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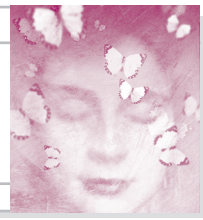
Oxytocin use in South Africa — a review



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Objective. Oxytocin is one of the most frequently used drugs in labour and there are many different dosage regimens. The aim of this study was to examine the use of oxytocin by obstetricians in South Africa.

Methods. A specially designed questionnaire was drawn up and distributed to specialists according to an address list obtained from the South African Society of Obstetricians and Gynaecologists.

Results. Three hundred and fifty questionnaires were distributed, with 174 processed for analysis. The majority of obstetricians (70.3%) reported that they would not use oxytocin for induction of labour in a patient with a previous lower-segment caesarean section, and 63.7% said that they would not consider the use of oxytocin in a patient with a multifetal pregnancy.

Most respondents used oxytocin for induction of labour in multigravid patients and 91.9% also used oxytocin for augmentation in these patients. However, clinicians would not use oxytocin if the patient was a grand multipara.

Conclusions. Most clinicians adhere to accepted protocols practised internationally, with a few exceptions. The use of oxytocin for both induction and augmentation of labour in women with one previous caesarean section is not practised in South Africa, despite evidence suggesting its safety.

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In 1906 Dale[1] showed that an extract from the posterior pituitary gland stimulated uterine activity. Three years later Blair Bell[2] reported its efficacy in the treatment of postpartum haemorrhage. In 1927 Bourne and Burn concluded that oxytocin may be valuable in cases where labour is prolonged secondary to 'sluggish pains'.[3] Du Vigneaud was the first person to synthesise this polypeptide hormone and in 1955 received the Nobel Prize for his work.[4]

Oxytocin is a nonapeptide hormone, produced in the hypothalamus, stored in the posterior pituitary gland, and secreted in a pulsatile way. Oxytocin receptors are found in the myoepithelial cells of the breast, the myometrium and the decidua.[5] Myometrial oxytocin sensitivity increases through pregnancy.[6] The concentration of myometrial receptors increases towards term and may be particularly high in patients with preterm labour.[7] Myometrial gap junctions also increase as gestation advances, possibly enhancing the sensitivity of the myometrium to uterotonic agents and helping to maintain effective contractions.[8]

In pregnancy, oxytocinase (circulating aminopeptidase) is produced by the placenta and significantly increases the metabolic clearance rate of oxytocin.[9] The exact pharmacological half-life of oxytocin is controversial[10] but available data suggest that a stable uterine response is obtained 40 - 60 minutes after initiating a constant-dose infusion.[11,12] Therefore the physiological half-life may be close to 10 minutes, since approximately four 'half-lives' are required to obtain constant plasma levels.[5]

Oxytocin is one of the most commonly used drugs in labour, and there are many different dosage regimens. However, if oxytocin is used incorrectly it can lead to major complications such as fetal hypoxia, hyperstimulation of the uterus and even uterine rupture. The aim of this study was to examine the use of oxytocin by practising obstetricians in South Africa.

Methods

A specially designed questionnaire was drawn up and reviewed by a panel of practising obstetricians. A total of

Table I. Oxytocin use in pregnancy — results of questionnaire

Question	Answer (*N*)	Percentage
Induction of labour		
1. Oxytocin use with unfavourable cervix	Yes 16	9.2
	No 157	90.8
2. Oxytocin use with intact membranes	Yes 68	39.5
	No 104	60.5
3. Time after ROM		
Primigravida		
Immediately	32	18.9
1 hour	62	36.7
6 hours	36	21.3
12 hours	11	6.5
24 hours	10	5.9
Other	17	10.1
Not at all	1	0.6
Multigravida		
Immediately	20	11.8
1 hour	52	30.8
6 hours	36	33.1
12 hours	10	5.9
24 hours	9	5.3
Other	22	13
4. Use with one previous caesarean section	Yes 51	29.7
	No 121	70.3
5. Use with viable twin pregnancy	Yes 62	36.3
	No 109	63.7
6 . Use with multigravida	Yes 159	94.6
	No 9	5.4
7 . Use with grand multipara	Yes 47	28.1
	No 120	71.9
8. Same regimen as with primigravidas	46	30.3
Lower dose than with primigravidas	106	69.7
9. Fetal heart monitoring		
Fetal stethoscope + intermittent CTG	4	2.4
Intermittent CTG	38	22.8
Intermittent + continuous CTG	7	4.2
Intermittent CTG + doptone	4	2.4
Continuous CTG	114	68.3
10. Administering method		
Electronic pump	150	90.4
Non-electronic device	14	8.4
None of the above	2	1.2
Augmentation of labour		
1. Oxytocin with intact membranes	Yes 71	41.3
	No 101	58.7

350 questionnaires (in both English and Afrikaans) were distributed to specialists according to an address list obtained from the South African Society of Obstetricians and Gynaecologists. Each questionnaire was divided into two sections: the first dealt with induction of labour and the second with augmentation of labour. Every questionnaire was accompanied by a covering letter explaining the aim of the study, as well as a stamped self-addressed envelope. All the questionnaires were returned anonymously. The forms were distributed between August and December 2002.

