Intrapartum Oxytocin (Mis)use in South Asia[1]

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Abstract: *Oxytocin is a natural hormone with uterine stimulant properties that plays a prominent role in obstetric practice. Clinical guidelines for oxytocin use intrapartum emphasise that injudicious use has serious potential for adverse outcomes for mother and baby. Oxytocin is readily available in South Asia and widely used in ways that flout these guidelines. Yet recommendations for active management of third stage of labour (AMTSL) include the administration of oxytocin to prevent post-partum haemorrhage (PPH). Troublingly, these proposals seem to ignore oxytocin's already extensive life independent of policy interventions. Taking oxytocin as an example, the paper argues that policy-makers urgently need to engage with the everyday realities of drug availability and use in South Asia.*

I
Introduction

Oxytocin is a natural hormone with uterine stimulant properties that plays a prominent role in obstetric practice. It was first synthesised by Du Vigneaud in 1953 [Mousa and Alfirevic, 2007]. In the late 1960s O'Driscoll advocated oxytocin use intrapartum as a component of active management of labour (AML i.e. first and second stage of labour, before the baby is born), a package aimed at limiting the length of labour in nulliparous women [O'Driscoll and Meagher, 1980]. Later, oxytocin was found to be effective in preventing and controlling post-partum haemorrhage (PPH) in the third

stage of labour [Prendiville, Elbourne, and McDonald, 2000]. PPH is regarded as a key cause of maternal mortality throughout the Global South—estimates for India suggest that between 31 per cent and 38 per cent of maternal deaths are due to haemorrhage [Registrar-General India, 2006: 17,15]. Proposals for the active management of the third stage of labour (AMTSL) include administration by local-level government health workers, such as nurse-midwives, of either oxytocin (by intramuscular injection) or misoprostol (administered by pill).

Yet oxytocin is widely available and used in the formal health care system in South Asia, even in apparently remote rural areas. Moreover, the clinical guidelines for intrapartum oxytocin use are often flouted, whether in urban nursing homes and hospitals or in rural home births. Injudicious intrapartum use of oxytocin has serious potential for adverse outcomes, including uterine rupture and foetal asphyxia. This understanding motivated us to include oxytocin in the Tracing Pharmaceuticals project and our concerns have subsequently been enhanced by the proposals for AMTSL that would extend its availability even further.

II
Clinical Guidelines for the Use of Oxytocin

We begin by outlining 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 is also used to "abort the fetus in cases of incomplete abortion or miscarriage" [www.drugs.com accessed 25/09/07], but we shall not discuss this use here.

Oxytocin in the intrapartum period

Augmentation of labour increases 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 in AML were based on their 14 years of practice in the National Maternity Hospital in Dublin [O'Driscoll and Meagher, 1980]. Apart from oxytocin, the AML package includes a strict definition of labour, amniotomy and continuous support during labour in order to avoid the potential risks associated with oxytocin use. Table 1 summarises the conditions under which they and others recommend that oxytocin be used intrapartum.

Table 1: Intrapartum Oxytocin Use: Clinical Guidelines*	
Exclusion of at-risk women	Contra-indications include: hypertonic uterine contractions, foetal distress, any condition where spontaneous labour or vaginal delivery are inadvisable, prolonged administration in oxytocin-resistant uterine inertia, severe pre-eclamptic toxaemia, severe cardiovascular disease, impaired placental function which might lead to hypoxia.
Parity	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). Multiparas are prone to uterine rupture and oxytocin stimulation increases the risk of rupture, so oxytocin should be used in multiparas only in exceptional cases determined by the obstetrician.
Examination prior to oxytocin administration	A strict definition of labour to admit only women in labour. Oxytocin use is conditional on there being a single foetus in vertex presentation.
Mode of administration	Artificial rupture of membranes is the first intervention offered in the case of slow progress of labour (less than 1cm dilatation per hour): this is often sufficient to augment labour. Moreover, oxytocin is often ineffective with intact membranes and can increase the risk of infusion of amniotic fluid into maternal circulation. 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.
Monitoring the woman & foetus during oxytocin administration	All labouring women should be assigned a personal nurse who is present from admission until the baby is born. After amniotomy, vaginal examinations should be performed hourly. To detect uterine hyperstimulation or foetal distress, the progress of labour and interventions should be detailed on a partograph, recording contractions, mother's blood pressure & foetal heart rate (the latter by direct auscultation for one minute every 15 minutes during the first stage and after each contraction during the second stage).
Setting/availability of emergency facilities:	AML recommended only for institutional deliveries in facilities with adequate equipment to deal with obstetric emergencies (e.g. Caesarean section or resuscitation of the infant).
* See O'Driscoll and Meagher [1980] and British National Formulary http://www.bnf.org/bnf/bnf/current/4499.htm?q= per cent22oxytocin per cent22# (accessed 4 March 2009)	

