Ectopic Pregnancy: Medical or Surgical Treatment? «Time for Assessment»

Results from Auvergne register

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Epidemiologic Register for Ectopic Pregnancy in Auvergne

- Created in 1992 (J.L Pouly, H. Fernandez, N. Job Spiro)
- General population basis (non biased information, the « real life »)
- 3 departments of Auvergne’s region (Allier, Cantal, Puy de Dôme)
- 20 medical centers, public and private
- All women, 15-45 years old, treated for EP
- 1992-2008: 3196 patients (200 cases/year)

To study EP incidence on a long period, old and new risk factors, different treatment’s results, cost-effectiveness and consequences on fertility and quality of life

Epidemiologic Register for Ectopic Pregnancy in Auvergne

- Pre-established questionary basis / patient:
  - Sociodemographic characteristics
  - Sexual, gynaecological, reproductive and smoking habits
  - Surgical histories and conditions of conception (contraception, IVF)
  - Serological tests and β-HCG levels
  - Characteristics of the EP (site, tubal rupture, haemoperitoneum…)
  - Characteristics of treatment procedures
- Interview by phone every 6 months / fertility
- Exhaustiveness ratio = 90% (capture-recapture technique)
**Auvergne’s Register for EP**

1992-2008, 3196 patients, treatments

- 1216 (38%) Radical treatment
- 1965 (61.5%) Conservative treatment
- 15 Missing

- 1447 (73.6%) Surgical treatment
- 718 (26.4%) Medical treatment

- 1306 (66.5%) Exclusive laparoscopy
- 141 (7.2%) Laparoscopy + Medical
- 457 (25.3%) Methotrexate
- 99 Others

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**Effectiveness of methotrexate**

1992-2008, results of Auvergne’s register

- 419 patients
  - Asymptomatic, β-HCG < 5000 IU
  - Mean pre-therapeutic HCG level = 1675 IU
  - Single dose regimen: one intramuscular injection of 50 mg/m²
  - Failure: need of a second line surgical treatment

- A significant increase in the use of MTX
  - 9.5% en 1992
  - 45.1% en 2008, *p*<0.0001

- Mean Failure rate: 24.6%
  - 50% en 1992
  - 13% en 2008, *p*<0.0001

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**Risk factors for failure of methotrexate**

1992-2008, results of Auvergne’s register

- Mean HCG level
  - Mean: 1272.4 IU (95% CI 992-1557)
  - Failure: 2920.2 IU (95% CI 1242.4-4598), *p*<0.06

- Univariate and multivariate analysis:
  - Sociodemographic characteristics
  - Contraceptive and reproductive history
  - Ectopic pregnancy characteristics

- Significant factors of failure in multivariate analysis:
  - History of combined oral contraception, 18.4% vs 30.4%, *p* = 0.001
  - **HCG level**
    - < 1300 IU Failure rate = 16.5%
    - > 1300 IU Failure rate = 39.9%, *p* < 0.0001

Rabischong et al. Fertil Steril 2011
**Comments/ Methotrexate**

- Mean failure rate (24.6%) higher than the literature
  - Results in a general population basis
  - Reflects real practice without bias of specialized centers
- Risk for failure, HCG level
  - Higher cut-off: 1,300 IU
- Significant decrease of failure rate in 15 years
  - Learning curve:
    - Better selection of patients?
    - Change in MTX administration protocol?
    - Better understanding and management of patients after MTX treatment?
- No consensus on the most appropriate administration protocol
  - Necessity of a therapeutic prospective trial


**Conservative Laparoscopic Treatment**

- Laparoscopy = surgical gold standard
- Indications: symptomatic patients (no indication for methotrexate)
- Laparoscopic salpingostomy = the oldest laparoscopic technique

- First case: 1973 by Manhès and Bruhat

**Laparoscopic Salpingostomy**

1992-2008, 1306 patients

- Standardized technique and instrumentation
- Contra-indications (relative)
  - Intratubal pregnancy
  - Massive hemorrhage with tubal rupture
  - EP > 4 cms, High pretherapeutic HCG levels
  - Risk of persistent trophoblast
- Indication / salpingectomy:
  - Whenever possible / Fertility
  - Posy score (Fertil Steril 1989)
  - Contralateral tubal evaluation ++
- Failure = second line of medical or surgical treatment

Rabischong B, Larrain D et al. Obstet Gynecol 2010
Conservative Laparoscopic Treatment
1992-2008, 1306 patients. Effectiveness?

