Comparing medical versus surgical termination of pregnancy at 13-20 weeks of gestation: a randomized controlled trial

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• Introduction – Gap in Knowledge
  – For 2\textsuperscript{nd} trimester TOP, both medical and surgical techniques are acceptable
  – Limited RCT comparing safety and efficacy:
    • Most studies are in pregnancies <13 weeks
    • Grimes et al 1980 RCT of 2\textsuperscript{nd} trimester intra-amniotic PG F2a vs D&E
    • Grimes et al 2004 RCT of mifepristone/misoprostol vs D&E was abandoned because of enrollment
• Introduction – Purpose of Study
  – Compare psychological outcomes and acceptability of MTOP vs STOP at 13-20 weeks

• Introduction – Hypothesis
  – MTOP will have greater psychological distress 2 weeks after procedure (impact of event scale)
  – Will compare effectiveness and acceptability (no hypothesis given)
• **Introduction**
  
  – Does the background specify the gap in knowledge and question being asked?
  
  – Is the hypothesis reasonable, testable, and clearly stated?
• Methods –
  – RCT
  – Setting: Tertiary teaching hospital, 2000-2004
  – Population: 13-20 weeks by BPD, minors included with parental consent
  – Exclusion: Congenital anomaly, contraindications to MTOP, previous C/S, non-English speaking
  – Randomization: computer generated table, opaque envelop
• Methods – Measures after enrollment
  – General Health Questionnaire
  – Hospital Anxiety and Depression Scale
• **Methods – STOP**
  
  – 17+ weeks: Gemeprost 1 mg pv 3 and 6 hrs before STOP
  
  – Multiparous 13-16 6/7: Gemeprost 1 mg 3 hrs before STOP
  
  – One surgeon, US BPD in OR, Hegar dilators, aspiration curette up to 15 weeks, Sopher forceps with US past 15 weeks, US at end, oxytocin if persistent bleeding
  
  – Flagyl per rectum
• Methods – MTOP
  • Doxycycline day before
  • Mifepristone 200 mg orally
  • Misoprostol 800 ug was placed in gyn clinic 36-48 hrs later (8 AM)
  • Misoprostol 400 ug orally every 3 hrs depending on bleeding for maximum 4 doses
  • If no abortion by midnight: mifepristone 200 mg orally and gemeprost 1 mg vaginally every 3 hours starting at 8 AM for maximum of 5 doses. If no abortion by next 8AM, STOP arranged. If placenta retained a further dose of prostaglandin given and wait 4 hours.
• Methods – 2 week Outcome measures
  – Primary outcome: IES (measure of stress reactions after traumatic events)
  – Secondary outcomes:
    – General Health Questionnaire (screen psych distress)
    – HADS score: (symptoms of anxiety and depression)
    – Physical symptoms: bleeding, duration of bleeding, duration of pain and maximum pain during TOP or after
    – Complications: (hemorrhage, failure, uterine evacuation of retained products, infection
    – Acceptability: would do again, better/worse than expected
    – Satisfaction with care: (counseling, care during, care after)
• Methods
  – Questionnaires
  – Hospital notes and general practitioner confirmed complications
• **Methods** —
  
  – Appropriate?
  – Generalizable?
  – Outcome measures ideal?
  – Methodology comments?
    
    • Randomization
    • Blinding
    • Efforts to reduce bias
    • Followup
• Methods – Statistical Analyses
  – Power analysis – based on 5 point difference in primary endpoint, SD 9, power 90%, Type-I error of 0.05, and 20% loss to follow up
  – Recruitment goal = 130
Methods – Statistics