Since 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 and Nageotte, 2007: 445]. A review of studies on the use of oxytocin and misoprostol in seven low-income countries showed that up to 50 per cent of deliveries in public hospitals were induced or augmented (up to 20 per cent in Ethiopia and Tanzania, and 40-50 per cent in the other five countries) [Lovold, Stanton, and 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, and 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 various practices across institutions and countries.

Recent evidence found oxytocin to be effective in shortening labour [Wei, Wo, Xu, Roy, Turcot and Fraser, 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, and 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 oxytocin dosage regimens [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. 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 also be 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 oxytocin use 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 proposed two systematic reviews in 2008. These will 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, childhood disability), and maternal death or serious morbidity [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, and Walkinshaw, 2008].

Although the clinical evidence is not always completely clear-cut, then, guidelines suggest that oxytocin should be administered intrapartum very cautiously and only under specific conditions because of the risks to the mother and her baby. 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].

Oxytocin in Active Management of Third Stage of Labour (AMTSL)

A Cochrane systematic review has found active management of the third stage superior to expectant management in terms of blood loss, PPH, and shortened labour [Prendiville et al., 2000]. AMTSL is a package of interventions including early cord clamping and cutting, controlled cord traction to deliver the placenta, and the routine administration of a prophylactic uterotonic drug just before, with, or immediately after, the birth of the baby [Begley, Devane, Murphy, Gyte, McDonald, and McGuire, 2008].

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 per cent CI 0.43 to 0.59; 7 trials, more than 3000 women) and the need for therapeutic oxytocics (RR 0.50; 95 per cent 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 per cent CI 0.71 to 0.95); side-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 uterotonics 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, it is more common to administer uterotonics 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 much of the Global South, especially in rural areas, health facilities are unlikely to have reliable electricity supplies or refrigeration facilities; heat-stable oxytocin is being developed, however. In addition, oxytocin and ergot preparations require syringe technologies and sterilisation equipment (although the "Uniject™" device 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.

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 the baby's delivery, and lower haematocrit levels and haemoglobin concentration up to six months after birth due to early cord clamping [McDonald and Middleton, 2008]. Little is known about the effects of particular components of AMTSL. 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.

AMTSL, 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 in Prendiville et al [2000] that AMTSL should be applied routinely in maternity hospitals. 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 best practice. Evidence on adverse neonatal outcomes is lacking. It is not known if

intrapartum interventions involving uterotonic drugs (such as oxytocin) enhance the risk of PPH [McDonald, Abbott, and Higgins, 2004], because intrapartum interventions have been studied separately from third stage interventions and little is known about how they impact on the need for further interventions postpartum.

