Multi-Level Pregnancy Tests in Medical Abortion Service Delivery

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Declaration of Interests

- No financial or personal relationships to disclose
Medical Abortion Trends

• Since introduction of medical abortion in the USA in 2001
  • Abortion rates have remained constant
  • A larger proportion of abortions are managed medically—25%

• In Europe medical abortion represents and even larger proportion of all abortions
  • 73.5% in Scotland
  • 48.6% in France
  • 87.5% in Sweden
MA Follow up:
WHAT WE DO AT PRESENT

- Ask all women to return for follow up
- Assume they will
- When (if) they come, ask them some questions
- Assess that
  - The abortion has occurred
  - There is no ongoing pregnancy
- Ask questions
- **Use technology to judge if abortion worked:**
  - Physical exam
  - hCG level in blood or urine
  - Ultrasonography
WHAT IS A MULTI-LEVEL PREGNANCY TEST?

- Identifies hCG using antigen/antibody reaction, like all other pregnancy tests
- Does not give a precise concentration of hCG in test liquid
- Does not give only a "yes/no" readout
- DOES Identify a range in which the precise level falls
- DOES provide the potential for serial measurements within these ranges
MULTI-LEVEL PREGNANCY TEST

Baseline
(same day as Mifepristone)

Follow-up
(1 to 2 wks later)
Current strategy for using MLPT to assess MA outcome

- Baseline MLPT - mifepristone
  - Day 1

- Home misoprostol
  - Day 2-3

- Follow-up MLPT at home - Call in results
  - Day 7 - 14

Stable or increase in hCG =
In-clinic follow up (1 out of 10 women)

Decrease in hCG range = All done! (9 out of 10 women)

Day 7 - 14
MLPT: Diagnostic Accuracy for Identifying Ongoing Pregnancy

<table>
<thead>
<tr>
<th>Ongoing pregnancy</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>No decline</td>
<td>21</td>
</tr>
<tr>
<td>Decline</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>21</td>
</tr>
</tbody>
</table>

Sensitivity: 100% (95% CL 84%, 100%)
Negative predictive value: 100% (95% CL 99.8%, 100%)
% with decline: 93% (95% CL 91%, 94%)
MLPT: Comparison to Routine Follow-up

Two RCTs:
Women presenting for MA at ≤ 63 days

MLPT Group
• MLPT before and 2 weeks after mife
• Ultrasound or exam if no decline in HCG or specified symptoms

Clinic Assessment Group
• Ultrasound or exam 2 weeks after mife
MLPT: No difference in detection of ongoing pregnancy, by service delivery strategy

<table>
<thead>
<tr>
<th>Enrolled</th>
<th>MLPT Strategy</th>
<th>Standard Clinic Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1913</td>
<td>1900 (99%)</td>
<td>1920</td>
</tr>
</tbody>
</table>

| Followed | 1862 (97%)    |

<table>
<thead>
<tr>
<th>Ongoing prog</th>
<th>MLPT</th>
<th>Standard Clinic Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>23 (1.2%)</td>
<td>25 (1.3%)</td>
<td></td>
</tr>
</tbody>
</table>

1/23 was missed (test showed decline in HCG on day 13).

RR = 0.90 (95% CI 0.51-1.58)

### How Soon Can the Follow-Up Test Be Used?

Data from Vietnam (N=292)

<table>
<thead>
<tr>
<th>Days post-mife</th>
<th>Specificity</th>
<th>Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 days</td>
<td>64%</td>
<td>100%</td>
</tr>
<tr>
<td>7 days</td>
<td>90%</td>
<td>100%</td>
</tr>
<tr>
<td>14 days</td>
<td>97%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Proportion of women for whom clinic-based follow-up would be recommended

<table>
<thead>
<tr>
<th>Day</th>
<th>MLPT</th>
<th>HSPT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 3</td>
<td>38%</td>
<td>94%</td>
</tr>
<tr>
<td>Day 7</td>
<td>12%</td>
<td>80%</td>
</tr>
<tr>
<td>Day 14</td>
<td>5%</td>
<td>39%</td>
</tr>
</tbody>
</table>
MLPT: Ease of use (n=3,453)

- Very easy/easy: 94.6%
- Neither easy nor difficult: 5.1%
- Difficult: [VALUE]

Stanford School of Medicine
Gynuity Health Projects
MLPT: Conclusions

- MLPTs could substantially reduce proportion of clinic-based follow-up after medical abortion.
- Ongoing pregnancy identified in virtually all cases and MLPT effectively identifies women needing clinic-based follow-up care.
- Follow-up can be as early as 3 days after mifepristone, but a 7-14 day follow-up results in fewer false positives.
- Acceptability was high in all settings; however, programmatic applications need development.
Follow-up with a multi-level pregnancy test (MLPT) could:

• Identify ongoing pregnancies at home; allowing for “virtual” follow-up for the majority of women (e.g. by telephone, Internet, etc.)