- Mean HCG level
  - Success: 2900.5 ± 7156.1
  - Failure: 3745.7 ± 5428.6
  - P= 0.20

- Univariate and multivariate analysis

- Mean failure rate = 6.6 %
  - (24.6 % with MTX)
  - Stable through all the period (15.9% in 1992 vs 6.4% in 2008, p<0.05)
  - Lower than the literature (~ 15 %) and single dose MTX

- Factor of failure:
  - HCG level:
    - < 1960 IU: failure rate = 5.1 %
    - ≥ 1960 IU: failure rate = 8.6 %, p= 0.03
    - But poor predictive value and clinical relevance of this cut-off

Rabischong, Larroque et Al: Obstet Gynecol 2010

Comments / Laparoscopic Salpingostomy
Importance of adequate instrumentation

- Monopolar diathermy needle

- Lavage-suction device with a 10 mm canula

Comments / Laparoscopic Salpingostomy
Importance of surgical technique

- Exposure

- Salpingostomy:
  - with monopolar diathermy
  - along the antimesenteric border
  - in the proximal part
  - incision of the three coats at once
  - sufficient incision of 10 mm

- Tubal aspiration (10mm canula)

- Avoid the milking

- Hémostasis:
  - Often useless
  - Lamin electrocoagulation
  - Clamping the mesosalpinx and have a coffee
Laparoscopic Salpingostomy
Surgical Technique

End of the debate ??
No
the real challenge remains the subsequent fertility...

Fertility Following Tubal Ectopic Pregnancy

✓ Rate of spontaneous IUP according to the type of treatment?
  highly controversial issue
✓ Risk factors of repeated ectopic pregnancy?
✓ Prospective follow-up of each patient until 45 y old in the Auvergne’s register to study the reproductive outcome after a tubal EP
Fertility Following Ectopic Pregnancy

Results of Auvergne’s Register. Patients

Factors influencing Fertility Following EP

Rate of IUP. Univariable analysis. 1064 patients

- Treatment, p=0.007
- History of infertility, p<0.0001
- History of live birth, p=0.007
- Tubal disease, p<0.0001
- EP with IUD, p<0.0001
- Age at baseline, p<0.0001

Fertility Following Ectopic Pregnancy

24-months cumulative rates of spontaneous IUP/ treatment

Kaplan-Meier. 1064 patients

24-months cumulative rate:
- Salpingectomy: 67.4 %
- Salpingostomy: 76.4 %
- Methotrexate: 75.6 %
Fertility Following Ectopic Pregnancy

Multivariable analysis of factors influencing fertility: Cox model

After adjustment for confounders, there was only a statistically not significant trend in favour of the conservative strategy.

Fertility Following Ectopic Pregnancy

Multivariable analysis for the two subgroup of women depending of history of infertility, tubal patency or age at the time of EP

- For patients with at least one of these three risk factors (subgroup 1), the IUP rate was significantly higher after conservative treatment compared with salpingectomy (HR 0.67; 95% CI 0.50-0.91)

- In this subgroup, no difference in fertility was found according to the type of conservative treatment, medical or surgical.
Recurrence Following Ectopic Pregnancy
Cumulative rates of repeat EP depending of the treatment

2-year cumulative rate of repeat EP
- 19% for salpingostomy
- 18.5% for salpingectomy
- 25.5% for methotrexate
- No difference according to the type of treatment, p=0.86

Recurrence Following Ectopic Pregnancy
Multivariable analysis of factors influencing the risk of recurrence (Cox model)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Adjusted Hazard Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of infertility</td>
<td>1.0</td>
<td>[0.3 - 0.8]</td>
</tr>
<tr>
<td>History of live birth</td>
<td>0.6</td>
<td>[0.6 - 0.9]</td>
</tr>
<tr>
<td>History of abortion</td>
<td>1.8</td>
<td>[1.2 - 3.0]</td>
</tr>
</tbody>
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- Previous voluntary termination of pregnancy was a risk factor of recurrence (HR 1.8; 95% CI 1.1-3.0)
- Interest in secondary prevention

Conclusions
Surgical or Medical treatment?
- The main strength of these results is that they reflect the daily gynecological practice
- The conservative strategy seems to be preferred whenever possible to preserve patient’s fertility without increasing the risk of recurrence
- The choice between conservative treatments does not rely on subsequent fertility, but more likely on their own indications and therapeutic effectiveness or the quality of life
- Risk factors of recurrence could be considered for secondary prevention
Thank You Very Much
For Your Attention!