Oxytocin Availability in South Asia

With these considerations this in mind, we now shift our focus from the guidelines for oxytocin use to its availability and use in South Asia. During the Tracing Pharmaceuticals project, we interviewed medical representatives, in urban and rural settings alike. They said that they do not actively promote oxytocin—mainly because oxytocin sales are sufficiently buoyant for producing companies not to perceive any need for high-profile and energetic marketing strategies these days. Our interviews with wholesale stockists and retailers endorse this interpretation.[6]

Table 2: Oxytocin Brands Available in India

Evatocin	***Neon Labs***	***INJ***	***Rs153.00***	***Rs15.30***
Foetocin	TTK	INJ	Rs13.00	Rs13.00
Gynotocin	ACE (Svizera)	INJ	Rs14.87	Rs14.87
Indox	Ind Swift	AMP	Rs14.30	Rs14.30
Oxybro Inj	Cadila (Vibra)	INJ	Rs15.00	Rs15.00
Oxystar	Cadila (Genstar)	INJ	Rs17.00	Rs17.00
Oxytocin Inj	Prem Pharma	INJ	Rs13.50	Rs13.50
Oxyton-5	Inga	INJ	Rs12.00	Rs12.00
Pitocin	Pfizer	INJ	Rs15.60	Rs15.60
Syntocinon	Novartis	INJ	Rs57.20	Rs11.44
Syntocinon	Novartis	INJ	Rs57.20	Rs11.44

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. Recommendations for the intramuscular injection of oxytocin in AMT-SL 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 such as we outline in this paper.

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. Our interviews and some spot checks on stocks in retail outlets, also indicated that oxytocin is well known, routinely kept in stock by wholesalers and retailers, and relatively cheap. Moreover, oxytocin can easily be purchased over-the-counter (as our research assistants did several times), despite being a prescription-only drug. Table 2

lists the brands of oxytocin marketed in India, their producers and prices: all are locally manufactured.

Urban Obstetricians and Intrapartum Oxytocin Use

Active management of labour is high profile in obstetrics circles in contemporary India. For instance, Daftary and colleagues have produced "an indigenously developed protocol of labour management" [2003], whilst 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, and Choudhary, 2006; Yuel, Kaur, and Kaur, 2008].

Systematic evidence about intrapartum oxytocin usage in institutional deliveries in South Asia is hard to come by, however. Nevertheless, the urban obstetricians we interviewed during the Tracing Pharmaceuticals project strongly advocated AML. They took intrapartum oxytocin use for granted as routine, normal and appropriate in their repertoire of interventions, the drug of choice for augmenting labour. One described oxytocin as 'the spinal cord of our speciality' (Interview, October 24, 2007 Bijnor, western Uttar Pradesh). Obstetricians, including those nearing retirement, said that they had been told during their medical training that oxytocin use intrapartum was appropriate and that such 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 per cent. 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, March 10, 2007 Delhi). 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 adjudicate on whether such usage is over and above what might be classed as 'medical need', although the clinical guidelines suggest that oxytocin use should be exceptional rather than routine.

Intrapartum oxytocin use, then, seems to be very common and highly valued in institutional deliveries in the region. Why this might be remains uncertain. 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]. A government obstetrician 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." (October 24, 2007 Bijnor). And in other research in Bijnor 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, the clinical guidelines for intrapartum oxytocin use are not necessarily being followed in institutional deliveries. Writing about Karnataka, Matthews et al. comment: "[m]ore than 90 per cent of all women, and more than 75 per cent 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, Ramakrishna, Mahendra, Kilaru, and Ganapathy, 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 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 irregularly and 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, and Costello, 2000]. Similarly, although the evidence is sparse and unsystematic, intrapartum oxytocin use in hospital deliveries in low-income countries more generally 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.

Intrapartum Use of Oxytocin in Rural Home Deliveries

Many studies in South Asia have shown that the bulk of health care, especially in rural

areas, is provided by private practitioners of various kinds—trained in various medical traditions or none—operating outwith the formal government health care system. Given the government sector's lack of capacity, perhaps the private sector plugs an important gap in provision. In this case, though, oxytocin is being administered in circumstances that raise serious disquiet. Table 3 summarises how oxytocin is being used intrapartum in rural home deliveries in South Asia. In itself, of course, using oxytocin during home deliveries flouts the clinical guidelines because the recommended monitoring and emergency facilities are absent. Moreover, oxytocin is usually administered by intramuscular injection. 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 12 Uttar Pradesh districts found that oxytocin was administered