- Intention-to-treat analysis
- Compared means and proportions with 95% confidence intervals.
- Analysis of covariance for GHQ and HAD to compare means between time points. Bootstrap procedures for data that was not normally distributed.
• **Methods – Statistics**
  – Does the power analysis seem reasonable
    • Are you convinced that a 5 point difference is meaningful?
    • 20% drop out is expected?
  – Does statistics plan address the questions being asked?
RESULTS
• Results
  – MTOP and STOP groups had similar characteristics
  – MTOP randomized 60 and 30 followed up
  – STOP randomized 62 and 36 followed up
  – Those who did not provide primary outcome were less likely to be in first pregnancy
## Baseline Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>MTOP n=60</th>
<th>STOP n=62</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years)</td>
<td>23.9</td>
<td>23.5</td>
</tr>
<tr>
<td>Mean gestation (weeks)</td>
<td>14.7</td>
<td>15.1</td>
</tr>
<tr>
<td>Mean GHQ-12</td>
<td>4.5</td>
<td>5.3</td>
</tr>
<tr>
<td>Mean HAD-A</td>
<td>8.3</td>
<td>9.6</td>
</tr>
<tr>
<td>Mean HAD-D</td>
<td>5.9</td>
<td>7.0</td>
</tr>
<tr>
<td>Primipara (n)</td>
<td>24</td>
<td>29</td>
</tr>
<tr>
<td>Previous TOP (n)</td>
<td>14</td>
<td>21</td>
</tr>
</tbody>
</table>
# Psychological and Preference Outcomes at 2 Weeks

<table>
<thead>
<tr>
<th>Variable</th>
<th>MTOP</th>
<th>STOP</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean IES-I</td>
<td>18.6</td>
<td>12.0</td>
<td>1.4 to 11.8**</td>
</tr>
<tr>
<td>Mean IES-A</td>
<td>18.2</td>
<td>17.3</td>
<td>4.0 to 5.8</td>
</tr>
<tr>
<td>Mean IES-T</td>
<td>36.8</td>
<td>30.1</td>
<td>-2.5 to 15.9</td>
</tr>
<tr>
<td>Mean GHQ-12</td>
<td>4.4</td>
<td>2.1</td>
<td>0.7 to 4.4**</td>
</tr>
<tr>
<td>Mean HAD-A</td>
<td>6.3</td>
<td>6.5</td>
<td>-1.8 to 1.8</td>
</tr>
<tr>
<td>Mean HAD-D</td>
<td>5.0</td>
<td>3.9</td>
<td>-1.1 to 2.9</td>
</tr>
<tr>
<td>Choose same TOP again?</td>
<td>53%</td>
<td>100%</td>
<td>-29% to -65%**</td>
</tr>
<tr>
<td>Experience worse than expected?</td>
<td>53%</td>
<td>0%</td>
<td>35% to 71%**</td>
</tr>
</tbody>
</table>

What can you state from these results? Any data look unusual to you?
<table>
<thead>
<tr>
<th>Variable</th>
<th>MTOP</th>
<th>STOP</th>
<th>95% CI</th>
<th>Opt for same-YES n =42</th>
<th>Opt for same-NO n=14</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Comp %</td>
<td>11.5</td>
<td>12.0</td>
<td>-13 to 12</td>
<td>14</td>
<td>7</td>
<td>-13 to 27</td>
</tr>
<tr>
<td>ERPC %</td>
<td>10</td>
<td>2</td>
<td>-1 to 17</td>
<td>14</td>
<td>2</td>
<td>-7 to 31</td>
</tr>
<tr>
<td>Overnight %</td>
<td>31</td>
<td>0</td>
<td>18 to 43**</td>
<td>43</td>
<td>7</td>
<td>9 to 63**</td>
</tr>
<tr>
<td>% Bleeding &gt; menses/severe</td>
<td>37</td>
<td>4</td>
<td>14 to 52**</td>
<td>50</td>
<td>12</td>
<td>10 to 66**</td>
</tr>
<tr>
<td>Pain after moderate or severe %</td>
<td>43</td>
<td>23</td>
<td>-4 to 44</td>
<td>50</td>
<td>29</td>
<td>-8 to 51</td>
</tr>
<tr>
<td>Mean pain duration</td>
<td>44</td>
<td>1.9</td>
<td>0.4 to 4.5**</td>
<td>2.7</td>
<td>4.8</td>
<td>-0.7 to 4.8</td>
</tr>
<tr>
<td>Mean VAS</td>
<td>6.8</td>
<td>4.6</td>
<td>0.7 to 3.8**</td>
<td>5.0</td>
<td>8.0</td>
<td>1.7 to 4.1**</td>
</tr>
</tbody>
</table>
• Complications
  – Similar numbers in both groups
  – MTOP: Evacuation for retained products x 5, one transfusion. Significantly more unexpectedly stayed overnight (mostly for late passage of tissue or need for D&C).
  – STOP: Blood loss >500 ml x 5 with no transfusion, cervical laceration x 1, evacuation for retained products x 1
• **Satisfaction**
  
