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A NATIONAL SURVEY OF OXYTOCIN USE DURING CAESAREAN SECTION IN ZIMBABWE

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ABSTRACT

***Background*: Post-partum haemorrhage is the leading cause of mortality for labouring women in Zimbabwe. Current literature supports the use of low dose oxytocin to prevent bleeding during Caesarean section. Internationally, clinical practice has been slow to change and the use of potentially harmful, higher than recommended dose is common.**
***Objective*: To describe the current clinical practice in Zimbabwe.**
***Design*: A self-administered questionnaire survey. Descriptive statistics were used to report the study results.**
***Setting*: In 2013 a national survey was conducted on the use of oxytocin by different types of clinicians, who provide either anaesthesia or surgery for Caesarean section.**
***Results*: Of a total of 221 (61%) questionnaires returned, 170 (80%) were completed fully. Only 23% of respondents would give an intravenous dose of 5.0 IU or less of oxytocin for elective Caesarean section. The majority of clinicians (77%) would administer more than 5.0 IU of oxytocin at elective. A significant number of nurse anaesthetists 16/59 (27%), and a non-negligible number of specialist anaesthetists 3/48 (6%) would even give 20 IU of oxytocin in elective cases rising to 30% and 13% respectively for emergency cases. In case of persistent bleeding due to uterine atony, oxytocin was more likely to be repeated (45%), rather than using misoprostol (25%) or ergometrine (19%).**
***Conclusion*: Most clinicians in Zimbabwe use oxytocin doses well above current internationally recommended. This illustrates the urgent need for updated national guidelines for the prevention of post-partum haemorrhage during Caesarean section.**

INTRODUCTION

The potential harmful effects of oxytocin received urgent attention after the United Kingdom Confidential Enquiry into Maternal Deaths1997-99 identified that a higher than recommended dose of oxytocin led to two maternal deaths (1). At the time, the British National Formulary recommendation was 5.0 IU slow intravenous bolus injection (2). The report on Confidential Enquiries into Maternal Deaths in South Africa 2005-2007 describes two deaths in which a high dose of oxytocin was contributory(3). Recent research has established the effective dose of oxytocin for elective Caesarean section (CS) at 0.35 IU (4,5). Dyer *et al*, suggested an oxytocin dose of 1.0-3.0 IU intravenously over 30 seconds for the prophylaxis of uterine atony in the healthy low risk parturient (6,7). For the treatment of uterine atony and postpartum haemorrhage (PPH) a higher dose of 3.0 IU is recommended (6,7). The Essential Drug List for Zimbabwe (EDLIZ) recommendation in 2006 was 5.0 IU (route unspecified) oxytocin after vaginal delivery of the baby, and was revised upwards to 10.0 IU in the 2011 edition (8). There was no specific guidance for CS.

Despite the growing evidence in support of a low dose of oxytocin, and published guidelines by authoritative bodies, clinical practice has been slow to change. Studies in the United Kingdom, Australia, New Zealand and Botswana showed wide variation in clinical practice (9-11). The aim of our study was to show whether in Zimbabwe clinicians had changed to low dose oxytocin in light of the current evidence and international recommendations, and to use our results to influence discussion on development of local, national and regional guidelines.

Zimbabwe has a population of 13million served by five central referral hospitals, eight provincial, 50 district-level, 46 mission plus other local-level rural hospitals. Obstetric services in peripheral hospitals are provided by Government Medical Officers (GMOs), midwives and nurses. Obstetric anaesthesia generally

is provided by Nurse Anaesthetists (NA). Typically NAs have a twelve months course to achieve a Diploma in Anaesthesia, and a six months course for a certificate. Depending on the hospital's proximity to an urban centre, private practitioners and visiting specialists may also provide obstetric, surgical or anaesthesia services. Some private practitioners have a one-year Diploma in Anaesthesia; others may just have done rotations in anaesthetics during their internship (currently 4 months). The next level above the district hospital is the Provincial hospital, located in a provincial urban centre, with establishment for ten to twelve GMOs and two or more NAs. The Provincial hospitals might, in addition to GMOs and NAs, be covered by medical specialists, private general and specialist practitioners with admitting rights and others also providing services on a full or part-time basis. A Provincial Hospital would do between 60 and 80 Caesarean sections while the central hospitals perform 2-300 a month.

