Tracing Pharmaceuticals in South Asia

Draft working paper

Use and Abuse of Oxytocin:
Millennium Development Goals 4 and 5 in South Asia

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Millennium Development Goals 4 and 5 in South Asia
Patricia Jeffery and Petra Brhlikova (University of Edinburgh)

Abstract:
The appropriate use of oxytocin is directly linked to Millennium Development Goals 4 and 5 (relating to child mortality and maternal health). The Active Management of Third Stage of Labour (AMTSL) is central to Safe Motherhood initiatives and recommendations for AMTSL include the administration of oxytocin by intramuscular injection to prevent post-partum haemorrhage (PPH), a key cause of maternal mortality throughout the developing world. Yet these proposals seem to ignore the realities of access to and use of medicines in the Global South. Many drugs, including oxytocin, have lives independent of policy interventions.

In this paper, we argue that focusing on pharmaceuticals use ‘on the ground’ can illuminate some of the problematic relationships between labouring women’s experiences in the Global South and the policies put in place to ameliorate them. Our project and other studies in India and Nepal indicate that oxytocin is readily available in the region and that there is unmonitored use of oxytocin intrapartum in rural home deliveries. Such use can result in adverse outcomes, including uterine rupture and foetal asphyxia. During our project, we interviewed obstetricians working in small towns or with rural work experience who generally seemed familiar with this use of oxytocin; those working in large cities, however, were generally unaware of this practice. Some policy-makers in Delhi and Kathmandu also did not know about this use of oxytocin; others, though, argued that the risks were outweighed by the benefits of making oxytocin widely available for post-partum administration. Taking oxytocin as an example, we argue that there is an urgent need for policy-makers to engage with the everyday realities of drug availability and use in the Global South.

Note: A Technical Appendix summarising the clinical guidelines for the use of oxytocin is attached at the end of the paper.
Introduction

In many parts of the Global South, maternal mortality ratios (MMR) have remained stubbornly high, although they are declining (if only) slowly in most parts of the world. Estimates suggest that MMRs in Asia declined by nearly 20% between 1990 and 2005: but a fall of 5.5% per year was needed to meet the Millennium Development Goal 5 for MMR reduction (Hill, AbouZahr, Walker, Say, Inoue, & Suzuki, 2007). In northern India, for instance, MMRs were about 700-750 around 1990 (Bhat, 2002) but had only declined to 517 (95% confidence interval 461-573) by 2001-03 (Registrar-General India, 2006a). Similarly, some progress has been made in reducing rates of child and infant mortality in South Asia, but mainly in the post-neonatal period. Between 1992-93 and 2005-06, the post-neonatal infant mortality rate in Uttar Pradesh declined from 40 to 25 whilst the neonatal mortality rate declined from 60 to 48 (Griffiths, Hinde, & Matthews, 2001: 607; International Institute for Population Sciences (IIPS), 1995a, b and 2007; International Institute for Population Sciences (IIPS) and Macro International, 2007).

Since the 1987 Safe Motherhood Conference in Nairobi, various Safe Motherhood initiatives aimed at reducing maternal and perinatal morbidity and mortality have been proposed. They include the training of Skilled Birth Attendants, advocacy of institutional deliveries and the Active Management of Third Stage of Labour (AMTSL). AMTSL is considered vital for reducing post-partum haemorrhage (PPH), which is a key cause of maternal mortality throughout the Global South. For instance, estimates for India suggest that between 31% and 38% of maternal deaths are due to haemorrhage (Registrar-General India, 2006b: 17 & 15). Post-partum infections and unsafe abortions account for about 11% and 10% respectively. Globally, recommendations for AMTSL include the administration of either oxytocin (by intramuscular injection) or misoprostol (administered by pill) to prevent PPH. These have been echoed in South Asia in proposals that oxytocin should be more readily available in government rural health centres for use in AMTSL by the local-level government health workers, such as nurse-midwives whose responsibilities include dealing with labouring and parturient women.

Yet oxytocin is already widely available outwith the formal health care system in South Asia, even in apparently remote rural areas and there is widespread unmonitored intrapartum use of oxytocin to augment labour. Such use can result in adverse outcomes, including uterine rupture and foetal asphyxia. Indeed, it was this understanding that initially motivated us to include oxytocin in the Tracing Pharmaceuticals project. In this paper, we outline the availability and rural use of oxytocin before focusing on our interviews with obstetricians and the policy-makers. Taking oxytocin as an example, we argue that there is an urgent need for policy-makers to engage with the everyday realities of drug availability and use in the Global South.

Oxytocin availability in rural South Asia

Accounts of how drugs are introduced into the market often focus on misleading literature, incentives to prescribers, and trade advertisements, and the medical representatives we interviewed often talked about their strategies to encourage practitioners to adopt particular drugs—free samples, opportunities for continuing medical education or to attend conferences, for instance. Such strategies may have been relevant when synthetic oxytocin was marketed after it was first synthesised in the 1950s. But our interviewees’ memories did not stretch that

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2 Space does not permit us to discuss misoprostol use in AMTSL.
far back and we do not know how oxytocin was initially marketed in South Asia. Nowadays, however, medical representatives in urban and rural settings alike say that they do not actively promote oxytocin—mainly because oxytocin sells steadily to urban clinics, small town pharmacies and so forth. At some stage, oxytocin sales have become sufficiently buoyant for producing companies not to perceive any need for high-profile and energetic marketing strategies. Our interviews with wholesale stockists and retailers endorse this interpretation. Our interviews and some spot checks on stocks in retail outlets, also indicated that oxytocin is well known and routinely kept in stock, by wholesalers and retailers alike. Table 1 lists the brands of oxytocin marketed in India, their producers and prices: all are locally manufactured.

We could not do a comprehensive study of oxytocin availability, but it can be readily obtained in disparate places, whether retail outlets near urban nursing homes and hospitals offering delivery facilities or small pharmacies in towns remote from large towns. Moreover, oxytocin can easily be purchased over-the-counter (as our research assistants did several times), despite being a prescription-only drug.

Table 1: Oxytocin brands available in India

<table>
<thead>
<tr>
<th>Brand name</th>
<th>Producer</th>
<th>Format</th>
<th>Price per pack</th>
<th>Price per 1ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evatocin</td>
<td>Neon Labs</td>
<td>INJ</td>
<td>Rs153.00</td>
<td>Rs15.30</td>
</tr>
<tr>
<td>Foetocin</td>
<td>TTK</td>
<td>INJ</td>
<td>Rs13.00</td>
<td>Rs13.00</td>
</tr>
<tr>
<td>Gynotocin</td>
<td>ACE (Svizera)</td>
<td>INJ</td>
<td>Rs14.87</td>
<td>Rs14.87</td>
</tr>
<tr>
<td>Indox</td>
<td>Ind Swift</td>
<td>AMP</td>
<td>Rs14.30</td>
<td>Rs14.30</td>
</tr>
<tr>
<td>Oxybro Inj</td>
<td>Cadila (Vibra)</td>
<td>INJ</td>
<td>Rs15.00</td>
<td>Rs15.00</td>
</tr>
<tr>
<td>Oxystar</td>
<td>Cadila (Genstar)</td>
<td>INJ</td>
<td>Rs17.00</td>
<td>Rs17.00</td>
</tr>
<tr>
<td>Oxytocin Inj</td>
<td>Prem Pharma</td>
<td>INJ</td>
<td>Rs13.50</td>
<td>Rs13.50</td>
</tr>
<tr>
<td>Oxyton-5</td>
<td>Inga</td>
<td>INJ</td>
<td>Rs12.00</td>
<td>Rs12.00</td>
</tr>
<tr>
<td>Pitocin</td>
<td>Pfizer</td>
<td>INJ</td>
<td>Rs15.60</td>
<td>Rs15.60</td>
</tr>
<tr>
<td>Syntocinon</td>
<td>Novartis</td>
<td>INJ</td>
<td>Rs57.20</td>
<td>Rs11.44</td>
</tr>
</tbody>
</table>

Source: CIMS India July-Oct 2006

Note: The dosage varies across products, with the majority containing 5iu/ml; Oxybro Inj contains 5iu/5ml, and Pitocin is available in the two dosages (5iu/ml and 5iu/5ml) at the same price. The dose is not known for Oxytocin Inj by Prem Pharma.

