South Africa. This is important for all women, but perhaps more so for women of low socio-economic status who may have little else by way of affirmation should their family life break down.

References

SID EfFECTS O F ORAL MISOPROSTOL IN THE THIRD STAGE OF LABOUR — A RANDOMISED PLACEBO-CONTROLLED TRIAL

G Justus Hofmeyr, V Cheryl Nikodem, Marinda de Jager, Andrew Drakely

Background. Misoprostol, an inexpensive, stable, orally active prostaglandin analogue, has been suggested for use in the prevention of postpartum haemorrhage. Potential side-effects, however, need to be quantified.

Objective. To compare the rate of postpartum shivering and pyrexia following oral misoprostol 600 μg and placebo.

Design. A double-blind placebo-controlled trial. Women in labour were randomly allocated to receive either misoprostol 600 μg orally or placebo after delivery. Conventional oxytocics were given immediately if blood loss was thought to be more than usual. Side-effects were recorded.

Postpartum blood loss in the first hour was measured by collection in a special flat plastic bedpan.

Setting. The labour ward of an academic hospital in Johannesburg, with 7 000 deliveries per annum.

Main outcome measures. Shivering and pyrexia.

Results. The groups were well matched. Misoprostol use was associated with more shivering (44% versus 11%, relative risk (RR) 4.03, 95% confidence interval (CI) 2.85 - 5.70), pyrexia ≥ 37.8°C (38% v. 6%, RR 6.23, CI 3.89 - 9.97), 1-hour systolic blood pressure ≥ 140 mmHg (33% v. 25%, RR 1.32, CI 1.03 - 1.70), and diastolic blood pressure ≥ 90 mmHg (10.5% v. 3.0%, RR 3.44, CI 1.67 - 7.11). There were no other significant differences. The study was not designed to be large enough to assess a difference in blood loss ≥ 1 000 ml (9% v. 9.7%, RR 0.93, CI 0.56 - 1.53). Possible effects on blood loss may have been obscured by the lesser use of additional oxytocics in the misoprostol group (14% v. 18%, RR 0.78, CI 0.54 - 1.13).

Department of Obstetrics and Gynaecology, Coronation Hospital and Effective Care Research Unit, University of the Witwatersrand, Johannesburg

G Justus Hofmeyr, MRCOG
V Cheryl Nikodem, MCur
Marinda de Jager, MCur
Andrew Drakely, MB ChB

May 2001, Vol 91, No 5 SAMJ
Conclusions. This study has shown the association of postpartum oral misoprostol 600 µg with shivering, pyrexia and hypertension. The increased blood pressure, as for the trend towards increased abdominal pain, may be secondary to the uterotonie effect of misoprostol. Large randomised trials are needed to assess the effectiveness of misoprostol in the prevention of postpartum haemorrhage, against which the disadvantages demonstrated here can be weighed.5 Af M6 2001; 91: 432-435.

The use of misoprostol, an inexpensive, stable, orally active prostaglandin analogue, for the prevention of postpartum haemorrhage, was first reported in 1996.1 If effective, this therapy would have profound implications for the health of childbearing women worldwide. A limiting factor may be side-effects of misoprostol.2 In a preliminary randomised trial, we observed shivering in 19% of puerperal women who received oral misoprostol 400 µg, compared with 5% of those who received placebo treatment.3 As shivering was not a primary outcome of the latter study, underreporting may have occurred. We have therefore conducted a prospective, randomised, placebo-controlled trial specifically to assess the side-effects of misoprostol use after delivery.

**Patients and Methods**

The study protocol was approved by the Committee for Research on Human Subjects of the University of the Witwatersrand. Women in labour at Coronation Hospital, Johannesburg, were asked to participate in the study, and to sign informed consent. Baseline data were recorded. Immediately after delivery the women were asked to swallow three tablets directly from the next in a series of numbered, opaque test tubes, with a sip of water. The tablets were either misoprostol 200 µg or placebo tablets similar in size and colour but not shape. Efforts to obtain identical placebo tablets were unsuccessful. This method of blinding proved to be effective. The containers were ordered according to a computer-generated random sequence, in balanced blocks of 18. The placenta was removed by cord traction once the uterus was palpated to have contracted firmly.

Within a minute after delivery, linen soiled with amniotic fluid was removed, a fresh, disposable absorbent linen saver sheet with plastic backing was placed under the woman, and a low-profile wedge-shaped plastic 'fracture' bedpan was slid under her buttocks. When active bleeding had stopped, any blood clots were expressed from the uterus, the bedpan was removed and a sanitary towel was applied. The blood in the bedpan was measured in a measuring jug. One hour after delivery, any bloodstained linen savers and sanitary towels were placed in a plastic bag and weighed in grams. The known dry weight of the linen savers and sanitary towels was subtracted to give the approximate volume of blood in millilitres. This was added to the measured blood volume from the bedpan to give the total measured blood loss in the first hour after delivery.