• Reduce reliance on ultrasound (and the “unnecessary” interventions that often result from U/S)

• Facilitate task-shifting efforts by enabling lower cadres of medical professionals to manage client follow-up

• Be “Bundled” with MA “Combi-pack”
Potential other marketable uses of MLTP

- Monitoring hCG in assisted fertility setting: Pilot study in 2 countries showed high concordance between urine hCG using MLPT and serum hCG for tracking increase in hCG (above 90%)
- Identification of pregnancy (similar to commonly available HSPT)
- Triage for Pregnancy of Unknown Location
- Ectopic and molar pregnancy evaluation & follow-up
Different Products
# Update on Global Availability

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Design of test</th>
<th>Countries where currently distributed</th>
<th>Anticipated market</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ameritek device, marketed as dBest®</td>
<td>5 bracket panel test, urine dipstick</td>
<td>Kazakhstan, China</td>
<td>Additional countries in the EE, Caucus region</td>
</tr>
<tr>
<td>Ameritek device to be marketed as Quanti5®</td>
<td>5 bracket panel test, urine dipstick</td>
<td>None</td>
<td>US (FDA application to be submitted soon)</td>
</tr>
<tr>
<td>CEMAG device to be marketed as TBD name</td>
<td>3 bracket panel test, urine dipstick</td>
<td>None</td>
<td>US (possibly Canada and Mexico)</td>
</tr>
<tr>
<td>TBD PHS - India product</td>
<td>5 bracket panel test, urine dropper</td>
<td>None</td>
<td>India, potentially global</td>
</tr>
<tr>
<td>Low sensitivity PTs (LSPTs)</td>
<td>2 bracket urine test, dipstick and dropper</td>
<td>Global</td>
<td>BUT, not enough!</td>
</tr>
</tbody>
</table>
MLPT: Conclusions

Strengths:
- Highly reliable for excluding ongoing pregnancy at ≤63 days; most women can avoid clinic visit
- No difference in detection of ongoing pregnancy between MLPT strategy and standard clinical evaluation
- Follow-up can be as early as 3 days after mifepristone, but a 7-14 day follow-up results in fewer false positives
- Women find the test easy to use and would like the option to use the MLPT for home follow-up in the future

Weaknesses:
- Nothing is perfect: missed 1 ongoing pregnancy
- Insufficient data after 63 days
Alternative follow-up: Why is this important?

- Costs
  - time,
  - labs,
  - procedures
  - *unnecessary visits have over-medicalized medical abortion for years*

- Future of medical abortion is at home
  - how can we contribute to the scientific evidence supporting this – and alternative follow-up in particular
HOW WE ASSESS

• Ask questions
• Use technology to judge if abortion worked:
  • Physical exam
  • hCG level in blood or urine
  • ultrasonography
WHAT REALLY HAPPENS

• Very poor return rate (In US, loss to f/u now around 30%, some clinics 50%)

• Very few women who return need any treatment (Success rates in large series now around 98%)

• Huge waste of resources, providers’ and women’s time
What would we like to have:

An accurate out-of-clinic method to identify growing/continuing pregnancies post MA that could eliminate the need for in-clinic follow up for most women

- Questionnaires are not accurate enough
- Usual pregnancy tests produce many false positives and/or cannot be used early
Clinical utility of semi-quantitative pregnancy tests

• To assess successful medical abortion
  – A mechanism for at-home follow up (vs. clinic-based follow up) for women after abortion
  – Tests show increasing or decreasing levels of hCG;
• only women not experiencing hCG drop would be asked to return for clinic follow-up
# EFFECTIVENESS OF SQPT

<table>
<thead>
<tr>
<th>TEST RESULT</th>
<th>Ongoing pregnancy</th>
<th>All other outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steady or increasing hCG</td>
<td>96.6 (28/29)</td>
<td>5.3 (68/1291)</td>
</tr>
<tr>
<td>Decreasing hCG</td>
<td>3.4 (1/29)^</td>
<td>94.7 (1223/1291)</td>
</tr>
</tbody>
</table>

Sensitivity: 96.6 %, Specificity: 94.7 %

Positive predictive value: 29.2%, Negative predictive value: 99.9%

Client’s reading is not available for women with no home pregnancy test data.

^ Suspected protocol violation. All data indicated complete abortion, but woman self-referred for clinic visit after telephone follow-up.
FUTURE NEEDS

• Development of patient and provider info on interpretation of test
• Simplification of information sheet for use by low or no-literacy audiences
• Research to examine best methods to contact women (phone, internet, text). Some already done in UK…bpas/Gynuity
• Investment to make SQPT widely available at affordable price for integration into medical abortion services globally