Oxytocin, then, already has a significant life outwith the realm of government policy and provision—indeed, a life that is also beyond its purview. As with fluoxetine, one of the other ‘Tracing Pharmaceuticals’ drugs, the very existence and availability of oxytocin drives its use, often with unintended consequences. But how much does this matter? Many studies in South Asia have shown that the bulk of health care is provided by private practitioners of various kinds—trained in various medical traditions or none—operating outwith the formal and government health care system. Given the government sector’s lack of capacity, perhaps the

3 We have been unable trace data that provide overall information for South Asia on oxytocin sales over time, so we cannot comment on these assessments.

4 Recommendations for the intramuscular injection of oxytocin in AMTSL are for 10iu and pharmaceutical companies might market oxytocin in such dosages in the future: this would provide room for confusion and quite possibly for even more dangerous use of intrapartum oxytocin.

5 We could not conduct a systematic study of how drugs were transported and stored. This aspect merits further work for heat-labile drugs such as oxytocin since turnover and seasonality may impact on the efficacy of drugs.
private sector plugs an important gap in provision. In this case, though, oxytocin is being administered in circumstances that give rise to considerable disquiet.

**Intrapartum Oxytocin use in rural South Asia**

Although the clinical evidence is not always completely clear-cut, guidelines suggest that oxytocin should be administered intrapartum very cautiously and only under specific conditions (see Technical Appendix for more details). The WHO practical guide from 1996, for instance, explicitly warned against the *intramuscular* administration of oxytocin because it is harmful for the foetus and increases the risk of uterine rupture. The guide also recommended that oxytocin augmentation should be restricted to labours supervised by obstetricians and to facilities that provide surgical services and (whenever possible) foetal surveillance by electronic monitoring (WHO, 1996). More recent WHO guidelines recommend either oxytocin IV infusion for labour augmentation, with the precautions outlined above (WHO, 2003a), or that oxytocin only be used for the prevention of PPH in the third stage of labour (WHO, 2003b).

Table 2 summarises the clinical guidelines for intrapartum oxytocin use and how oxytocin is being used intrapartum in rural home deliveries in South Asia. In themselves, home deliveries flout the guidelines, since the recommended monitoring cannot achieved. Moreover, oxytocin is generally administered by intramuscular injection to augment labour. A few studies indicate how frequently oxytocin is used, whilst others merely indicate that its use is commonplace and well-known. A study conducted in twelve Uttar Pradesh districts found that oxytocin was administered in 48.2% of home deliveries (n=2,992) across the state (ranging from 74.7% in Muzaffarnagar to 16.7% in Chitrakoot). Almost two-thirds of the women reporting injections had had more than one. Traditional birth attendants (TBAs) and auxiliary nurse-midwives (ANMs) were the primary decision-makers for using the injection (29.8% and 29.6% respectively) and informal private practitioners and ANMs were the primary injection service providers (48.2% and 32.8% respectively) (Das et al., 2005). A study in rural Kanpur reported similar patterns of use, although absolute levels were lower (23%, n=527), and there was a statistically significant relationship between injection use and the presence of a provider (trained or otherwise) (Sharan et al., 2005). Research in two villages in Bijnor district, western Uttar Pradesh, indicates that between 1983 and 1987, oxytocin was being administered in about 15% of deliveries (n=237) by the government pharmacist as part of his (illegal) private practice (Jeffery, Jeffery, & Lyon, 1989:111-112). In 1998–2002, oxytocin injections were administered by untrained private rural medical practitioners (male) in 48% of deliveries (n=346) (Jeffery & Jeffery, 2008: 72). In the early 2000s, these practitioners charged between Rs100 and Rs150 per injection, a considerable mark-up on the retail price of around Rs20 for a phial of 10IU of oxytocin, but not prohibitively expensive even for poor families. A Karnataka study reports that ‘injections to increase pains (probably oxytocics) were injected in 21% of all home deliveries, including 51% of those attended by government auxiliary nurse-midwives (Matthews, Ramakrishna, Mahendra, Kilaru, & Ganapathy, 2005:397; Ramakrishna, Ganapathy, Matthews, Mahendra, & Kilaru, 2008: 96; see also George, Iyer, & Sen, 2005 for a report on elsewhere in rural Karnataka). Similarly, writing about rural Rajasthan, Iyengar notes that intramuscular oxytocin injections are ‘widely used’ intrapartum (Iyengar, Iyengar, Martines, Dashora, & Deora, 2008: S27), whilst Van Hollen describes its use as ‘almost routine’ for the local multi-purpose health worker during home
Table 2: Intrapartum Oxytocin Use: Clinical guidelines and practice in rural home deliveries in South Asia

<table>
<thead>
<tr>
<th></th>
<th>Clinical guidelines</th>
<th>Rural home deliveries in South Asia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Parity</strong></td>
<td>Normally only for nulliparous women (to reduce risk of uterine rupture)</td>
<td>Multiparous women often receive oxytocin, although oxytocin use is more common among primagravidae (Das, Agarwal, Tripathi, &amp; Parveen, 2005; Sharan, Strobino, &amp; Ahmed, 2005). In the 2002-4 Bijnor study, Patricia and Roger Jeffery found that 62.3% of primagravidae (n=53) (whose labours can normally be expected to be longer than others) received injections, compared with 45% of women of higher parities (n=293) (unpublished data).</td>
</tr>
<tr>
<td><strong>Examination prior to administration of oxytocin</strong></td>
<td>After exclusion of all at-risk women, examination to ensure that administered only to women already in labour, with one foetus in vertex position</td>
<td>TBAs generally do external examinations but do not necessarily ascertain cervical dilatation before oxytocin is administered; male practitioners generally perform no examinations; thus neither stage of labour (first or second) nor presentation of foetus are necessarily ascertained. Several women in the Bijnor study reported foetal breech or transverse presentations that were not diagnosed before the administration of oxytocin.</td>
</tr>
<tr>
<td><strong>Mode of administration</strong></td>
<td>Cautious &amp; monitored administration by intravenous infusion, which can easily be stopped</td>
<td>Intramuscular injection (sometimes more than one); effective dose cannot be ascertained or regulated</td>
</tr>
<tr>
<td><strong>Monitoring the woman &amp; foetus during oxytocin administration</strong></td>
<td>Regular vaginal examinations, monitoring of contractions, mother’s blood pressure &amp; foetal heart rate etc. to detect uterine hyperstimulation or foetal distress</td>
<td>TBAs may perform internal examinations but they and rural practitioners do not use monitoring equipment to detect foetal distress, assess frequency &amp; strength of contractions or measure mother’s blood pressure etc. after oxytocin administration</td>
</tr>
<tr>
<td><strong>Setting/availability of emergency facilities</strong></td>
<td>Recommended only for deliveries in institutions with adequate equipment to deal with obstetric emergencies (such as might entail a Caesarean section)</td>
<td>No equipment in rural homes for dealing with small/weak babies (resuscitation equipment, incubator etc.), &amp; no operating facilities (anaesthesia, blood bank etc.); taking labouring women elsewhere presents problems of transport, time &amp; distance</td>
</tr>
</tbody>
</table>