Because conventional oxytocics were not given routinely, the protocol required that close observation be maintained, and conventional therapy be given immediately if the bleeding was considered to be more than usual. The caregiver could choose to use intramuscular Syntometrine 1 ampoule or oxytocin 10 IU, or in more severe cases an intravenous infusion of oxytocin 20 IU in 1 000 ml saline.

All data were entered onto a database (Epping) 6 for analysis. The randomisation code was broken only after entry and checking of data. Comparisons were by the chi-square test with Yates' correction or Fisher's exact probability test if any cell was < 5, and relative risks with Taylor Series 95% confidence intervals.

**Results**

There were no withdrawals after randomisation and all outcomes were analysed in the allocated group.

The randomisation process was successful in producing well-matched groups (Table I). The outcome variables are shown in Table II. Shivering, pyrexia ≥ 37.8°C and hypertension were significantly more common in the misoprostol group. There was somewhat less frequent use of conventional oxytocics in the misoprostol group.

<table>
<thead>
<tr>
<th>Number</th>
<th>Misoprostol</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>300</td>
<td>300</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>26.6 (5.6)</td>
<td>27.4 (5.8)</td>
</tr>
<tr>
<td>Primiparous</td>
<td>94 (31%)</td>
<td>85 (28%)</td>
</tr>
<tr>
<td>Parity 4+</td>
<td>10 (3.3%)</td>
<td>7 (2.3%)</td>
</tr>
<tr>
<td>Episiotomy/tear</td>
<td>146 (49%)</td>
<td>141 (47%)</td>
</tr>
<tr>
<td>Birth weight (grams)</td>
<td>3 047 (528)</td>
<td>3 076 (528)</td>
</tr>
</tbody>
</table>

Results are expressed as mean values (standard deviation) or numbers (%). There were no statistically significant differences.

**Discussion**

The use of placebo treatment was considered acceptable by the University Ethics Committee, specifically within the context of a research environment in which blood loss was closely and accurately monitored, and conventional oxytocics were administered as soon as blood loss was thought to be more...
abdominal pain is likely to reflect increased uterine contraction. Similarly, the near-significant increase in finding demonstrated a clear uterotonic effect of misoprostol in the increased uterine contractility. Lowering of blood pressure with misoprostol. As misoprostol in investigation or treatment of 'unexplained' postpartum pyrexia. Clinicians be aware of puerperal misoprostol. In only one case in the current trial did the temperature exceed brisk than usual. Placebo use has also been considered acceptable in a recent Swedish trial. Two previous reports have suggested that postpartum misoprostol causes shivering in as many as 60% of women, but these studies lacked the control groups necessary to quantify this effect. After completing the current study, we participated in a World Health Organisation multicentre pilot trial comparing misoprostol 600 µg and 400 µg and Syntocinon 10 units intramuscularly. Although different cut-off points were chosen, both trials documented a clear thermogenic effect of puerperal misoprostol. The potential benefit of misoprostol may be greater in an environment in which conventional oxytocics are not available.

CONCLUSIONS
This study has quantified certain side-effects of postpartum misoprostol. It is essential for clinicians who use misoprostol in the postpartum period to be aware of these side-effects. Very large randomised trials, such as the trial currently being undertaken by the World Health Organisation, are needed to determine the effectiveness of oral misoprostol in the prevention of postpartum haemorrhage, against which the ready use of conventional oxytocics, which were required more frequently in the control group, is likely to have obscured any benefit from misoprostol. The potential benefit of misoprostol may be greater in an environment in which conventional oxytocics are not available.

We acknowledge support from the South African Medical Research Council and the University of the Witwatersrand, and the excellent assistance of the nursing staff at Coronation Hospital.

Table II. Comparison of outcome variables between women randomly allocated to receive misoprostol 600 µg or placebo for third stage of labour management