Table 3: Intrapartum Oxytocin Use: Practice in Rural Home Deliveries in South Asia

Exclusion of at-risk women	Regional variations in proportions of women covered by antenatal care in the formal health sector; most regimes do not include antenatal visits in late pregnancy, when many contra-indications would first become obvious.
Parity	Multiparous women often receive oxytocin, although its use is more common among primagravidae [Das et al., 2005; Sharan et al., 2005]. In the Bijnor study, 62.3 per cent of primagravidae (n=53) received injections, compared with 45 per cent of women of higher parities (n=293) (unpublished data).
Examination prior to administration of oxytocin	TBAs generally do external examinations but do not necessarily ascertain cervical dilatation before oxytocin administration; male practitioners generally perform no examinations: thus stage of labour, presentation and number of infant(s) are not necessarily ascertained. Several women in the Bijnor study reported footling breech or transverse presentations that were undiagnosed before oxytocin administration.
Mode of administration	Intramuscular injection (sometimes more than one); effective dose cannot be ascertained or regulated.
Monitoring the woman & foetus during oxytocin administration	TBAs may perform internal examinations but there is no monitoring equipment to detect foetal distress, assess frequency & strength of contractions or measure mother's blood pressure etc. after oxytocin administration.
Setting/availability of emergency facilities	No equipment for dealing with emergencies (resuscitation equipment, incubator etc. for small/weak babies, no operating facilities, anaesthesia, blood bank etc.); taking labouring women elsewhere presents problems of transport, money, time & distance.

Note: This table should be compared with Table 1, which outlines the clinical guidelines for intrapartum oxytocin use. The points listed in Table 3 are probably widely applicable in South Asia although few of the studies cited in the text explicitly mention them. This listing draws mainly on the research on childbearing in Bijnor district (western Uttar Pradesh) conducted by Patricia Jeffery and Roger Jeffery.

in 48.2 per cent of home deliveries (n=2,992) across the state (ranging from 74.7 per cent in Muzaffarnagar to 16.7 per cent 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 per cent and 29.6 per cent respectively) and informal private practitioners and ANMs were the primary injection service providers (48.2 per cent and 32.8 per cent respectively) [Das, Agarwal, Tripathi, and Parveen, 2005]. A study in rural Kanpur reported similar patterns of use, although absolute levels were lower (23 per cent, n=527), and there was a statistically significant relationship between injection use and the presence of a provider (trained or otherwise) [Sharan, Strobino, & Ahmed, 2005]. Research in two villages in Bijnor district, western Uttar Pradesh, indicates that between 1983 and 1987, oxytocin was being administered in about 15 per cent 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 per cent of deliveries (n=346) [Jeffery and 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 5iu 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 per cent of all home deliveries, including 51 per cent of those attended by government auxiliary nurse-midwives [Matthews et al., 2005:397; Ramakrishna, Ganapathy, Matthews, Mahendra, and Kilaru, 2008: 96; see also George, Iyer, and 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 by the local multi-purpose health worker as 'almost routine' during home deliveries in Tamilnadu [Van Hollen, 2003a, b]. Bang, Bang, Baitule, Reddy, and Dashmukh [2005] report that in rural Maharashtra oxytocin injections were administered by unqualified private practitioners) in between 21.2 per cent and 23.1 per cent of the cases they studied 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, and Jeffery, 2007].

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. Oxytocin may also be used intrapartum in urban home deliveries: a study in a poor area of Delhi reported oxytocin use in 68.9 per cent of home deliveries, administered by private 'doctors' in 86.8 per cent of cases [Caleb, 1995]. Similar use has also been documented in Sudan and Guatemala [Lovold et al., 2008].

An additional feature of oxytocin is its cultural acceptability. In the local understanding of pregnancy, a woman's body becomes increasingly 'hot' (in the humoral sense) until uterine contractions are sparked off. According to the Bijnor study, desi [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 barhāne kā tikkā [pain/contraction enhancing injection]. Other sources talk of garmī ri huī [Iyengar et al., 2008: S27] or garmī ki suī (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].