**Note:** The points listed in the right hand column of Table 2 are probably widely applicable in South Asia although few of the studies cited in the text explicitly mention them. This listing draws mainly on research on childbirth in Bijnor district (western Uttar Pradesh) conducted by Patricia Jeffery and Roger Jeffery (funded by Social Science Research Council [now Economic and Social Research Council] in 1982-3 and 1985 and by Wellcome Trust in 2002-4).
deliveries in Tamilnadu (Van Hollen, 2003a, b). Bang, Bang, Baitule, Reddy, & Dashmukh (2005) report that in rural Maharashtra oxytocin injections were administered in between 21.2% and 23.1% of the cases they studied (by unqualified private practitioners) and that they raised the risk of birth asphyxia and stillbirth threefold. Similar usage was acknowledged in personal communications from colleagues in Bangladesh and Pakistan (Jeffery, Das, Dasgupta, & Jeffery, 2007). Similar use has been documented elsewhere, including in Sudan and Guatemala (Lovold, Stanton, & Armbruster, 2008). Oxytocin may also be used intrapartum in urban home deliveries: a study in a poor area of Delhi reported oxytocin use in 68.9% of home deliveries, administered by private ‘doctors’ in 86.8% of cases (Caleb, 1995).

During the Tracing Pharmaceuticals project, our interviews with rural practitioners (mostly untrained and working in a private capacity) also indicated that they are very familiar with oxytocin and that some routinely administered it by IM injection to augment labour. A few talked about the dangers of using oxytocin in home deliveries, but many administered oxytocin in circumstances comparable to those outlined above, generally at the behest of the labouring woman and/or her female attendants, or because the TBA recommended its use.

One additional feature of oxytocin is its cultural acceptability. In local understandings of pregnancy, a woman’s body becomes increasingly ‘hot’ (in the humoral sense) until uterine contractions are sparked off. According to the Bijnor study, desī [folk] methods of ‘heating’ a woman’s labour—‘heating’ drinks such as tea containing unrefined sugar, loosening her plaits, unlocking padlocks etc.—were still common in the early 1980s (Jeffery et al., 1989: 103ff.). They had almost disappeared by the early 2000s and village women and their attendants regarded intrapartum oxytocin injections as the most effective method of speeding labour, especially in labours perceived to be lengthy and in which the contractions had ‘cooled’ (become infrequent or less intense). They were popular with women wanting their labour to end quickly and many women had several injections within a few hours. They called these injections dard barhåne kå tikkå [pain/contraction enhancing injection]. Other sources talk of garmī ri huï (Iyengar et al., 2008: S27) or garmī ki suî [heating injection], and other variants on the theme are widespread in the region. Further, as many sources suggest, hyperdermic needles are powerful icons of ‘modernity’. Based on her study in rural Sitapur [UP], Pinto argues that injections enable local practitioners to re-assert their quasi-institutional authority through association with modern biomedicine (Pinto, 2004, 2008). In line with this, Das et al. found that intrapartum oxytocin use was greatest among women of higher socio-economic status and the relatively more educated, suggesting that it was used less because of need and more because of ability to pay and an association with ‘modernity’ (Das et al., 2005).

This evidence suggests that intrapartum oxytocin use is in rural home deliveries departs in several important ways from the recommended precautions that we outlined above. More work is required to establish how commonplace such use is and to assess its impact on rates of maternal mortality, stillbirths and neonatal mortality and morbidity.

**Urban obstetricians and oxytocin**

What surprises us, however, is how little concern has emanated from the professional and policy circles that are closely involved with issues of reproductive and child health. How far do urban professionals, for instance, appreciate what is happening in the rural hinterland? During our project, we interviewed obstetricians in Delhi, Lucknow, Bijnor, Kolkata (India) and Kathmandu, Butwal and Tansen (Nepal). On that basis, we conclude that obstetricians working in smaller towns and those who had work experience in rural or small town settings were generally aware of unmonitored intrapartum use of oxytocin in rural home deliveries.
For example, an obstetrician at the government District women’s hospital in Bijnor called oxytocin the ‘spinal cord of our speciality’ and outlined its use in her current practice. She then commented on labouring women coming to the hospital from the rural hinterland who had been ‘handled’: such women talk about having a ‘garm [hot] injection’ which she described as a ‘wrong use of medication’, sometimes given even to women with a ‘previously operated delivery’ because the TBAs do not know the complications. Some labouring women had also begun arriving having had misoprostol inserted in their vagina without their knowledge:

So in that way, oxytocin was better known because it was injectible and people could tell us that “yes, they have given some injection” and we could know that she has been handled. With the tablet of misoprost, sometimes it becomes … difficult to know the patient has been handled or not [PJ: Yes] and in what way we should manage. So in a way I think this drug [misoprostol] is being used badly by some quacks, the persons who does not know the ABC. They are not the paramedical staff, neither paramedical staff, because paramedical staff got training—they know something or the other about this. So these days, especially since last one or two months, I am receiving the cases from the rural area though they are 99% handled. [24 October 2007 Bijnor]

In a large government hospital in Kolkata, a male obstetrician nearing retirement talked about his 18 years working in rural West Bengal, beginning in 1976: ‘Absolutely interior parts. And there we used to get cases of ruptured uterus [PJ You did?] Ruptured uterus only because of giving these injections’, a practice which he said has declined in the recent past since there are more qualified practitioners now in rural Bengal. Another Kolkata obstetrician who had seen cases of complications caused by intrapartum oxytocin injections during his rural employment confirmed that the use of oxytocin injections had declined in rural West Bengal in recent years and said this was because villagers were more prepared to seek an institutional delivery if the labour became complicated. [Interview, 16 Nov 2007]

Several obstetricians working in Butwal (Nepal) also talked about intrapartum oxytocin injections in the local rural areas. One commented:

Yes, there are a lot of cases and that is misuse of oxytocin. Because those who are not trained enough … for instance, people who do not have the knowledge as to what complications can arise due to the use of oxytocin or on which cases oxytocin should only be administered … they use it for delivery and even some people give oxytocin IM … or even administer bolus dose IM which have led to intrauterine foetal death or even uterine rupture … we have come across such cases. [15 January 2008 Butwal]

When asked if the guidelines for oxytocin use had not been followed, he retorted:

In the hospitals, protocols regarding the use of oxytocin have been adhered to, but not outside the hospital in outlying areas. In the outlying areas what protocols are there? … Well, what protocols have been maintained outside the hospital in Nepal, you tell me? [15 January 2008 Butwal]

When asked if people administering oxytocin in the rural areas were trained health workers who had learnt about oxytocin from hospital doctors, he commented:

6 Similarly, during the Bijnor project in 2002-4, doctors running private nursing homes and clinics in the town often admitted ‘handled cases’—labouring women whom they considered had been ‘mishandled’ by dāīs [TBAs] and rural practitioners.
More than the health personnel like CMAs and ANMs, the ones who are doing it are “non-medical practitioners” for instance, quacks, those who are called “jhole [cloth bag] doctor” or those who have learnt to give injections, especially “jhole doctors” in the Terai region who carry drugs in their bags [jholā] and go from one house to another. These people have been administering oxytocin IM and cases of rupture have come. And these people are using it since it’s the lack of knowledge of those villagers in those outlying areas of the Terai belt. [...] From the hills it is usually cases of obstructed labour. But more cases of unregulated use of oxytocin use usually comes from the Terai belt. [15 January 2008 Butwal]

Obstetricians with rural experience are thus well aware of oxytocin (mis)use but obstetricians in the larger metropolitan cities, however, generally seemed unaware that IM injections of oxytocin are sometimes administered intrapartum in rural home deliveries. Some denied that oxytocin would even be known or available in rural areas. In several interviews, Patricia had to repeat herself to emphasise that she was asking about IM injections, as several interviewees did not initially absorb Patricia’s account and simply assumed that the oxytocin was being administered IV. In a couple of cases, the interviewee summoned junior colleagues who had rural experience and asked them to confirm our view that oxytocin is both available and used in the rural areas.

Systematic evidence about intrapartum oxytocin usage in institutional deliveries in the region is hard to come by. The urban obstetricians we interviewed strongly advocated the ‘active management of labour’ (AML, i.e. first and second stage before the baby is born). They took intrapartum oxytocin use for granted as routine, normal and appropriate in their repertoire of interventions, the drug of choice for augmenting labour. The obstetricians, including those nearing retirement, said that they had learnt about oxytocin during their medical training and that its intrapartum use had been widespread throughout their working lives. Several obstetricians provided off-the-cuff estimates of intrapartum oxytocin usage in their institutions—sometimes upwards of 70%. Some of this apparently high usage might be because a high proportion of institutional deliveries are difficult labours. Nevertheless, oxytocin was also being used in pre-booked deliveries, which suggests a more routinised use, even when labours are progressing normally. A senior midwifery lecturer in Delhi described her arguments with staff at the Safdarjang Hospital—the government hospital where her trainee midwives received their practical training—when she wanted her students to experience ‘normal deliveries’. The hospital staff said they routinely administered oxytocin to all women in the labour wards because of pressure of numbers: women’s labours could not be protracted, because of bed shortages and a rapid through-put needed to be maintained. [Interview, 10 March 2007] Our own observational data (e.g. from two sessions of several hours each observing the labour room of a large teaching hospital in Kolkata), also suggest that oxytocin is used in a large proportion of institutional deliveries. We cannot, however, adjudicate on whether this level of usage is over and above what might be classed as ‘medical need’.

In addition, AML is high profile in obstetrics circles in contemporary India. For instance, Daftary and colleagues have produced ‘an indigenously developed protocol of labour management’ (Daftary, Desai, & Nanavati, 2003), whilst Dr Shyam Desai, in his presidential address to the Federation of Obstetric and Gynaecological Societies of India (FOGSI), placed AML—including labour acceleration using oxytocics—at the heart of Safe Motherhood initiatives in India (Desai, 2005). The use of oxytocics for augmentation is part of ‘programmed labour’ discussed in several sources (e.g. Meena, Singhal, & Choudhary, 2006; Yuel, Kaur, & Kaur, 2008).
Whilst we cannot be definite, intrapartum oxytocin use seems to be very common and highly valued in institutional deliveries in the region. Why this might be remains uncertain. Several interviewees had been told during training that its use was appropriate. Oxytocin use may be a form of ‘crowd control’ to ensure that labour room beds are vacated quickly (cf. Van Hollen’s discussion of busy hospitals in Chennai city: Van Hollen, 2003a, b). The Bijnor obstetrician cited above suggested that intrapartum oxytocin use enables (private) doctors to regulate the time when women deliver: ‘Because everything is money-oriented exactly. They want to work in day, take rest in night. [24 October 2007 Bijnor] And in the Bijnor research in 2002-4, lay people frequently (and cynically) suggested that the financial interests of non-government health care providers lead them to administer drugs (or conduct even more lucrative Caesarean sections). Perhaps for several reasons, intrapartum oxytocin use seems to be normalised in institutional deliveries in the region.

Moreover, it seems that the clinical guidelines for intrapartum oxytocin use are not necessarily being followed in urban institutions. Writing about Karnataka, Matthews et al. comment: ‘[m]ore than 90% of all women, and more than 75% of women with no complications, were given repeated injections or intravenous infusions of oxytocics to hasten labour. Women in private and mission hospitals were more likely to have a doctor present during the delivery, but even here most women received repeated injections of oxytocics to speed up labour’ (Matthews et al., 2005: 399 our emphasis). An unpublished study in Jamshedpur also found that oxytocin use was routine in two hospitals (one government, one run by Tata), administered by different grades of staffs, sometimes IV but sometimes IM. In the government hospital, women received very little attention or monitoring, whereas monitoring was routine in the Tata hospital (Judith Sim, personal communication, 12 March 2009). During our observations of procedures in a Kolkata teaching hospital, women admitted to the labour ward were examined (to assess cervical dilatation and the baby’s presentation) and most were straightaway attached to IV saline drips containing oxytocin. Thereafter, checking of the drip, internal examinations, foetal heart monitoring etc. were done infrequently and at irregular intervals. There was no continuity of care. Labouring women were left to their own devices, often two to a bed, whilst staff spent much of their time congregated at a desk at one end of the ward. Discussing institutional deliveries and the incidence of neonatal encephalopathy in Kathmandu, Ellis comments that ‘the most striking potentially preventable risk factor for adverse outcome’ was ‘induction of delivery’ using oxytocin infusion (Ellis, 1999: 167; see also Ellis, Manandhar, Manandhar, & Costello, 2000). Similarly, although the evidence is sparse and unsystematic, intrapartum oxytocin use in hospital deliveries in low-income countries seems to be associated with enhanced risks of stillbirth, neonatal resuscitation, neonatal deaths and uterine rupture (Lovold et al., 2008). In brief, institutional deliveries are no guarantee either of quality of care or of safety.

Beyond this, we must consider the linkages between urban institutions and the widespread intrapartum use of oxytocin in rural deliveries. Most of the obstetricians we interviewed were strikingly incurious about how oxytocin use might have become widespread in the rural areas. We have been unable to tap into any firm historical accounts. Several participants at the Tracing Pharmaceuticals inception workshops in Delhi and Kathmandu suggested that the widespread use of bovine oxytocin to enhance milk production might be crucial. Bovine oxytocin is readily available over-the-counter—but would TBAs and rural practitioners make the connection between oxytocin use to enhance milk production and its use in augmenting women’s labour?