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Misoprostol</th>
<th>Placebo</th>
<th>RR</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>133 (44)</td>
<td>1 (0)</td>
<td>4.03</td>
<td>2.85 - 5.70</td>
<td>0.0000</td>
</tr>
<tr>
<td>Temperature ≥ 37.5°C</td>
<td>114 (38)</td>
<td>2 (0.7)</td>
<td>2.00</td>
<td>0.37 - 10.8</td>
<td>0.68</td>
</tr>
<tr>
<td>Temperature ≥ 40°C</td>
<td>1 (0.3)</td>
<td>1 (0.3)</td>
<td>1.00</td>
<td>0.06 - 15.9</td>
<td>0.10</td>
</tr>
<tr>
<td><strong>Secondary outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>5 (1.7)</td>
<td>1 (0.3)</td>
<td>5.00</td>
<td>0.59 - 42.5</td>
<td>0.22</td>
</tr>
<tr>
<td>Vomiting</td>
<td>4 (1.3)</td>
<td>2 (0.7)</td>
<td>2.00</td>
<td>0.37 - 10.8</td>
<td>0.68</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>1 (0.3)</td>
<td>1 (0.3)</td>
<td>1.00</td>
<td>0.06 - 15.9</td>
<td>0.10</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>47 (15.7)</td>
<td>31 (10.3)</td>
<td>1.52</td>
<td>0.99 - 2.32</td>
<td>0.07</td>
</tr>
<tr>
<td>Blood pressure at 1 hour</td>
<td>2 (0.7)</td>
<td>2 (0.7)</td>
<td>1.00</td>
<td>0.14 - 7.05</td>
<td>1.00</td>
</tr>
<tr>
<td>Systolic ≥ 140 mmHg</td>
<td>100 (33)</td>
<td>75 (25)</td>
<td>1.32</td>
<td>1.03 - 1.70</td>
<td>0.04</td>
</tr>
<tr>
<td>Diastolic ≥ 90 mmHg</td>
<td>31 (10.5)</td>
<td>9 (3.0)</td>
<td>3.44</td>
<td>1.67 - 7.11</td>
<td>0.0006</td>
</tr>
<tr>
<td>Blood loss ≥ 1 000 ml</td>
<td>27 (9)</td>
<td>29 (9.7)</td>
<td>0.93</td>
<td>0.56 - 1.53</td>
<td>0.88</td>
</tr>
<tr>
<td>Additional oxytocic needed</td>
<td>42 (14)</td>
<td>54 (18)</td>
<td>0.78</td>
<td>0.54 - 1.13</td>
<td>0.22</td>
</tr>
<tr>
<td>Third stage ≥ 30 min</td>
<td>6 (2)</td>
<td>3 (1)</td>
<td>1.99</td>
<td>0.50 - 7.87</td>
<td>0.50</td>
</tr>
<tr>
<td>Manual removal of placenta</td>
<td>2 (0.7)</td>
<td>2 (0.7)</td>
<td>1.00</td>
<td>0.14 - 7.05</td>
<td>1.00</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>1 (0.3)</td>
<td>1 (0.3)</td>
<td>1.00</td>
<td>0.05 - 5.50</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Results are expressed as numbers (%). RR = relative risk; CI = confidence interval.
Kangaroo Mother Care
Restoring the Original Paradigm for Infant Care and Breastfeeding

Kangaroo Mother Care is a method of care for all newborn babies, but especially prematures. This is the eagerly awaited original video of Dr Nils Bergman’s highly popular talks on the subject. The video provides the latest up-to-date research and evidence to prove that the newborn thrives best in its original “rightful” place - on its mother’s chest. Kangaroo Mother Care has the following vital components:

Skin to skin contact
The naked baby is placed against the mother’s skin, where the temperature is perfectly controlled all the time. A mother’s temperature will naturally rise 2°C to warm a cold baby. The baby’s breathing is markedly improved.

Breastfeeding
The baby is given the full benefits of the perfect food. Mother’s milk contains the exact proteins required, and for premature babies, the protein content increases automatically for better growth. The composition is such that the baby rarely suffers colic and constipation. Mother’s milk contains antibodies against infection.

Never separate mother and child
The stress of separation causes hormones to be released which interfere with digestion and all other normal functions of the baby’s body: the baby is in survival mode rather than growing normally. Kangaroo Mother Care enables the baby to relax, and improves the heart rate and temperature. High levels of stress hormones can have permanent adverse effects on the baby’s brain, resulting in behaviour disorders and lower IQ later in life.

Mother’s love
Kangaroo Mother Care leads to better bonding between mother and baby, and empowers the mother, who knows instinctively that she is giving her baby superb nursing care for a secure and healthy future.

The video provides full details on why Kangaroo Mother Care works, and why it is so important for all newborn babies. It is intended for doctors and health workers dealing with healthy and “at risk” mothers-to-be, and for prospective mothers and fathers. Kangaroo Mother Care is now official government policy in the Western Cape, and is soon to be adopted by other provinces.

Order your copy of this life-changing video for R150 including VAT and postage.

Orders: The South African Medical Association
Private Bag X1, Pinelands 7430.
Tel (021) 531-3081, fax (021) 531-4126
E-mail: jsrydom@sammedical.org

---

References