Results

Of the 350 questionnaires distributed, 185 questionnaires were returned. Eleven doctors were either abroad or retired, and therefore not practising in South Africa. One hundred and seventy-four questionnaires were processed, giving a response rate of 51.3% (Table I).

Induction of labour

In the section dealing with induction of labour, 90.8% of obstetricians would not use oxytocin in patients who had an unfavourable cervix (Bishop score of less than 6) and 60.5% said that they would not consider the use of oxytocin if the patient had intact membranes.

If a primigravida's membranes had ruptured, 18.9% of clinicians said that they would administer oxytocin immediately, 36.7% said they would wait 1 hour, and 21.3% said they would wait 6 hours before starting with an oxytocin infusion.

In the case of multigravid women, 11.8% of obstetricians said they would start oxytocin immediately, 30.8% said they would wait 1 hour, and the majority of clinicians (33.1%) said they would wait 6 hours.

Table I, continued

2.	Use with one previous caesarean section	Yes 60	34.6
		No 113	65.3
3.	Use with viable twin pregnancies	Yes 68	39.3
		No 105	60.7
4.	Use with multigravida	Yes 159	91.9
		No 14	8.1
5.	Use with grand multipara	Yes 48	27.7
		No 125	72.3
6.	Same regimen as with primigravida	51	33.6
	Lower regimen than with primigravida	101	66.4
7.	Contractions/10 min	2 : 2	1.2
		3 : 124	74.7
		4 : 35	21.1
		5 : 5	3
8.	Time after prostaglandin (hrs)		
	1	4	2.6
	2	9	5.8
	3	8	5.1
	4	40	25.6
	5	5	3.2
	6	78	50
	More	12	7.7
9.	Dosage increase after		
	15 min	24	14.6
	30 min	119	71.9
	45 min	13	7.9
	60 min	8	4.9

ROM = rupture of membranes; CTG = cardiotocogram.

With regard to previous caesarean sections, 70.3% of obstetricians said they would not use oxytocin in patients with a previous lower-segment caesarean section.

A total of 63.7% of doctors said they would not consider oxytocin use in a patient with a multifetal pregnancy.

Most respondents said they would use oxytocin for induction of labour in multigravid patients; only 5.4% said they would not use it. However 71.9% of doctors said they would not use oxytocin to induce labour in grand-multiparous patients. Most doctors (69.7%) said they would use a lower-dose regimen with multigravid than with primigravid patients.

With regard to monitoring the patient, 68.3% said they would use continuous cardiotographic (CTG) monitoring while administering oxytocin, 22.8% said they would use intermittent CTG monitoring, while the remainder said they would use a combination of fetal stethoscope and CTG monitoring.

Augmentation of labour

The second section of the questionnaire dealt with augmentation of labour. It showed that 58.7% of obstetricians would not use oxytocin in a patient with intact membranes and 65.3% would not augment patients who had had a previous (lower-segment) caesarean section.

The majority of doctors (60.7%) said they would not use oxytocin augmentation in a patient with a multifetal pregnancy.

The majority of respondents (91.9%) said they would use oxytocin to augment labour in multigravid women; however if the patient was a grand multipara, 72.3% said they would not use oxytocin. In multiparous patients, 66.4% of doctors said they would use a lower dose than in primigravidas.

Most clinicians (74.7%) agreed that the desired number of contractions is 3 in 10 minutes, whereas 21.1% of doctors preferred 4 strong contractions in 10 minutes. Only 3% of doctors accepted 5 strong contractions in 10 minutes. Most obstetricians (71.9%) said they would wait 30 minutes before increasing the oxytocin dosage if contractions were suboptimal, while 14.9% said they would increase the dosage every 15 minutes.

If a prostaglandin analogue was used for induction of labour, 25.6% of obstetricians said they would wait 4 hours before starting oxytocin infusion, 50% said they would wait at least 6 hours, and 7.7% of respondents said they would wait longer than 6 hours.