A more plausible account—proposed by several interviewees—is the connection between rural medical practitioners and urban facilities. For instance, one commented that many
providers in the periphery—‘jholā chhāp’ practitioners—had worked in urban facilities, where they learnt by observation. They would have seen oxytocin being administered, and for them ‘ignorance is bliss’—they would know nothing about the side-effects. She said that very high doses are often administered. [9 March 2007 Delhi] Similarly, when asked how rural practitioners learned about oxytocin, one Kolkata obstetrician initially said ‘They took this lesson from these veterinary doctors. In cows’ delivery they used to give oxytocin injection intramuscularly, just to hasten the delivery.’ But when Patricia asked him to elaborate, he commented:

They learnt it mostly from MBBS doctors. You see, I have seen it, let me admit, even in medical colleges. I have seen people … in the last stage, in the end stage of the second stage of labour during delivery, just to hasten it, just to quicken, hasten the thing, they used to give a bolus injection of oxytocin. They [rural practitioners] learnt it basically from MBBS doctors, and to some extent also from the veterinary doctors, that giving the injection, this injection hastens the delivery. [23 Nov 2007 Kolkata]

Many rural medical practitioners have no formal medical qualifications. Others have training in Ayurveda, Unani or homeopathy, but their practice usually includes, or is even dominated by, cosmopolitan remedies. Rural practitioners have often had previous urban employment as compounders (pharmacists), ward boys etc. in urban facilities: they probably learnt their trade primarily by observing clinical practices there and adopted them in their rural practices. Interviews with rural practitioners also indicate that they maintain relationships with urban facilities, often accompanying labouring women whom they refer there (in the 2002-4 Bijnor study, villagers alleged that they take a commission for doing so). There are, then, many opportunities for them to observe oxytocin use in urban facilities.

If urban usage fails to follow clinical guidelines, rural practitioners are unlikely to appreciate the dangers of administering oxytocin IM in situations where they cannot adequately monitor the labour’s progress or provide emergency back-up care if matters go awry. Indeed, even if urban practices do follow clinical guidelines, rural practitioners might not emulate them if they are unaware of the rationales for them. In sum, the enthusiasm of MBBS doctors for using (and sometimes misusing) oxytocin intrapartum in urban nursing homes and hospitals probably leads directly and indirectly to its use and misuse in the rural areas—a series of unintended consequences that the urban practitioners we interviewed were generally unwilling to acknowledge.

Oxytocin in the policy domain

The National Family Health Survey (NFHS)—the main source of national-level information about pregnancy, delivery and post-partum care in India—has collected nothing on intrapartum oxytocin use in its 1992-1993, 1998-1999, and 2005-2006 rounds. Similarly, no question about intrapartum oxytocin use was included in the questionnaire for a study of local delivery practices and neonatal care conducted during 2006-7 in UP (among other states) and sponsored by the Sector Investment Programme by Government of India in partnership with the European Commission—the ‘Concurrent Assessment of Health and Family Welfare Programs and Technical Support to Districts of Uttar Pradesh’.

Similarly, policy documents advocating AMTSL are silent about intrapartum oxytocin use and the widespread availability of oxytocin outwith the state sector in India. For example, proposals for preventing PPH and encouraging AMTSL were launched in Delhi in February 2007. A MacArthur Foundation grant had enabled White Ribbon Alliance-India (WRA-I) to collaborate with the Ministry of Health and Family Welfare, UNFPA, UNICEF, WHO India,
the Federation of Obstetric and Gynaecological Societies of India (FOGSI), the Trained Nurses Association of India (TNAI) etc. to produce *Promoting Skilled Attendance at Birth in India – A Brief Report* that outlined the guidelines and protocols for an essential package for maternal and child health under the Reproductive and Child Health-II programme. Proposals included increasing the availability of skilled attendance at birth and access to EmOC [emergency obstetric care]. A crucial innovation would permit auxiliary nurse-midwives (ANMs) to perform several procedures hitherto (supposedly) forbidden to them, for instance administering injections, including oxytocin to manage PPH. Gaining agreement to this proposal had entailed complex brokering between medical profession representatives (who generally opposed it) and nursing representatives (who favoured it). At the report launch, several speakers acknowledged that ANMs attend only a small minority of rural births in many parts of India and that training Skilled Birth Attendants (SBAs) to provide full coverage would take years. In one-to-one conversations later, several participants acknowledged that oxytocin is already being widely administered intrapartum in rural India and that this is a risky practice. One person involved in writing the WRA-I report said that some concerns had been raised during the preparatory meetings about whether ANMs should be supplied with oxytocin because of worries about its potential for misuse in rural areas (as well as about storage issues and the need for sterile needles). Ultimately, however, oxytocin was included in India’s AMTSL package because it is considered more efficacious than misoprostol in arresting PPH. [9 March 2007 Delhi]

During our interviews in Delhi and Kathmandu with people working in organisations such as WHO, UNICEF, UNFPA with interests in reproductive and child health, some expressed surprise when we asked about intrapartum oxytocin use in rural home deliveries. One insisted that oxytocin was being used in rural Nepal only during third stage of labour: staff had been told never to administer oxytocin during pregnancy and MCHWs had been trained to use it only in the third stage. She said she ‘would like to believe this is what happens’ but admitted she did not have the ‘intelligence’ to suggest otherwise and had not been able to go to villages herself [14 Sep 2007 Kathmandu]. Several other interviewees, though, were aware of intrapartum oxytocin use in the rural areas. One said:

In fact all of us have been aware that people do … I mean it [oxytocin] has been misused. But then I think the kind of ideal condition would be to empower and to train our health workers because as obstetricians and as MBBS doctors also we are all so scared of giving oxytocin. Like if it is only 2 units we would not be able to go beyond 2 units. I think it’s just ignorance, ignorance about the complications that could arise out of, you know, such inadvertent use of oxytocin that is leading people to, kind of you know, to misuse it. So while we train our health workers, while we educate them on each and every aspect of skilled birth attendance, I think this thing needs to be kind of reiterated, you know, as to how some women have actually died because of uterine rupture and other complications which arose because the attendants were not sure of, but were actually misusing drugs like oxytocin. [PJ: Yes, yes ] But then there have been so many drugs, for that matter you know, which have been misused and one good strategy, and the only strategy is to actually equip people with knowledge about the use as well as about the side effects … [20 March 2008 Delhi]

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7 In some regions of India (especially the north), very few delivering women have trained attendants at all, whereas institutional deliveries are more common in the south. Thus generalisation is probably rather misleading.
Another said issuing oxytocin to community-level workers in government service to prevent or arrest PPH would pose no additional problem since its use would be restricted to institutional deliveries:

But the fact of the matter is that in the Government of India programme there was a conscious decision that in outreach settings where an ANM is delivering at home in certain situations or in sub-centres where she is not under the medical doctor’s supervision, the misoprostol remains the drug of choice [for PPH] because the stability and the whole issues of management. But wherever she is in institutions, if she is delivering a baby in a primary health centre under doctor’s supervision, there are other nurses around then the oxytocin remains the drug of choice. And we have the experience from other countries from Indonesia, from Africa and other places where the community-based workers have been providing misoprostol successfully. So I think there should not be much of a problem there and gradually in India the focus is being given to institutions so we are safely covered over there. But for interim misoprostol is there … still prevents the PPH. [31 March 2008 Delhi]

Another considered that the safety issues raised by intrapartum oxytocin use in rural deliveries must be evaluated in relation to maternal mortality due to PPH:

It’s already there. We know that it’s already there. [PJ: Within the institutions?] Within institution, outside institution. There is a large malpractice or illegal use of these substances. … You see this [oxytocin for management of PPH] is a good concept but reality in a way is far ahead. We do have oxytocics’ use for abortion and illegal abortion or oxytocics in India, particularly in rural India, by so called Rural Medical Practitioners or quacks for a cost to let women abort. Now, how do we deal with this? This is an important issue for further evidence or research. But certainly it’s inconsequential when we have to deal with the issue of maternal mortality and particularly again both the third stage management or the treatment of PPH. [PJ: By that you mean it’s more dangerous not to have oxytocics available?] Obviously. [PJ: Because the real problem is maternal mortality?] Exactly. [24 March 2008 Delhi]