MATERIALS AND METHODS

Institutional approval was granted from the Joint Parirenyatwa Hospital and College of Health Sciences Research and Ethics Committee (JREC/39/13), and the Medical Research Council of Zimbabwe (MRCZ/A/1760). A pilot study targeting 24 anaesthetists and obstetricians was conducted in one central hospital. After amendments to the questionnaire, a survey of the dose of oxytocin used by clinicians providing anaesthesia, or performing surgery for CS was conducted over a three months period (September 1st to November 30th , 2013). This ranged from specialist anaesthetist, obstetrician, nurse anaesthetist to medical officer level. General Practitioners were recorded as Medical Officers for this survey. We were specifically interested in the intravenous oxytocin dose [bolus or infusion] clinicians would administer for elective or emergency CS in different clinical scenarios: i) Elective CS, ii) Emergency CS, iii) CS following prolonged labour, and iv) CS following induction of labour with oxytocin. In addition we intended to seek if, and what other uterotonic drugs were used in case of persistent uterine bleeding.

A list of anaesthesia providers throughout Zimbabwe was obtained from the professional associations: the Zimbabwe Anaesthetic Association (physician anaesthetists), Clinical Anaesthetists Association (Nurse Anaesthetists). The Zimbabwe Society of Obstetrician and Gynaecologists supplied a list of obstetricians. The Council of Affiliated Associations (CAA), and the Medical and Dental Professions Council sent lists of doctors working at district and provincial level. The Ministry of Health and Child Care provided a list of all hospitals in the country, which enabled distribution of survey forms and in contacting hospital human resource units. A letter explaining the purpose of the oxytocin survey and the questionnaire were sent to all identified practitioners. Hospitals outside the major urban centres of Harare and Bulawayo were contacted directly by telephone to establish their current staff complement and to verify that they had received the survey questionnaires (LK). Finally, the clinicians who had been contacted were asked by the researchers (EC, FDM) to pass on the questionnaire to others who were either anaesthetic or obstetric service providers for CS. Questionnaires were sent by email, courier, and hand delivered and were followed up by telephone (EC, LK, FDM). In some instances telephone interviews were conducted by the research staff (LK). Point persons were identified (EC, SS) in some provincial and district hospitals to assist with collecting and following up the forms. Email reminders and telephone calls were made to non-responders. Completed forms were returned in the same way.

Data entry and analysis was conducted using EPIDATA V3.1 and STATA v.13.

The Questionnaire
Demographic Information
Clinician Type:
Obstetrician / Anaesthetist / Nurse Anaesthetist / Medical Officer Level
Hospital Institution Level:
Central Referral / Provincial / District / Mission / Rural Hospital / Private Clinic
Service Type
Government / Private / Mission [not for profit private]
Clinical Questions

1. In a healthy pregnant woman, not in labour, at term having uneventful elective Caesarean Section, which dose of oxytocin do you use ?
   a)<5.0 IUb) 5.0 IU c) 10.0 IU d) 20.0 IU
2. If the same woman had an infusion instead, what infusion regimen would / do you use?

a) 5.0 IU in 500mls over 2-3 hrs or 10 IU in 1000mls over 4-8 hrs
b) 10.0 IU in 500mls over 2-3hrs or 20 IU in 1000mls over 4-8 hrs
c) 30 or 40 IU in 1000mls over 4-8 hrs
d) I do not use infusion
e) Other regimen

3. In a healthy pregnant woman, in labour, at term presenting for emergency Caesarean Section, which dose of oxytocin do you use ?

a) <5.0 IU b) 5.0 IU c) 10.0 IU d) 20.0 IU

4. If the same woman had an infusion instead, what infusion regimen would / do you use ?

a) IU in 500mls over 2-3 hrs or 10 IU in 1000mls over 4-8 hrs
b) 10.0 IU in 500mls over 2-3hrs or 20 IU in 1000mls over 4-8 hrs

c) 30 IU or 40 IU in 1000mls over 4-8 hrs
d) I do not use infusion
e) Other regimen