Of the 174 respondents, 73.1% were in private practice, 13.2% in academic institutions, 11.4% worked in both private practice and academic institutions, and 2.4% worked in non-academic government hospitals.

Discussion

A total of 350 questionnaires were posted and 185 returned, of which 174 (51.3%) could be processed. According to Babbie *et al.*[13] a response rate of 50% or more is adequate for robust analysis and interpretation.

Labour is induced when delivery will benefit the health of the fetus and/or the mother.[14] Obstetricians should be familiar with the indications for induction of labour, and the chance of successful induction depends a great deal on the condition of the cervix. According to Hofmeyr,[15] the cervix

undergoes physiological change during pregnancy. In the first trimester the cervix consists mostly of tightly aligned collagen (50%), 20% smooth muscle and the remainder is ground substance, including elastin and glycosamino-glycans. As pregnancy advances, hyaluronidase increases from 6% to 33%, whereas other glycosaminoglycans (dermatin and chondroitin), which bind collagen more tightly, decrease. Collagenase, the vascularity of the cervix and its water content increase during pregnancy. In 1964 Bishop[16] designed a pelvic scoring system (which has since been modified) to assess the condition of the cervix. The chance of successful induction with oxytocin depends a great deal on the Bishop score; a score of ≥ 9 was associated with a > 50% delivery rate within 5 days without any intervention.

Local application of prostaglandin E_2 gel (dinoprostone) is widely used for cervical ripening and induction of labour.[17] Oxytocin may also be used for this purpose, but controlled studies have indicated that oxytocin is not very effective when the cervix is unfavourable when compared with local prostaglandins.[18] The present study showed that most obstetricians (90.8%) would not use oxytocin infusion for induction if the cervix was unfavourable. When induction is commenced with prostaglandins, the latest evidence-based guidelines[19] specify that the interval between prostaglandin doses should be 6 hours. However, the shortest safe time interval between prostaglandin administration and the initiation of oxytocin use has not yet been established. According to the manufacturer's guidelines, oxytocin should be delayed for 6 - 12 hours following prostaglandin administration.[17] Over 50% of obstetricians in South Africa follow the abovementioned guidelines.

Another common method of induction of labour is artificial rupture of the membranes. With the HIV pandemic it is vital to know the patient's HIV status, since amniotomy can lead to vertical transmission. There is still uncertainty in the literature regarding the safe time interval between amniotomy and commencement of oxytocin infusion. The general consensus is that prostaglandins are released during low amniotomy and this stimulates labour. Oxytocin should be started 1 hour after amniotomy to allow the locally released prostaglandins to facilitate contractions and to avoid possible uterine hyperstimulation. The majority of clinicians surveyed nationally employ this regimen, although 21.3% wait 6 hours after amniotomy before starting oxytocin.

Another interesting fact that came to light in this study was that most obstetricians in South Africa would not use oxytocin for either induction or augmentation of labour in a patient with a previous (lower-segment) caesarean section. Could this possibly be explained by Edwin Cragin's well-known statement in 1916: 'once a caesarean, always a caesarean'?[20] One of the biggest fears among obstetricians who allow a trial of scar is the risk of uterine rupture. Arulkumaran *et al.*[21] reported the risk of scar rupture to be small if progress of labour in response to oxytocin is satisfactory. They suggested that a satisfactory rate of cervical dilatation in the presence of optimal uterine activity is predictive of a favourable outcome when oxytocin is used for dysfunctional labour after a previous caesarean section.[21]

Several studies[22-27] consider the risk of scar rupture in patients with a previous caesarean section who received oxytocin for either induction or augmentation of labour (Table II). Flamm *et al.*[23] had no uterine rupture in their study and no maternal or perinatal mortality. Paul *et al.*[25] investigated low-dose oxytocin use in patients with a scarred uterus and found a dehiscence rate of 3%. There was no 'true' rupture secondary to oxytocin use. In 1991 Rosen *et al.*[28] published a meta-analysis describing the morbidity of vaginal birth after caesarean section. It included 31 studies with more than 11 000 patients, and the (intended) route of delivery was observed to have made no difference to the rate of uterine dehiscence or rupture. The use of oxytocin, a recurrent indication for the previous caesarean section and the presence of an unknown type of uterine scar were also not associated with dehiscence or rupture.[28]

This study showed that obstetricians are reluctant to use oxytocin for either induction or augmentation of labour in patients with multifetal pregnancies. The literature on the use of oxytocin in twin pregnancies is very limited. In 1967 Niemand *et al.*[29] looked at the use of oxytocin augmentation in 127 women with twin pregnancies, of whom two-thirds were multigravid. Oxytocin was commenced during the

