistent medical activity.<sup>13,14</sup> Most of the diagnoses of EP are now performed at an early stage, before life-threatening tubal rupture that is today an infre-

quent occurrence.<sup>10</sup> Three treatments can be proposed for unruptured EP in a modern algorithm: expectant management, MTX injection, and laparoscopy. Laparotomy is an invasive option that significantly increases the cost of the treatment and should no longer be indicated.<sup>15,16</sup> In selected cases, MTX appears as effective as laparoscopy in terms of cure rate and subsequent intrauterine pregnancy rate. Thus, systematic use of MTX instead of laparoscopy for small EP could decrease demands for medical resources.

In this study, we assessed the resources required by MTX and conservative laparoscopy in small and more advanced EP. Because this study is not randomized, potential bias could exist. In fact, patients in groups I and II are comparable for clinical, sonographic, and biologic criteria at presentation, and, in addition, demographic features and medical history of those patients were not significantly different (**Table 2**). Laparoscopy was performed in women (group II) who refused MTX or didn't fulfil the conditions we required for the follow-up (compliance, residency, for example). Conversely, group III was constituted of patients who had more severe clinical or biological characteristics.

Our results are similar to those previously reported in European countries for cure rates after laparoscopy, length of hospitalization, and persistent EP rate after laparoscopy.<sup>17</sup>

Finally, we selected parameters that are unquestionable indicators of the consumption of medical goods and services.

MTX and laparoscopy differed quite considerably for resource consumption. MTX resulted in a low rate of hospitalization and a short hospital stay. Conversely, follow-up after medical therapy was significantly longer than after laparoscopy and required significantly more office visits and biological tests. Laparoscopy provided opposite issues: a long hospital stay and a short follow-up requiring less physician time and biological tests. Interestingly, groups II and III had similar outcomes in terms of length of hospital stay and follow-up requirements, although clinical presentations differed greatly.

It appears that the most logical indications for MTX are EP, which can be treated on an out-patient basis, with a short follow-up and a high success rate after one single injection. Follow-up appears to be time-consuming for physicians, patients, and laboratories. Surprisingly, few

studies have addressed this topic.<sup>18</sup> Establishing a more rational protocol is of major interest, to provide sufficient medical security for patients' quality of life. Patients' point of view should be better considered. It has been reported that MTX could have a detrimental impact on women's health-related quality of life.<sup>19</sup> The length of the medical "pressure" and the repetition of tests could explain that patients treated medically perceive themselves as unhealthy and alter their quality of life.

In this series, MTX therapy led to a high rate of subsequent readmissions. They were most of the time related to pelvic pain and were managed conservatively. But they gave rise to consistent medical consumption in terms of days of hospitalization and biological tests. Efforts should be made to educate physicians and patients to reduce the invasiveness of the management of such predictable events.

Laparoscopy resulted in a high number of days of hospitalization. It has been demonstrated that, hospital charges constituted the main part of the direct cost.<sup>14</sup> It is then logical that laparotomy generates higher costs than laparoscopy, and that laparoscopy induces higher costs than medical ambulatory treatments. It is now demonstrated that single-dose MTX provides significant cost savings, when compared with conservative laparoscopy.<sup>20,21</sup> Efforts should, thus, be made to reduce hospital stay after laparoscopic treatment of EP. Outpatient surgery is an interesting alternative, but is not a common policy in France today. Outpatient laparoscopic treatment of EP is feasible but it requires the cooperation of the hospital with city practitioners, nurses, and social workers.<sup>22</sup> In our experience, most prolonged hospitalizations were not related to medical problems, but to unfavourable social situations (data not shown). We wish to emphasise that to be really effective and profitable reduction in the number of days of hospital stay should lead to the reduction in hospital beds at patients' disposal, allocating medical goods and assigning health workers towards other activities, for example cancer screening.

This series confirms that the treatment of unruptured EP with IM MTX gives similar results when compared with laparoscopy. MTX therapy is simple and does not require hospitalization, but follow-up is time-consuming and requires a lot of biological tests. Today, this follow-up is mainly carried out in the hospital, but this could be achieved by local physicians and independent laborato-

ries in the near future. Laparoscopy mainly consumes resources during the hospital stay. Technical acts (anaesthesia and surgery) and hospital charges cannot be avoided; however, the length of postoperative hospital stay could be shortened. This may constitute a goal for the future in France.

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