Later in the same interview, we mentioned a neonatologist whom we had interviewed in Kolkata who was concerned about the effects of intrapartum oxytocin use on the unborn baby, for instance, causing asphyxia or increasing bilirubin levels in the brain:

We very much share this concern. Nevertheless, we need also to look case by case. This is a medical intervention. It is in a way demystified by a policy decision with the intention to tackle a very important point which is again complications of third trimester. … What comes first, difficult to say, right? Scientifically I had to share this concern he [neonatologist] has. Misuse of oxytocin certainly increases stillbirth or intrauterine death, certainly increases risk of hyper-bilirubinia and very important brain damage in children, particularly low birth weight or very low birth weight, particularly that proportion of children below 1500 gms. It’s a very difficult decision to make. Again I would specify, instead of largely advocating the use of injectible oxytocin, I would restrict, probably, to the advocacy of widely practising and using oxytocins within the facility and the medical supervision if possible. [24 March 2008 Delhi]

Conclusions

Maternal mortality (and morbidity) has catastrophic effects on household wellbeing, with children orphaned and the loss or incapacity of adult workers. Equally, child mortality—here
especially stillbirths and perinatal deaths—almost certainly means that women undergo more pregnancies than they might otherwise, with the associated risks of maternal mortality or ‘depletion’. The enduringly high levels of maternal and child mortality in many countries of the Global South are reflected in the MDGs 4 and 5—which most countries in South Asia will probably not attain. Clinical guidelines for intrapartum oxytocin use suggest that it should be administered extremely cautiously and only under certain circumstances because of the potential risks to mother and baby. These guidelines, however, are often flouted in South Asia in home institutional deliveries alike. Of course, oxytocin misuse is not the only serious issue at stake for Safe Motherhood. Yet oxytocin provides a window on issues that have been inadequately addressed in the plethora of proposals and programmes to combat maternal and child mortality.

First, despite new funding streams, systemic incapacities of government health care provision will remain, almost certainly for years to come. Institutional deliveries supervised by Skilled Birth Attendants are seen as the prime means of attaining Safe Motherhood goals—yet the majority of births will not plausibly meet the criteria of ‘safe’ within the foreseeable future. SBA training programmes in India would anyway have taken years to meet their target levels—but they have been slow to get moving. There are simply not enough institutional beds to accommodate all labouring women—whilst in remote areas, such as hilly areas in Nepal or central India, it would be impossible to ensure that all women can reach institutions and have ‘safe’ deliveries in a timely fashion. In any case, institutional deliveries as they are currently practised cannot always be deemed ‘safe’ according to the criteria set by WHO and others: the rampant and careless use of oxytocin intrapartum is just one of the many problems endemic in institutions. Thus institutional deliveries with SBAs are unlikely to prove the panacea that they are proclaimed to be. To be realistic, women in South Asia (in many areas, the vast majority of women) will continue to deliver their babies at home—and much greater attention must be paid to ensuring ‘safe’ motherhood in home deliveries.

Our second point follows from this: public documents proposing the PPH management with IM oxytocin injections do not mention intrapartum oxytocin use outwith the state health care sector. Yet our research makes clear that many drugs, including oxytocin, have existences independent of policy interventions—indeed, existences known to some of the actors involved in creating Safe Motherhood proposals. Policy documents, however, tend to present government programmes as if they are hermetically sealed from the wider world in which they are embedded. The failure to address and comprehend the ground realities beyond the purview of government programmes threatens to jeopardise many policy interventions. In reproductive and child health, a huge range of activities takes place beyond the government sector or the programmes that are financed by overseas donors, NGOs and the like. Put another way, there is a lively market in health care and in the distribution of drugs. The private sector in health care provision is huge and diverse and, of course, inflected with market incentives and the imperative to make money. For these very reasons, it should not be rendered invisible in policy interventions. Indeed, the implications of the health care market for Safe Motherhood initiatives must be addressed if policy interventions are to have their hoped-for impact. If most women in South Asia will continue to deliver outwith the government sector, attempts to reduce maternal and infant mortality rates must acknowledge the ground realities.

On their own, then, Safe Motherhood initiatives cannot guarantee that motherhood will become safer, because they do not address the wider context in which women undergo childbearing. But can mechanisms be put in place to guarantee that home deliveries (as well as institutional deliveries, whether in private nursing homes or in the government sector) meet
the safety criteria of Safe Motherhood initiatives? Tackling this question would require thinking through how to establish and sustain a plethora of regulatory systems encompassing the marketing and distribution of drugs (such as oxytocin) and the supervision and monitoring of medical practitioners of various kinds even in remote rural areas. Suffice it to say here that this is a crucial element in any attempt to protect labouring women from exposure to unsafe birthing practices and to ensure that safe obstetric care is provided to all women wherever they live and give birth.

Tracing pharmaceuticals ‘on the ground’ and understanding how they are embedded in wider social and economic contexts provides an important entry point for analysing the extremely problematic relationships between the conditions of reproductive and child health in the Global South and the policies put in place to ameliorate them. Starting from how drugs are actually being used raises many challenging questions about whether programmes developed at the national and even global level will meet with the success that their proponents desire.

**Bibliography:**


Technical Appendix:

Clinical Guidelines for the use of Oxytocin

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Oxytocin is a natural hormone with uterine stimulant properties. It was described and first synthesised by Du Vigneaud in 1953 (Mousa & Alfirevic, 2007). In the late 1960s O’Driscoll advocated the use of oxytocin intrapartum as a component of ‘the active management of labour’ (AML) package aimed at limiting the length of labour in nulliparous women (O’Driscoll & Meagher, 1980). Later, oxytocin was found to be effective in preventing and controlling PPH in the third stage of labour (Prendiville, Elbourne, & McDonald, 2000). In addition to its intrapartum and postpartum use, oxytocin is also used to ‘abort the fetus in cases of incomplete abortion or miscarriage’ (www.drugs.com accessed 25/09/07). Here we review the clinical evidence and guidelines related to oxytocin use to augment labour (in first and second stages) and to prevent and treat PPH in the third stage of labour.

**Oxytocin in the intrapartum period**

Augmentation of labour is performed to increase the frequency, duration and strength of contractions. In the first stage, the intention is to cause the cervix to dilate and in the second stage, to cause the head to descend. The clinical guidelines formulated by O’Driscoll and Meagher for oxytocin use within the active management of labour (AML) were based on their 14-years of practising AML in the National Maternity Hospital in Dublin (O’Driscoll & Meagher, 1980). Apart from the use of oxytocin, the AML package includes a strict definition of labour, amniotomy and continuous support during labour. To avoid potential risks associated with the use of oxytocin, their recommendations considered several factors:

1. **Parity:** Augmentation of labour by oxytocin was recommended only for nulliparous women. In multiparas, inefficient uterine action is rare and slow progress of labour is more likely to be associated with other causes (e.g. foetal malpresentation or malformation). In addition, multiparas are prone to uterine rupture and oxytocin stimulation increases the risk of rupture. Therefore oxytocin should be used in multiparas only in exceptional cases which should be decided only by the obstetrician.