5. In a healthy pregnant woman, who is having an oxytocin induction of labour, presenting for emergency Caesarean Section, which dose of oxytocin do you use ?

a) <5.0 IUb) 5.0 IUc) 10.0 IUd) 20.0 IU e) Other doses

5. In a healthy pregnant woman, in prolonged labour, presenting for emergency Caesarean Section, which dose of oxytocin do you use ?

a) <5.0 IUb) 5.0 IUc) 10.0 IUd) 20.0 IUe) >20.0 IU

6. In a healthy pregnant woman who has had the recommended dose of oxytocin at Caesarean Section, but still is bleeding, what practice do you follow :

a) Repeat doses oxytocin by infusion or boluses
b) Ergometrine intramuscular
c) Cytotec suppositories [misoprostol]
d) Other

RESULTS

A total of 221 forms were returned (Table 1) out of 361 sent(61%). Of these 170 (80%) were completed fully. Of the 51 incomplete forms 21 (9.5%) did not indicate what type of hospital they worked, six (3%) did indicate station but not designation and 24 forms (11%) did not indicate the station or the clinical designation. The response rate was: 92% of specialist anaesthetists (76% working in a central hospital), 45% of obstetricians (58% in a central hospital) and 54% of nurse anaesthetists (only 23% working in central hospitals). Only 16,5 % of the medical officers registered responded to the questionnaire.

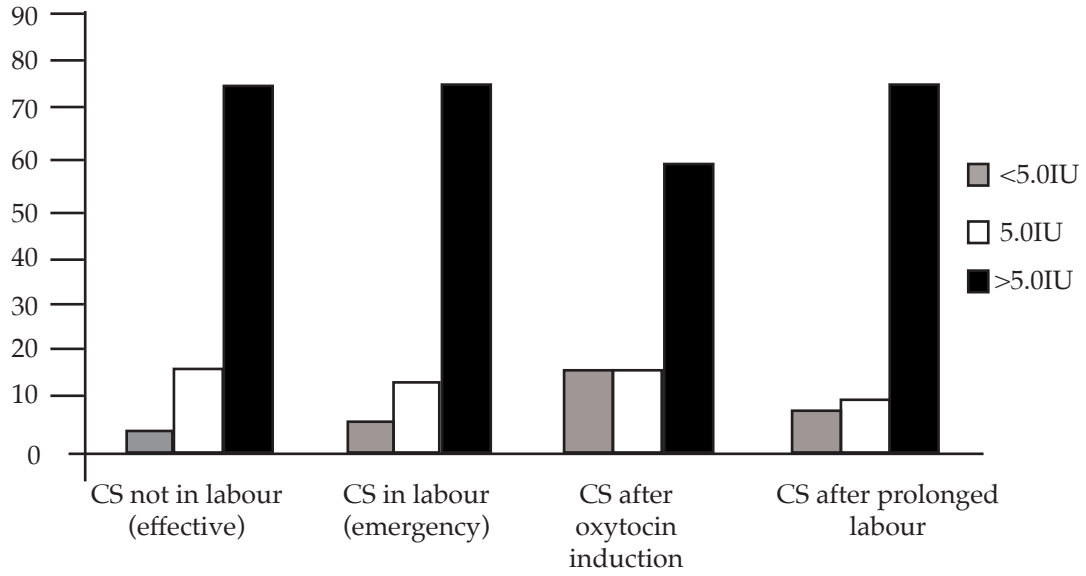
Table 1
Characteristics of responders to the questionnaire

	Anaesthetists	Obstetricians	Nurse Anaesthetists	Medical Officers	Unknown Designation	Total
Central Hospital	35	21	15	10	1	82
Peripheral Hospital	3	2	42	13	2	62
Private Practice	3	6	4	16	3	32
Unknown Location	5	7	4	5	24	45
Total	46	36	65	44	30	221
Total registered	50	80	120	266		
% respondents	92%	45%	54%	16.5%		