  – No difference in counseling pre-TOP, care during TOP or care post-TOP between groups.
  – All categories rated very high 97-100%.
  – Satisfaction not driven by complication or symptoms.
• Results –
  – Is the primary question answered by this research?
  – Were the results presented in a way that was logical and understandable?
  – Any other data or analyses that would enhance the research?
• Discussion – Primary Findings
  – Possible improvement in psychological outcome with STOP
  – Most women were satisfied with their care and women seemed to prefer STOP
    • More women would choose STOP again
    • No woman in the STOP group thought it was worse than expected
    • More overnight stay, bleeding and pain reduced preference for MTOP
• Discussion
  – Difficulty with recruitment and retention in such studies
  – Previous first trimester RCT studies find no differences in psychological outcomes between MTOP and STOP
  – Limited conclusions secondary to sample size
  – Women seemed to prefer STOP
  – Patient-centered abortion service should offer choice of MTOP or STOP after 13 week gestation
• Discussion – Limitations
  – Did not achieve sample size of 130
  – Research nurse could only approach 32%
  – Primary outcome data on 60% - additional data collection methods may help
  – Did not record if women saw the fetus
Discussion – Psychological Outcome

- Justified use of IES and restated main finding
- Compared to literature – 3 RCT of MTOP and STOP psychological outcomes in first trimester with no differences
- Increase intrusive thoughts MTOP may be due to the medical experience bleeding/pain/overnight stay or to seeing the fetus
- MTOP IES scores in second trimester were higher than those reported in literature for first trimester terminations
• Discussion – Complications
  – Complications are higher than seen in first trimester terminations
  – MTOP complications were similar to the literature (9.6% requiring evacuation).
  – No prior studies assess pain and bleeding after discharge from MTOP
  – STOP complications were low – single experienced surgeon, US-guidance (6.9% with hemorrhage – higher than Grimes study)
Discussion - Preferences

- Literature suggests pain, seeing fetus, prolonged bleeding and possible psychological consequences influence TOP satisfaction and preference
- More women stated a preference for STOP (desire to be asleep) at recruitment
- More women preferred STOP during study – overnight stay, pain, bleeding
• Discussion – Social Comment
  – Despite safety of STOP and preference for STOP by many women, access is limited
  – Gynecologists are opting out of providing STOP after 12 weeks
  – Novel training strategies are needed
Discussion

- Other areas you would like to see addressed?
- Is there any important literature that was not covered?
- Do you agree with the interpretation of results?
- Any other limitations?
• Conclusions
  – MTOP was associated with more pain, bleeding and overnight stays
  – MTOP may be associated with more distress 2 weeks after the procedure, but larger trials are needed
  – More women would prefer STOP, but some choose MTOP to avoid general anesthesia and surgery
  – Women should be offered a choice of method
Conclusions

- Do the data support the conclusions?
- Did they avoid overstatements?
Clinical Context

- How can we apply this to our care of women locally?
- Is there anything you would want to change in how you currently practice?
- Are women currently offered both STOP and MTOP?
- Does the low complication rate, low IES and better experience in STOP encourage you to start offering STOP?
- What do we have in place to optimize the experience and outcomes, especially after MTOP, knowing that satisfaction was affected by need for overnight stay, bleeding and pain?
CIRHT
The Center for International Reproductive Health Training
at the University of Michigan