2. **Diagnosis and assessing the progress of labour:** The guidelines use a strict definition of labour to admit only women who are in labour. The progress of labour and interventions should be recorded on a partograph (on which contractions etc. are recorded through time). Artificial rupture of membranes is the first intervention offered in the case of slow progress of labour (less than 1cm dilatation per hour). O’Driscoll and Meagher (1980) argue that artificial rupture of membranes is often sufficient to augment the labour. Moreover, oxytocin is often ineffective with intact membranes and can increase the risk of infusion of amniotic fluid into maternal circulation. The use of oxytocin is further conditional on there being a single foetus in the vertex presentation. After amniotomy, vaginal examinations should be performed on an hourly basis.

3. **Monitoring the woman and foetus during oxytocin administration:** Oxytocin may cause hyperstimulation of the uterine muscles and the effective dose varies across women. To ensure optimal contractions, oxytocin should be administered cautiously by intravenous infusion and stopped immediately if hyperstimulation or foetal distress occurs. All labouring women were assigned a personal nurse who was present from their admission until the baby was born. The personal nurse monitored and recorded...
contractions and foetal heart rate (by direct auscultation for one minute every 15 minutes during the first stage and after each contraction during the second stage).

4. Setting/availability of emergency facilities: The practice of AML was recommended only for institutional deliveries in facilities with adequate equipment to deal with obstetric emergencies (such as might entail a Caesarean section).

Since the AML was first proposed in the 1960s, the practice with or without modifications ‘has been widely adopted across the world’ (WHO, 1996). The recent literature suggests that oxytocin is used intrapartum in the majority of deliveries in the US ‘with augmentation being more the rule than the exception’ (Freeman & Nageotte, 2007: 445). A review of studies on the use of oxytocin and misoprostol in seven low-income countries showed that up to 50% of deliveries in public hospitals were induced or augmented (up to 20% in Ethiopia and Tanzania, and 40-50% in the other five countries) (Lovold, Stanton, & Armbruster, 2008).

Such high percentages of induced and augmented labours are worrying in the context of developing countries where ‘current evidence-based guidelines are rare, care is less regulated, and staffing and monitoring capabilities are limited … [o]xytocin is often administered without the aid of a precise dose/time regulatory infusion pump, external fetal monitor […] or one-on-one care’ (Lovold et al., 2008: 277). The concerns over the frequent use of oxytocin intrapartum, however, extend to developed countries. Oxytocin as a drug associated with ‘a heightened risk of harm’ and one that may ‘require special safeguards to reduce the risk of error’ was recently included in the list of high-alert medications (Clark, Simpson, Knox, & Garite, 2009: 35.e1). Clark et al. point out that recommendations on oxytocin administration currently used in practice are vague and that ‘in many instances, the apparent efficacy and safety of the various anecdotally derived means of administration (“the way we have always done it”) owe their success primarily to the resiliency of maternal-fetal biology rather than carefully considered scientific evidence’ (Clark et al., 2009: 35.e1). Guidelines for oxytocin use in augmentation of labour are often based on and reflect diverse practices across institutions and countries.

Recent evidence found oxytocin to be effective in shortening labour (Wei et al. 2007), but data from clinical trials did not support the belief that oxytocin reduces the rate of Caesarean sections (NICE [National Collaborating Centre for Women’s and Children’s Health], 2007). Although more evidence from clinical trials is currently available, systematic evidence for oxytocin use is still lacking (Bugg, Siddiqui, & Thornton, 2008). Clinical trials are often small, exclude at-risk women, look at varied practices and report only selected maternal and neonatal outcomes. The problem also lies with the definition of ‘delay’ in the first and second stage of labour and, in practice, various criteria have been used (NICE [National Collaborating Centre for Women’s and Children’s Health], 2007), as well as various dosage regimens of oxytocin (Bugg et al., 2008; NICE [National Collaborating Centre for Women’s and Children’s Health], 2007).

A summary of the evidence relating to augmentation of the first stage of labour suggests no differences in outcomes, other than shortening its duration (NICE [National Collaborating Centre for Women’s and Children’s Health], 2007). There was no evidence of abnormal foetal heart rate or of changes in the Caesarean section rate due to oxytocin augmentation. Nevertheless, the NICE guidelines emphasise the need to monitor the foetal heart rate continuously when oxytocin is used for augmentation. The evidence comparing low-dose regimens (starting dose and an increment of up to 2mU/min) and high-dose regimens (starting dose and an increment of 4mU/min or more) shows that high-dose regimens result in shorter labours, lower Caesarean section rate and higher chance of vaginal delivery but more
hyperstimulation of the uterine muscles. The data on neonatal outcomes were insufficient to draw any conclusions on neonatal morbidity and mortality. Current specific recommendations on oxytocin augmentation in the first stage include a consultation with the obstetrician about whether oxytocin should be considered. For multiparas, a full assessment, including an abdominal palpation and vaginal examination, is required. When oxytocin is used, the foetus needs to be continuously monitored; the time between dose increments should be at least 30 minutes and the dose should be increased until there are 4-5 contractions in 10 minutes. Women should be also advised to have a vaginal examination four hours after oxytocin is started. No evidence for oxytocin augmentation in the second stage of labour was identified. Moreover, since there is a risk of uterine rupture NICE guidelines do not recommend oxytocin use in this stage.

The WHO recommendations, however, do not distinguish between augmentation in the first and second stages of labour (WHO, 2003a). They suggest a starting dose of 2.5 units in 500ml of dextrose (or normal saline). The dose should be increased until 3 contractions lasting 40 seconds in 10 minutes are attained with maximum infusion rate of 60 drops per minute. If satisfactory contractions are not established, the concentration of oxytocin should be increased to 5 units in 500ml dextrose (or normal saline) with the same rate of infusion and increments as above. Women should be carefully observed throughout, and their pulse, blood pressure and contractions monitored; the foetal heart should be monitored every 30 minutes and the IV infusion should be stopped in the event of abnormal foetal heart rate or of uterine hyperstimulation. Apart from these differences, the guidelines provided by NICE and by WHO are alike in requiring oxytocin to be administered by IV infusion and the continuous monitoring of contractions and foetal heart rate.

Although the NICE guidelines summarise some high-quality evidence on the use of oxytocin in the first stage of labour, their conclusion emphasizes the importance of further research into the start dose and increments of oxytocin infusion. The data on neonatal outcomes were also insufficient. To provide clear recommendations for practice, the Cochrane Collaboration Group has proposed two systematic reviews in 2008. These aim to evaluate the available evidence on the effect of oxytocin administered because of slow progress in the first stage of labour with respect to uterine hyperstimulation and its impact on changes in foetal heart rate, Caesarean section rate, and incidence of serious neonatal morbidity or perinatal death (e.g. birth asphyxia, neonatal encephalopathy, disability in childhood), and serious maternal morbidity or death (Bugg et al., 2008). A comparison will also be made between various dose regimes of oxytocin (i.e. starting doses and the increments in oxytocin infusion) (Mori, Ullman, Pledge, & Walkinshaw, 2008).