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, however, have often had previous urban employment as compounders (pharmacists), ward boys, etc. in urban facilities. One explanation for how oxytocin use might have become widespread in the rural areas was proposed by several interviewees: that rural practitioners learn their trade primarily by observing clinical practices in urban facilities and adopt 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 injection in situations where they cannot adequately monitor the labour or provide emergency 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 behind them. In sum, the enthusiasm of obstetricians 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.

Conclusions

This paper has focused on intrapartum use of oxytocin in South Asia. More work is required to establish how commonplace intrapartum oxytocin use is in South Asia, whether in rural home deliveries or in urban institutions. We also do not know how much of that use departs from the clinical guidelines for its use and there are no data providing systematic information on the impact of such use on maternal mortality and morbidity, stillbirths and neonatal mortality and morbidity. 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, for instance.

Nevertheless, advocacy of AMTSL includes proposals to issue local-level health workers with oxytocin to avert and (if necessary) arrest post-partum haemorrhage. Policy documents, however, tend to present government programmes as if they are hermetically sealed from the wider world in which they are embedded. With respect to the use of oxytocin in AMTSL, they are silent about its significant life out with the realm of government policy and provision—indeed, a life that is also beyond its purview. The lack of concern about oxytocin misuse that has emanated from the professional and policy circles involved with issues of reproductive and child health is troubling. Our interviews with policy-makers and employees of NGOs in Delhi and Kathmandu, for instance, indicate that they are often aware of the kinds of oxytocin usage we have described, that they consider PPH a more significant issue than oxytocin misuse (despite the lack of evidence base) and that they are naïvely complacent about the prospects of retaining control over the oxytocin issued for AMTSL purposes.

The policy recommendations have no robust mechanisms to prevent oxytocin designated for PPH prevention from being used intrapartum, whether in local-level facilities by government staff themselves or by seepage into the private sector. The health care market is huge, diverse and, of course, inflected with market incentives and the imperative to make money: its implications for Safe Motherhood initiatives must be addressed. To be realistic, women in South Asia (in many areas, the vast majority of

women) will continue to deliver their babies outside the government sector—and much greater attention must be paid to these ground realities if policy interventions are to have their hoped-for impact (and not to be undermined by their undesirable unintended consequences). Of course, intrapartum oxytocin (mis)use is not the only serious issue at stake for Safe Motherhood. But tracing how pharmaceuticals such as oxytocin are being used "on the ground" and understanding how they are embedded in wider social and economic contexts provides crucial support for our view that policy-makers urgently need to engage with the everyday realities of drug availability and use in the Global South.

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2 The 'medicalisation' of childbirth has not been uncritically accepted within professional circles, as well as beyond, but we cannot address this issue here.

3 There are many possible variations of these three interventions. First, several uterotonic agents are available, 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 of hospitals in developing countries, see Stanton, Armbruster, Knight, Ariawan, Gbangbade, Getachew et al. (2009).

4 When misoprostol was used there was a higher risk of severe PPH (RR 1.32, 95 per cent CI 1.16 to 1.51; 16 trials, 29042 women) and greater use of additional uterotonics but fewer blood transfusions (RR 0.81, 95 per cent 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˚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.

5 Definitions of AMSTL differ slightly. FIGO-ICM prefer 10iu 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 10iu 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 per cent20Active per cent20management per cent20of per cent20the per cent20third per cent20stage

6 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.

7 We could not conduct a systematic study of drug transport and storage. This aspect merits further work for heat-labile drugs such as oxytocin, since turnover and seasonality may impact on drug efficacy.

8 Research on childbearing in Bijnor district (western Uttar Pradesh) was conducted by Patricia Jeffery and Roger Jeffery and funded by Social Science Research Council [now Economic and Social Research Council] in 1982-3 and 1985 and by Wellcome Trust in 2002-4).