Table II. Successful oxytocin administration during trials of labour after previous caesarean sections

Series	Year	Oxytocin		No oxytocin	
		Trials of labour	Vaginal delivery (%)	Trials of of labour	Vaginal delivery (%)
Meehan[22]	1988	261	235 (90)	298	240 (81)
Flamm *et al.*[23]	1987	282	194 (69)	1 291	1 005 (78)
Silver and Gibbs[24]	1987	64	40 (63)	N/A	N/A
Paul *et al.*[25]	1985	257	177 (69)	594	537 (90)
Chelmow and Laros[26]	1992	62	46 (74)	442	245 (55)
Phelan *et al.*[27]	1987	793	557 (70)	N/A	N/A

first stage of labour and continued through to the third stage. They suggested that overdistension of the uterus is apparently not a contraindication to intravenous oxytocin and that there are no significant untoward effects from its use. Eighty-five per cent of women who displayed the dysfunctional type of labour commonly found in twins had vaginal deliveries. Fausett *et al.*[30] published a retrospective study in 1997 comparing twin with singleton pregnancies in terms of maximum dose of oxytocin used and successful vaginal deliveries. Oxytocin stimulation in twins resulted in fewer interruptions of the infusion for fetal heart rate abnormalities (5% for twins versus 26% for singleton pregnancies) and less hyperstimulation (6% v. 18%).

Recently Harle *et al.*[31] conducted a case-controlled study comparing oxytocin induction with expectant management in uncomplicated twin pregnancies. They concluded that induction of labour may be proposed to patients with uncomplicated twin pregnancies after 36 weeks' gestation without increasing maternal or fetal morbidity.

Despite the literature, doctors are still hesitant to use oxytocin for either induction or augmentation of labour in patients with multifetal pregnancies, as is evident in this study. According to the Royal College of Obstetricians and Gynaecologists (RCOG)[32] no conclusion can be drawn from the available evidence regarding the merits of an active policy for induction of labour in twin pregnancies. If there is careful monitoring of both the fetus and the mother and if the presenting twin is cephalic, oxytocin may be used with caution in twin pregnancies.

Almost 70% of South African obstetricians were reluctant to use oxytocin in a grand-multiparous patient, whether for induction or augmentation of labour. The data on oxytocin use in grand-multiparous patients are very limited. Ben-Aroya *et al.*[33] published a retrospective study in 2001. Their objective was to determine whether the use of oxytocin for the augmentation of labour in grand-multiparous women would increase the risk of peripartum complications. During the period from 1989 to 1997, 424 grand-multiparous women received intravenous oxytocin for augmentation of labour. All the women had fetal heart rate and uterine contraction monitoring. There was no significant difference between the oxytocin group and the control group regarding the rates of placental abruption, fetal distress, caesarean section, retained placenta and Apgar scores of less than seven at 5 minutes. They did, however, find a significantly higher vacuum delivery rate in the oxytocin group compared with the controls (3.5% v. 1.4% respectively, $p = 0.001$).

One should exercise caution in augmenting multiparous patients, especially grand multiparas, where the cause of poor progress may be unrecognised disproportion. Augmentation with oxytocin might lead to uterine rupture and fetal death. Any excessive stimulation of the uterus should therefore be very carefully avoided, or diagnosed early when oxytocin is used in the multiparous or grand-multiparous patient.

Regarding the administration of oxytocin, 74.7% of South African obstetricians are satisfied with 3 strong contractions in 10 minutes, whereas 21.1% said they would increase oxytocin infusion until there are 4 strong contractions per 10 minutes. Some institutions use the cut-off of 5 contractions per 10 minutes with at least 1 minute of uterine diastole,[34] but the RCOG recommends a maximum of 3 strong contractions every 10 minutes,[32] and this study confirmed this policy.

Several articles have been published regarding the incremental interval (ranging from 15 minutes to 60 minutes) of oxytocin increase. If one bears in mind that a stable uterine response is only obtained 40 - 60 minutes after initiating a constant oxytocin dose infusion, then in order to prevent uterine hyperstimulation, oxytocin should only be increased every 30 minutes. Most reports[32] indicate that the use of longer intervals between increases reduces uterine hyperstimulation, decreases the maximum used and total dose of oxytocin and decreases the rate of caesarean section. The American College of Obstetricians and Gynecologists[35] also recommends 30-minute incremental intervals. Orhue *et al.*[36] stated that 30-minute incremental increases in the infusion rate of oxytocin were superior to a 15-minute protocol in reducing the incidence of hyperstimulation and precipitous labour in nulliparous women.

The use of oxytocin has been associated with possible side- effects for both the mother and fetus. An important adverse effect of administering oxytocin is its antidiuretic action.[37] This effect decreases urine flow and places women receiving oxytocin at increased risk of dilutional hyponatraemia (water intoxication). Therefore the total fluid intake during oxytocin administration should be monitored carefully.[38] The development of dilutional hyponatraemia is enhanced when oxytocin is administered in an electrolyte-free dextrose solution or at a rate exceeding 20 mU/min.[39] The preferred solutions are therefore either 0.9% sodium chloride or lactated Ringer's solution.

Oxytocin appears to have a high therapeutic index because broad ranges of infusion rates and concentrations seem to be both safe and effective.[34] O'Driscoll *et al.*[40] introduced active management of labour in nulliparous women to shorten labour at a time when the caesarean section rate was stable at 6%. Their regimen included early amniotomy and prompt intervention with high-dose oxytocin in the event of inefficient uterine contractions. However the efficacy and safety of this protocol was not universally accepted. Locally, Pattinson *et al.*[41] compared labour outcomes in nulliparous women using either aggressive or expectant management protocols, and concluded that aggressive labour management reduces the caesarean section rate in nulliparous women, but it requires more intensive nursing. Satin *et al.*[42] studied a high-dose oxytocin regimen (6 mU/minute dosage increments) versus a low-dose regimen (1 mU/minute dosage increment) for labour stimulation. They found that the high-dose regimen

was associated with a significantly increased caesarean section rate for fetal distress (6% v. 3%, $p = 0.05$), but a lower incidence of instrumental deliveries, fewer caesarean sections for dystocia and fewer failed inductions.

The present study required obstetricians to state the regimens used in their units, but unfortunately this specific question was answered poorly and no conclusion could be drawn. It is clear that many different regimens are used by clinicians. The RCOG guidelines[33] recommend that oxytocin infusions should be given in the smallest possible volume, using an accurate infusion pump and should be commenced at a rate of 1 mU/min, increased at intervals of not less than 30 minutes (until 3 strong contractions every 10 minutes) up to a maximum rate of 12 mU/min. According to the guidelines the total dose of oxytocin used should not exceed 5 units.

To the best of our knowledge this study is the first of its kind to be conducted in South Africa. It is reassuring to note that most of the obstetricians in South Africa follow accepted practice (Table III). However, as demonstrated by

Table III. Oxytocin — international recommendation v. South African obstetrician use

	International recommendation	South African use
Induction of labour		
1. Primigravida : time after ROM	1 hour*	Immediately: 18.9% After 1 hour: 36.7% After 6 hours: 21.3% After 12 hours: 6.5%
2. Multigravida: time after ROM	1 hour*	Immediately: 11.8% After 1 hour: 30.8% After 6 hours: 33.1% After 12 hours: 5.9%
3. Use with 1 previous c/s	Not contraindicated[20,27]	29.7% use oxytocin
4. Use with viable twins	Few data Probably safe[30]	36.3% use oxytocin
Augmentation of labour		
1. Use with 1 previous CS	Not contraindicated[20,27]	34.6% use oxytocin
2. Use with viable twins	Few data Probably safe[30]	39.3% use oxytocin
3. Use with multipara	No data	91.9% use oxytocin
4. Use with grand multipara	No data Probably dangerous	27.7% use oxytocin
5. Desired number of contractions	3 in 10 minutes[33]	2: 1.2% 3: 74.7% 4: 21.2% 5: 3%
6. Fetal heart rate monitoring	Continuous CTG	68.3%
7. Time after prostaglandin use	6 hours[16]	1 hour: 2.6% 2 hours: 5.8% 4 hours: 25.6% 6 hours: 50%
8. Increment intervals	30 min[34]	15 min: 14.6% 30 min: 71.9% 45 min: 7.9% 60 min: 4.9%

*Acceptable practice.

CS = caesarean section; CTG = cardiotocogram.

their limited use of oxytocin in women who had previous caesarean sections or with twin pregnancies, their approach is too cautious. It is very reassuring that most obstetricians use continuous fetal heart rate monitoring, and that the others use intermittent monitoring in some way or another. No one used auscultation exclusively in these cases. On the other hand, it is also alarming that some obstetricians use unsafe practices such as the use of oxytocin immediately after the membranes have been ruptured or within 6 hours of prostaglandins having been used, and that they increase the dose rate every 15 minutes or try to achieve a contraction frequency of 5 in 10 minutes. It is essential that these potentially dangerous practices are addressed in continuing professional development programmes.

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