Nevertheless, although the clinical evidence is not always completely clear-cut, there is concern that oxytocin should be administered with care and that the labouring woman and her baby should be continuously monitored. Specifically, the WHO practical guide from 1996 warned against the intramuscular administration of oxytocin because it is harmful for the foetus and increases the risk of uterine rupture; moreover, in the absence of unequivocal evidence on the risks and benefits of oxytocin augmentation, they concluded that oxytocin augmentation should be restricted to labours supervised by obstetricians and to facilities that provide surgical services and (whenever possible) foetal surveillance by electronic monitoring (WHO, 1996). More recent WHO guidelines recommend either oxytocin IV infusion to be administered for augmentation of labour, with the precautions outlined above (WHO, 2003a), or that oxytocin only be used for the prevention of PPH in the third stage of labour (WHO, 2003b).
Clinical evidence suggests that oxytocin and syntometrine are the drugs of choice for preventing PPH. Meta-analyses of clinical trials showed that prophylactic oxytocin is effective in reducing both blood loss greater than 500ml (RR 0.50; 95% CI 0.43 to 0.59; 7 trials, more than 3000 women) and the need for therapeutic oxytocics (RR 0.50; 95% CI 0.39 to 0.64) (Cotter, Ness, & Tolosa, 2001). When compared to oxytocin alone, syntometrine (a combination of oxytocin and ergometrine) is associated with a small but significant reduction in the risk of blood loss between 500 and 1000ml (RR 0.82; 95% CI 0.71 to 0.95); side effects such as nausea, vomiting and elevated blood pressure are, however, more common due to ergometrine (Su, Chong, & Samuel, 2007). Syntometrine should therefore not be administered to women with pre-eclampsia or cardiac conditions. More data on the side effects, optimal dose and route of administration of oxytocin are needed, however (Cotter et al., 2001). In addition, the question of optimal timing remains open: timing might affect the blood perfusion to the baby and the loss of maternal blood during the delivery, whilst uterotonic administered before the delivery of the baby may cause acute perinatal asphyxia (Begley et al., 2008). The main recommendation is to administer the relevant drugs at the delivery of the anterior shoulder, but this might require additional staff to be present at the labour. Typically, the practical approach is to administer uterotonic intramuscularly or by IV infusion immediately after the birth of the baby. Oxytocics are, however, sometimes administered at the crowning of the head or even after the delivery of the placenta (Cotter et al., 2001).

On the other hand, oxytocin and ergot preparations are not stable in tropical climates: according to the product information for Syntocinon (a leading brand of synthetic oxytocin), it should be kept below 25°C and should not be frozen. In many parts of the Global South, rural health facilities in particular are unlikely to have reliable electricity supplies or refrigeration facilities. In addition, oxytocin and ergot preparations require syringe technologies and sterilisation equipment (although the possible introduction of “Uniject™” syringes might circumvent this). Thus, whilst oxytocin is very effective in preventing and controlling PPH, several recent clinical trials have studied the effectiveness of prostaglandins and particularly misoprostol, which is cheap, can be administered in pill form and is not heat labile.3

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2 There are many possible variations of these three interventions. First, there are several uterotonics that can be used, with variations in timing, dose and route of administration (e.g. oxytocin can be administered as IV infusion or intramuscularly, syntometrine as an IM injection, and ergometrine IV or IM). Secondly, there are also possible variations in the timing of cord clamping and cutting and in the initiation of controlled cord traction. Variations in practice across health centres and countries mean that some women receive mixed management, a combination of expectant and active management that does not include all the components of either (Begley et al., 2008). For a discussion of the disparities in standards for AMTSL and in their implementation in practice for hospitals in developing countries, see Stanton, Armbruster, Knight, Ariawan, Gbangbade, Getachew et al. (2009).

3 When misoprostol was used there was a higher risk of severe PPH (RR 1.32, 95% CI 1.16 to 1.51; 16 trials, 29042 women) and greater use of additional uterotonic but fewer blood transfusions (RR 0.81,
Other recent studies evaluated the impact of the various interventions entailed in AMTSL and showed some adverse neonatal outcomes, including an increased risk of acute perinatal asphyxia if uterotonics are administered before delivery of the baby, and lower haematocrit levels and haemoglobin concentration up to six months after birth due to early cord clamping (McDonald & Middleton, 2008). Based on this, a new systematic review on ‘Active versus expectant management in the third stage of labour’ has been proposed (Begley et al., 2008). Currently, only a protocol is available. Moreover, little is known about the effects of particular components of AMTSL or about how interventions involving uterotonic drugs (such as oxytocin) during the first and second stages of labour contribute to the risk of PPH (McDonald, Abbott, & Higgins, 2004). Active management, then, is associated with some adverse effects (e.g. nausea, vomiting and hypertension when ergometrine was used as a part of the routine care) as well as having effects on the baby. Nevertheless, organisations such as International Confederation of Midwives (ICM), International Federation of Gynaecology and Obstetrics (FIGO) and WHO have accepted the proposal by Prendiville et al. (2000) that active management of the third stage of labour should be applied routinely in maternity hospitals.

In sum, then, there are still some question-marks over the evidence about exactly how and when oxytocin should and should not be used. Some good quality clinical trials have been conducted but often they were small, based on different practices, and often reporting only selected maternal and neonatal outcomes. Therefore it is hard to compare them and to draw any conclusions and recommendations for the best practice. More seems to be known about the use of oxytocin in AMTSL but the evidence on adverse neonatal outcomes is again lacking. Moreover, interventions in the first and second stage of labour were studied separately from interventions in the third stage and little is known about how intrapartum interventions impact on the need for further interventions postpartum.

Nevertheless, clinical guidelines advocate that oxytocin should be used very cautiously, since oxytocin use is associated with several risks for the mother and her baby. As our research in the Tracing Pharmaceuticals projects has indicated, the recommended precautions are often

95% CI 0.64 to 1.02; 15 trials, 27858 women) than when injectable uterotonics (oxytocin IM or IV, ergometrine, ergometrine plus oxytocin) were used. Oral misoprostol (600mcg) was associated with higher rates of side-effects, such as nausea, vomiting, diarrhoea, shivering and pyrexia (greater than 38 degrees C) when compared with injectable uterotonics as well as placebo. Results from a small number of trials suggest that side-effects associated with misoprostol use are dose related and that rectal misoprostol resulted in less pyrexia and shivering than oral misoprostol (Gulmezoglu, Forna, Villar, & Hofmeyr, 2007). Although less effective in preventing PPH than oxytocin, misoprostol showed promising results when compared to placebo and for its easier administration was tested in home-deliveries in developing countries (Derman, Kodkany, Goudar, Geller, Naik, Bellad et al., 2006; Miller, Lester, & Hensleigh, 2004). More research on the optimal dose and mode of administration is needed if misoprostol is to be recommended for resource-poor settings.

4 The definitions of AMSTL differ slightly. FIGO-ICM prefer 10 IU oxytocin administered by IM injection, or IV injection, drip or push after induction or augmentation within one minute of foetal delivery, with 0.2 mg ergometrine administered in the same way as oxytocin or 600mcg misoprostol (oral tablet) or other prostaglandins as second-line drugs. WHO prefer 10 IU by IM injection oxytocin within one minute of the baby’s delivery, and if oxytocin is not available they recommend 0.2 mg IM ergometrine or prostaglandins; they also specify that a check is made before giving these medications that there are no additional baby(s): for more details, see http://www.who.int/reproductive-health/impac/Clinical_Principles/Normal_labour_C57_C76.html#C73%20Active%20management%20of%20the%20third%20stage
thrown to the wind, by untrained rural practitioners involved in home deliveries and by trained practitioners working in urban nursing homes and hospitals alike.

Technical Appendix Bibliography:


