
An Unfinished Agenda in Maternal Health: Meeting the Needs of Women with Preeclampsia/Eclampsia and Postpartum Hemorrhage

Washington, DC
June 13, 2017
Outline

• MCPC background and revision process
• MCPC PE/E and PPH updates
• Redesign of WHO IMPAC derivative tools: initial discussions
MCPC Background

• Reference manual for midwives and doctors working at district hospital level in low resource settings.

• Uses symptom-sign based step-by-step approach (e.g. vaginal bleeding in early pregnancy).
  - Section 1: Clinical principles
  - Section 2: Symptoms
  - Section 3: Procedures
  - Section 4: Appendix.

• The first edition published in 2000 (re-printed 2007)
Revision Process

• **User Survey** conducted in 2015 to solicit feedback from key stakeholders to inform revisions of MCPC

• Core team of **WHO, partners and external experts** prioritized 18 chapters for revision

• **WHO and MCSP** members assigned as technical co-leads for each chapter

• Revisions had to be consistent with previously updated **WHO guidelines and recommendations**

• **WHO Guideline Review Committee (GRC)** requirements: external review conducted by 2 expert external reviewers for each revised chapter
### 18 Revised MCPC Priority Chapters

<table>
<thead>
<tr>
<th>Chapter Category</th>
<th>Chapters Revised</th>
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| **Clinical Principles (Section 1)** | • Emotional and psychological support  
• Emergencies  
• General care principles  
• Antibiotic therapy  
• Operative care principles  
• Normal labour and childbirth  
• Newborn care principles |
| **Symptoms (Section 2)** | • Vaginal bleeding in early pregnancy  
• Vaginal bleeding after childbirth  
• Elevated blood pressure, headache, blurred vision, convulsions or loss of consciousness  
• Fever during pregnancy and labour  
• Fever after childbirth  
• Difficulty in breathing  
• Prelabour rupture of membranes  
• Immediate newborn conditions or problem |
| **Procedures (Section 3)** | • Induction and augmentation of labour  
• Manual removal of placenta  
• Repair of vaginal and perineal tears |
PE/E: Key Areas of Revision

- **Revised classification** framework for Hypertensive Disorders of Pregnancy
- **Prevention** of PE/E
  - Calcium supplementation
  - Low-dose aspirin;
- Use of **SBP** in diagnosis and management of PE/severe PE
- Use of **laboratory findings** for severe PE
- Use of **antihypertensive** in management of HTN, including acute severe systolic HTN
- **Anticonvulsant therapy** for severe PE/E
- **Timing of delivery** in women with severe PE and Eclampsia
- **Postpartum monitoring**
- **Specialized post-partum care and follow up**
Clinical Criteria for Diagnosis of HTN in Pregnancy

- SBP > 140 mm Hg and/or DBP > 90 mm Hg (two consecutive readings four hours or more apart)
- Severe SBP > 160 and/or DBP > 110 mm Hg
Prevention

- **Calcium supplementation** (in areas with low dietary intake)
  - 1.5–2.0 g elemental calcium/day
  - All women, but particularly those at high-risk of PE*

- **Low-dose (75 mg) acetylsalicylic acid (aspirin)**
  - Initiated 12 - 20 weeks of gestation for women at high risk of PE*

*Risk Factors for Developing PE/E:
- Previous severe PE/E, diabetes, chronic hypertension, obesity, renal disease, autoimmune disease and multiple pregnancies.
### Treatment of acute severe hypertension:

**SBP > 160 mmHg and/or DBP > 110 mmHg**

<table>
<thead>
<tr>
<th>Antihypertensive Options</th>
<th>Dosing</th>
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</table>
| **Hydralazine**          | **Intravenous treatment:**
|                          | • Administer 5 mg IV, slowly; Repeat every five minutes until blood pressure goal is achieved. |
|                          | • Repeat hourly as needed or give 12.5 mg IM every 2 hours as needed. |
|                          | • The maximum dose is 20 mg per 24 hours. |
| **Labetalol**            | **Oral treatment:**
|                          | • Administer 200 mg; Repeat dose after one hour until blood pressure goal is achieved. |
|                          | • The maximum dose is 1200 mg in 24 hours. |
|                          | **Intravenous treatment:**
|                          | • Administer 10 mg IV. If response is inadequate after 10 minutes, administer 20 mg IV. |
|                          | • The dose can be doubled to 40 mg and then 80 mg with 10-minute intervals between each increased dose until blood pressure is achieved. |
|                          | • The maximum total dose is 300 mg; then switch to oral treatment. |
| **Nifedipine** (immediate-release capsule) | **Oral treatment:**
|                          | • Administer 5–10 mg orally. Repeat dose after 30 minutes until blood pressure goal is achieved. |
|                          | • The maximum total dose is 30 mg in the acute treatment setting. |
| **Alpha Methyldopa**    | **Oral treatment:**
|                          | • Administer 750 mg orally. |
|                          | • Repeat dose after three hours until blood pressure goal is achieved. |
|                          | • The maximum dose is 3 grams in 24 hours. |

