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## Comparison of the cost of ectopic pregnancy management : Surgery versus methotrexate

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- Objective** : *To estimate the cost savings per case of methotrexate therapy versus surgery for ectopic pregnancy*
- Setting** : *Department of Obstetrics and Gynecology, Nopparat Rajathanee Hospital, Bangkok, Thailand.*
- Design** : *Prospective study.*
- Subject** : *All patients treated for ectopic pregnancy from October 1998 to September 1999.*
- Intervention** : *Questionnaires were used to collect data during admission and follow up.*
- Main Outcome measures** : *Direct costs were determined from billing statements during admission and outpatient costs during follow up. Indirect costs were estimated from monthly income and length of disability from work.*
- Result** : *One hundred and ten ectopic pregnancies were treated, 94 patients by surgical treatment and 16 by methotrexate treatment. An average total cost of surgical treatment was 13,479.30 Baht per case and 8,014.06 Baht per case for the methotrexate treatment, with resultant cost savings of 40.55 percent per case.*

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**Conclusion** : *Methotrexate treatment can be alternative therapy for ectopic pregnancy. Appropriate use of methotrexate will not only reduce morbidity but also the cost.*

**Key words** : *Ectopic pregnancy, Methotrexate, Cost.*

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- วัตถุประสงค์** : เพื่อประมาณค่าใช้จ่ายที่ลดลงต่อรายจากการใช้ Methotrexate รักษาผู้ป่วยตั้งครรภ์นอกมดลูก
- สถานที่ที่ทำการศึกษา** : กลุ่มงานสูติ-นรีเวช โรงพยาบาลนพรัตนราชธานี กรมการแพทย์ กระทรวงสาธารณสุข
- รูปแบบการวิจัย** : การศึกษาไปข้างหน้าแบบพรรณนา
- ผู้ป่วยที่ได้ทำการศึกษา** : ผู้ป่วยตั้งครรภ์นอกมดลูกที่ได้รับการดูแลรักษาในช่วงเดือนตุลาคม พ.ศ. 2541 ถึงเดือนกันยายน พ.ศ. 2542
- วิธีการศึกษา** : ออกแบบสอบถามเพื่อเก็บข้อมูลขณะรับการรักษาตัวในโรงพยาบาล และขณะตรวจติดตาม
- วัตถุประสงค์** : ค่าใช้จ่ายโดยตรงพิจารณาจากใบเสร็จรับเงินขณะรับการรักษาตัวในโรงพยาบาล และค่าใช้จ่ายขณะตรวจติดตามเป็นผู้ป่วยนอก ค่าใช้จ่ายโดยอ้อมประมาณการจากการสูญเสียรายได้ประจำเดือน และระยะเวลาที่ไม่สามารถประกอบอาชีพได้
- ผลการศึกษา** : ผู้ป่วยตั้งครรภ์นอกมดลูกจำนวนทั้งหมด 110 ราย ได้รับการผ่าตัดรักษาจำนวน 94 ราย รักษาโดยใช้ Methotrexate 16 ราย เฉลี่ยค่าใช้จ่ายทั้งหมดในการผ่าตัดรักษาเป็นจำนวนเงิน 13,479.30 บาท ต่อราย และในการที่รักษาโดยใช้ Methotrexate 8,014.06 บาท ต่อราย เป็นผลให้การใช้ Methotrexate สามารถช่วยประหยัดค่าใช้จ่ายได้ร้อยละ 40.55 ต่อราย
- วิจารณ์และสรุป** : Methotrexate เป็นวิธีการหนึ่งในการรักษาผู้ป่วยตั้งครรภ์นอกมดลูก การใช้ Methotrexate ในผู้ป่วยที่เหมาะสมนอกจากจะช่วยลดการเจ็บป่วยแล้ว ยังช่วยลดค่าใช้จ่ายอีกด้วย

Ectopic pregnancies continue to be the leading causes of maternal death in the first trimester, mostly as a result of hemorrhage.<sup>(1)</sup> Despite the increased incidence, maternal deaths due to ectopic pregnancy are declining as a result of early diagnosis and therapy. The apparently increased incidence of ectopic pregnancy may be the result of sooner diagnosis from the use of sensitive and specific assays for hCG and due to developed transvaginal ultrasound for detecting some ectopic pregnancies that in the past may have resolved spontaneously before diagnosis.<sup>(2,3)</sup> Once a surgical emergency, ectopic pregnancy has now evolved into a disease amenable to conservative surgical and even medical therapy.

Because of increasingly reliable nonsurgical diagnosis eliminating surgical complication and lowering costs, systemic methotrexate is emerging as the standard medical regimen in the United States and Europe.<sup>(4)</sup> In this study, we examine the costs associated with management of ectopic pregnancy and we estimate the cost savings of methotrexate therapy for ectopic pregnancy.

### Materials and Methods

Questionnaires were completed for all patients having ectopic pregnancy during postoperative hospitalisation or before methotrexate therapy from October 1, 1998 to September 30, 1999 at Nopparat Rajathanee Hospital, Bangkok, Thailand. The standard surgical treatment of ectopic pregnancy was routine treatment via laparotomy. Patients eligible for methotrexate<sup>(5)</sup> therapy were included by the following conditions: (1) hCG titer  $\geq 2,000$  mIU/ml with no

intrauterine pregnancy by transvaginal ultrasonography, (2) hCG titer increased after curettage, if performed, (3) they were hemodynamically stable, (4) transvaginal ultrasonography demonstrated an unruptured ectopic pregnancy  $\leq 3.5$  cm in greatest dimension and/or absent of fetal cardiac activity in an extrauterine gestational sac, (5) hCG titer  $< 10,000$  mIU/ml, (6) no biochemical evidence of hepatic, renal, or hematologic dysfunction, (7) no evidence of HIV infection (8) they signed an informed consent agreement after clear counselling. If the patients, hCG titer  $< 2,000$  mIU/ml and a serum progesterone  $< 5.0$  ng/ml, they underwent curettage. All patients were treated with a single-dose intramuscular injection of methotrexate ( $50$  mg/m<sup>2</sup>) and hCG titer was repeated weekly until normal ( $< 10$  mIU/ml).

Hospital charges (included investigation fee) were recorded from billing statements standardized by the Department of Medical Services, Ministry of Public Health. Outpatient costs during follow-up visits included costs for transvaginal ultrasonographic examination and hCG titer measurement. The hospital charges and outpatient cost were used to estimate direct cost, indirect costs were estimated according to lost productivity, based on average income. Disability was factored at one month for laparotomy, and half a month for methotrexate therapy. We also reported a the patients requested hospital social welfare in both groups.

Statistical analyses were performed with two tailed t-test, chi-square and Fisher's exact test where appropriate. For all analyses, statistical significance was assumed at the  $p < 0.05$  level.

## Results

During a period from October 1, 1998 to September 30, 1999, we had 10, 189 deliveries and altogether 110 cases of ectopic pregnancy, giving an overall incidence of 10.8 ectopic pregnancies per 1,000 deliveries. The mean age of the patients was  $27.08 \pm 6.24$  years (range 15-41years). Most of them were employees (Table 1), 9.09 % were students.

Eighty five percent were married, 13.64 % were single and 1.82 % were divorced (Table 2). No significant difference between surgical patients and methotrexate treated patients in age, gravida, parity, abortion, gestational age and patient's incomes was found, except the hematocrit level were significantly lower because some surgical patients needed emergency laparotomy and blood transfusion (56/94) (Table 3).

Five cases (4.55 %) had a history of previous ectopic pregnancy, 4 cases (3.64%) had previous

tubal resection (Table 4); all of these patients treated surgically. Total patients treated by laparotomy were 94 patients, most of ectopic pregnancies were located at the fallopian tubes (95.75 %), 2.13 % at the ovaries, 1.06 % intraabdominal and 1.06 % at the cervix (Table 5).

There were 16 patients treated by using single-dose intramuscular methotrexate, all successfully, with mean time to resolution of hCG of  $5.06 \pm 2.08$  weeks (range 2-9 weeks). The mean length of hospital stay was  $3.75 \pm 1.29$  days with no significant difference when compared with surgical patients (Table 6). The average total costs of methotrexate therapy and surgical treatment were 8,014.06 Baht per case and 13,479.30 Baht per case, respectively. The total cost savings for methotrexate therapy compared with traditional laparotomy was approximately 40.55 per cent per case.

Table 1. Occupation.

Occupation	Surgery	Methotrexate	Total
1. Housewives	26 (27.66 %)	5 (31.25 %)	31 (28.18 %)
2. Employees	51 (54.26 %)	5 (31.25 %)	56 (50.91 %)
3. Business	2 (2.13 %)	1 (6.25 %)	3 (2.73 %)
4. Civil servants	4 (4.26 %)	2 (12.50 %)	6 (5.46 %)
5. Student	8 (8.51 %)	2 (12.50 %)	10 (9.09 %)
6. Other	3 (3.19 %)	1 (6.25 %)	4 (3.64 %)
<b>Total</b>	<b>94</b>	<b>16</b>	<b>110</b>

Table 2. Marrital Status.

Marrital Status	Surgery	Methotrexate	Total
1. Single	13 (13.83 %)	2 (12.50 %)	15 (13.64 %)
2. Married	79 (84.04 %)	14 (87.50 %)	93 (84.55 %)
3. Divorced	2 (2.13 %)	0	2 (1.82%)
<b>Total</b>	<b>94</b>	<b>16</b>	<b>110</b>

Table 3. Patient Characteristic.

Patient characteristic	Surgery (N = 94)	Methotrexate (N = 16)	p-value
1. Age (mean, year)	27.32 ± 6.26	25.19 ± 6.28	0.211
2. Gravida	2.27 ± 1.17	2.00 ± 1.03	0.390
3. Parity	0.89 ± 0.94	0.69 ± 0.70	0.407
4. Abortion	0.40 ± 0.79	0.31 ± 0.60	0.680
5. Hematocrit (%)	29.93 ± 5.34	33.94 ± 2.69	0.0*
6. Income (Baht)	3156.36 ± 3330.40	4125.00 ± 4645.79	0.316

\* Significance at p &lt; 0.05

Table 4. Past History.

Past history	Surgery (N = 94)	Methotrexate (N = 16)	Total (n = 110)
1. Previous ectopic	5 (5.32 %)	0	5 (4.55 %)
2. Previous pelvic surgery	2 (2.13 %)	0	2 (1.82 %)
3. Previous TR	4 (4.26 %)	0	4 (3.64 %)
4. History of Salpingitis	18 (19.15 %)	1 (6.25 %)	19 (17.27 %)

Table 5. Location.

Total	Surgery	Methotrexate	Total
1. Fallopian tube	90 (95.75 %)	16 (100 %)	106 (96.36 %)
2. Ovary	2 (2.13 %)	-	2 (1.82 %)
3. Abdominal	1 (1.06 %)	-	1 (0.91 %)
4. Cervical	1 (1.06 %)	-	1 (0.91 %)
<b>Total</b>	<b>94</b>	<b>16</b>	<b>110</b>

Table 6. Outcome.

Outcome	Surgery	Methotrexate	p-Value
1. Hospital stay	4.11 ± 1.09	3.75 ± 1.29	0.243
2. Blood Transfusion	1.51 ± 1.58	0	0.0*
3. Hospital fee (Baht)	10,425.22 ± 21,83.86	3,860.94 ± 3,002.86	0.0*
4. Hospital fee & OPD fee (Direct cost) (Baht)	10,425.22 ± 21,83.86	5,654.69 ± 3,084.77	0.0*
5. Indirect cost (Baht)	3,159.36 ± 3,330.40	2,359.30 ± 2,511.99	0.362
6. Total cost (Baht)	13,479.3 ± 3,987.54	8,014.06 ± 4,841.41	0.0*
7. Total hospital fee (Baht)	979,971.00	61,775.00	
8. Total deductible cost of hospitalization (Baht)	318,693.00	1,731.00	
9. Number of patient request social welfare	44	1	

\* Significance at p < 0.05

There were 44 surgical patients and 1 methotrexate treated patient who requested hospital social welfare. The total deductible costs of hospitalization was 318,693.00 Baht (32.52 %) and 1,731.00 Baht (2.80 %) in surgical group and methotrexate group, respectively.

#### Discussion

Ectopic pregnancy markedly affects future reproductive capabilities. Most ectopic pregnancies occur during the years of peak fertility and prompt treatment is important for conservation of reproductive potential. With earlier diagnosis, treatment has shifted from an immediate life-saving intervention to conservative methods of management; to preserve fertility, reduce morbidity, duration of hospitalization, and costs of the treatment.<sup>(6,7)</sup>

Single-dose methotrexate<sup>(8-10)</sup> appears to be as effective as the previously published multidose

regimen but has the advantages of requiring less methotrexate, having less cost and eliminating side effects. Hajenius, et al<sup>(11)</sup> reported the comparable effectiveness of methotrexate therapy and laparoscopic salpingostomy but with less morbidity and cost for the methotrexate therapy. Additionally, Vermesh et al<sup>(11)</sup> had been shown that the hospital cost savings for laparoscopic treatment compared with traditional laparotomy. Thus, methotrexate may provide an alternative to surgery for treatment of appropriately selected patients with ectopic pregnancy.

Patients treated for ectopic pregnancy with methotrexate frequently can continue to work during the therapy or return to work in less than 1 week. In contrast, return to work usually takes 4 to 6 weeks after laparotomy.<sup>(12)</sup> In this study, indirect costs were estimated from lost productivity based on income, and disability was factored at 1 month for laparotomy, and half a month for methotrexate treatment. The



average indirect costs to the surgical patient were 3,159.36 ± 3,330.40 Baht and 2,359.30 ± 2,511.59 Baht for methotrexate treated patients with no significantly difference. If the indirect costs from disability to work are estimated at 4 days for methotrexate treatment, as Creinin MD and Washington AE<sup>(12)</sup> reported, the costs would be more reduced. Although, the total costs had a significant difference in both groups of patients, the average total cost of surgical treatment was 13,479.30 Baht per case and 8,014.06 Baht per case of methotrexate treatment, with a resultant cost savings of 40.55 % per case.

Forty four (46.8 %) patients in the surgical group requested for hospital social welfare and only one (6.25 %) patient in the methotrexate group did. Total deductible costs of hospitalization was 318,693.00 Baht (32.52 %) and 1,731.00 Baht (2.80 %) for the surgical treated patients and methotrexate treated patients, respectively. In this study there were 16 patients (14.55 %) eligible for treatment with methotrexate. Other reports<sup>(8,9)</sup> found 33.4 - 44.8 % of patients eligible for methotrexate therapy. Therefore, the more patients eligible for methotrexate therapy, the more the deductible cost of hospitalization could reduced.

Methotrexate treatment can be alternative therapy for ectopic pregnancy. Appropriate use of methotrexate will reduce patient's cost and also reduce the deductible cost of hospitalization.

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