*Source: Elevated blood pressure, headache, blurred vision, convulsions or loss of consciousness chapter*
Eclampsia: Trends in Incidence and Case Fatality Rates in High Income Countries

- By 1970s, **99% reduction** in eclampsia-related maternal deaths
- **Over 90%** of decline due to reduced incidence of eclampsia

Primary Reason: **Early detection, Timely Delivery**
**Not** MgSO4 or anti-hypertensives

Severe Pre-Eclampsia: Diagnosis and Timing of Childbirth

**Diagnosis of Severe Pre-Eclampsia**

- New onset hypertension and proteinuria after 20 weeks gestation:
  - SBP ≥ 160 and/or DBP ≥ 110 after 20 weeks of gestation
  - Proteinuria 2+ on dipstick
- Pre-eclampsia with any of the following present, diagnose severe pre-eclampsia:
  - Neurologic: Headache, vision changes, hyper-reflexia, clonus
  - Pulmonary: Difficulty breathing (rales on auscultation due to fluid in lungs)
  - Hepatic: Upper abdominal pain, nausea/vomiting, liver enzymes elevated > 2x baseline
  - Renal: Serum creatinine > 1.1 mg/dL or doubling of baseline, oliguria (< 400 cc urine 24 hrs)
  - Hematologic: Platelets < 100,000 cells/mcl

**Summary Guidance for Optimal Timing of Delivery for Severe Pre-Eclampsia**

- **Gestational age < 24 weeks (pre-viable fetus)**
  - MgSO4, anti-hypertensive medications
  - Induce labour
- **Gestational age 24-34 weeks**
  - MgSO4; anti-hypertensive medications; antenatal corticosteroids (ACS) if safety conditions met:
  - Close maternal and fetal monitoring; expedite birth if maternal and fetus status not stable
- **Gestational age 34-36 6/7 weeks**
  - Same management as for 24-34 weeks except NO ACS
- **Gestational age 37 0/7 weeks**
  - MgSO4, anti-hypertensive medications and expedite delivery
Use of medicines in the management of PPH – new medications in 2nd edition
(Formerly: Use of Oxytocic Drugs)

<table>
<thead>
<tr>
<th></th>
<th>Dose and Route</th>
<th>Continuing</th>
<th>Maximum Dose</th>
<th>Precaution and Contraindication</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Misoprostol</strong></td>
<td>Sublingual</td>
<td>Repeat 200-800mcg</td>
<td>Not more than 1600 mcg</td>
<td></td>
</tr>
<tr>
<td><strong>PGE1</strong></td>
<td>800 mcg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Tranexamic Acid</strong></td>
<td>IV (slowly)</td>
<td>Repeat after 30 mins if bleeding continues (adjusted for renal function)</td>
<td>Not more than 10mg/kg body weight, three to four times daily</td>
<td>History of coagulopathy or active intravascular clotting, convulsions</td>
</tr>
<tr>
<td></td>
<td>1g</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
PPH Management

Sections added and/or revised:
- **Medicines** for PPH management
- **Nonpneumatic antishock garment**
- Surgical Interventions revised, including addition of **B-lynch suture**
- **Intrauterine Balloon Tamponade**

- IV Fluid Management
- Blood
Summary of MCPC User Survey Findings (Prior to Revision):
Significant Redesign is Needed

- While organization is useful (e.g., symptom-sign approach), it is not particularly user friendly
- Guidelines not up to date, which creates confusion
- Current format not responsive to large amount of emerging, new evidence constantly
  - Real-time updating of individual chapters rather than the entire manual
- Should Include Clinical Algorithms
- Should include more relevant Illustrations (e.g., UBT, B-Lynch)
- Use of technology to facilitate more rapid and effective publishing/dissemination of updated WHO recommendations
Integrated Management of Pregnancy & Childbirth (IMPAC) Manuals

Managing Complications in Pregnancy and Childbirth (MCPC)

Managing Newborn Problems

Pregnancy, Childbirth, Postpartum and Newborn Care (PCPNC)

Symptom-sign, step-by-step approach

Flow chart syndromic approach, with links to treatment in other parts
WHO Technical Meeting on ‘Redesigning the WHO Guidelines Derivative Tools for Maternal and Perinatal Health’ May 16-17, 2017

Considerations

• Urgent demand from countries for updated IMPAC materials
• WHO MNH recommendations (e.g. ANC) focus on specific questions and are not comprehensive - need for up to date comprehensive IMPAC guidance
• Compare use of clinical pathways/algorithms to other formats
• Unifying of MCPC/PCPNC content and format
• Digital vs paper
• Pragmatic approach - more iterative and rapid
• Regional differences, expectations, requirements
• Different levels of internet access
• Develop and pilot select content
• Pilot in a few settings to assess feasibility & acceptability
• End user testing: who, where, how
Next steps

- Adapt and unify MCPC/PCPNC platform
- Digital as primary process, with print PDF functionality
- By end of 2017
  - Agree on and develop new formats (pathway and 1 – 2 others) to test on same condition: one complication (e.g., PE/E) and one routine
  - Conduct targeted end user survey on formats
    - Clinical-based user testing of formats (different facility types, provider levels, location)
  - Iterative development of outputs
  - Develop larger, formal collaborative proposal and management structure for continuous revision process
  - Link with potential donors and partners
2018 and Beyond

• Based on 2017 learning, select a "primary" format
• Establish section editors, management structure, procedures etc.
• Start populating selected format with additional content (conditions)
• Develop full proposal
  • Becomes core component of QoC initiative to address knowledge gaps, provide best-practice evidence, etc
Summary

• MCPC has received much needed updates
• Process is arduous and present format does not optimally meet needs of end users
• Digital and clinical pathway/algorithm formats hold significant promise to meet needs of frontline health care worker
Thank you!
Tranexamic Acid and the WOMAN Trial Results

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Outline

• WOMAN study results
• Implications of study results for management of PPH
• Randomized, double-blind, placebo-controlled trial
• Assesses the effects of early administration of tranexamic acid on death, hysterectomy, and other relevant outcomes in women with PPH
• March 2010 – April 2016, 20,060 women enrolled at 193 hospitals in 21 countries
• Women with PPH received TXA 1 gm IV* or matching placebo along with usual care (2nd dose if bleeding continued after 30 mins, or restarted within 24 hrs)

*Dose: 100 mg/ml IV at 1 mL/min
Main Results

- **Deaths from bleeding significantly reduced by 19%** with use of TXA
- **Reduced by 31%** if given within 3 hrs of giving birth; no reduction if given after 3 hrs
- Risk of hysterectomy was not reduced
- Risk of laparotomy to control bleeding was significantly reduced (36%)
- Risk of thromboembolic events did not differ significantly

<table>
<thead>
<tr>
<th></th>
<th>Tranexamic acid group (n=10036)</th>
<th>Placebo group (n=9985)</th>
<th>RR (95% CI)</th>
<th>p value (two-sided)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding</td>
<td>155 (1.5%)</td>
<td>191 (1.9%)</td>
<td>0.81 (0.65–1.00)</td>
<td>0.045</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>10 (0.1%)</td>
<td>11 (0.1%)</td>
<td>0.90 (0.38–2.13)</td>
<td>0.82</td>
</tr>
<tr>
<td>Organ failure</td>
<td>25 (0.3%)</td>
<td>18 (0.2%)</td>
<td>1.38 (0.75–2.53)</td>
<td>0.29</td>
</tr>
<tr>
<td>Sepsis</td>
<td>15 (0.2%)</td>
<td>8 (0.1%)</td>
<td>1.87 (0.79–4.40)</td>
<td>0.15</td>
</tr>
<tr>
<td>Eclampsia</td>
<td>2 (0.02%)</td>
<td>8 (0.1%)</td>
<td>0.25 (0.05–1.17)</td>
<td>0.057</td>
</tr>
<tr>
<td>Other</td>
<td>20 (0.2%)</td>
<td>20 (0.2%)</td>
<td>0.99 (0.54–1.85)</td>
<td>0.99</td>
</tr>
<tr>
<td>Any cause of death</td>
<td>227 (2.3%)</td>
<td>256 (2.6%)</td>
<td>0.88 (0.74–1.05)</td>
<td>0.16</td>
</tr>
</tbody>
</table>

Data are n (%), unless otherwise indicated. RR = risk ratio.

Table 2: Effect of tranexamic acid on maternal death
Implications

• Administration of tranexamic acid to women with PPH significantly reduces death due to bleeding, with no evidence of adverse events/complications

• TXA should be given as soon as possible following onset of PPH (atony, trauma), and alongside use of uterotonics

  ➢ Note: MCPC 2017 - If oxytocin and other uterotonics fail to stop the bleeding or if the bleeding may be partly due to trauma, administer tranexamic acid.

• Availability of IV tranexamic acid in LMICs
• Effectiveness/bioavailability of oral tranexamic acid
Thank you!
For more information, please visit www.mcsprogram.org

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