Figure 1 summarises results of the doses of oxytocin respondents would administer in four different situations. Only 23% of respondents gave a dose of 5.0IU (18%) or less (4.5%) in elective cases. At least 60% of all clinicians would give more than 5.0 IU oxytocin in all obstetric situations as an intravenous bolus, 76% in elective CS, and 77% in established and prolonged labour. Taken separately, 27% of NA would give 20IU in elective CS while 6% of physician anaesthetists would do the same. For CS in labour 30% NA would give 20IU or more compared to 13% physician anaesthetists.

Figure 1

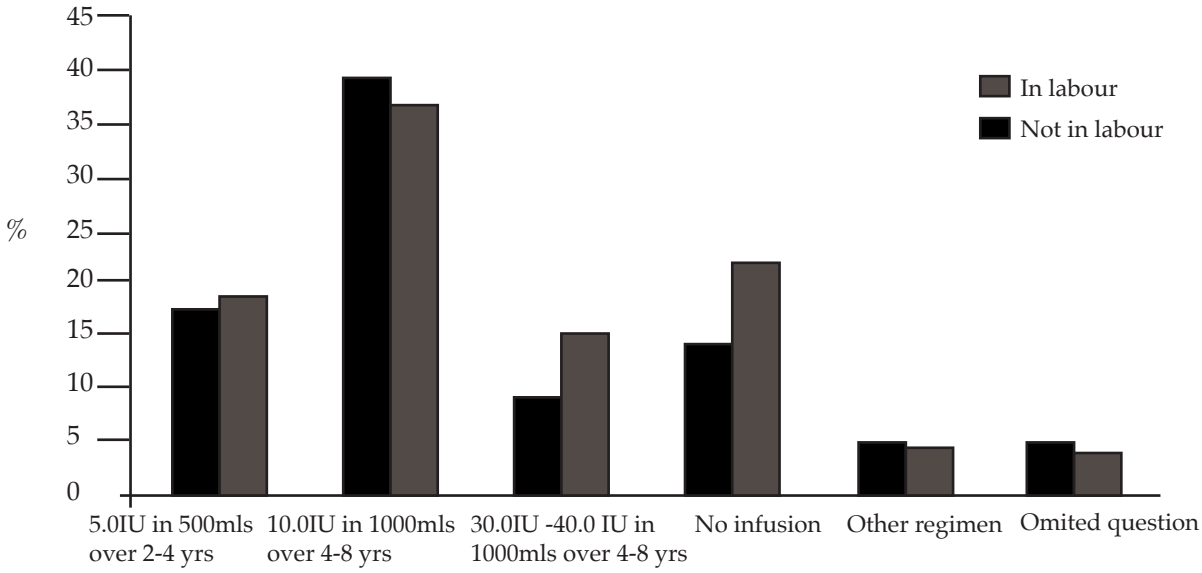
Percentage of respondents giving intravenous oxytocin boluses in four different settings of CS



In figure 2 we show the use of oxytocin infusion within the Caesarean section setting. Of the replies received 18% preferred a 5.0 IU infusion over 2-4 hours in elective and emergency CS. Almost 40% preferred to run 10.0IU over a period of up to 8hours.'No infusion' at all was the option for 14.2%for "not in labour" and 22% for "in labour" clinical scenarios.

Figure 2

Respondents who would give oxytocin infusion in Caesarean section setting



Percentage respondents giving oxytocin infusion

Table 2 shows the response rate in scenarios where women who continued to bleed due to uterine atony after an initial dose of oxytocin. Forty-five percent of clinicians preferred to use further doses of oxytocin while the remaining would either use misoprostol (25%), ergometrine (19%) or a combination (8.0%).

Table 2

Responses for what clinician would use for a woman bleeding from uterine atony after oxytocin

I would use	Percentage (%)
Repeat oxytocin by infusion	45.2
Misoprostol suppositories	24.9
Ergometrine	19.0
Other	7.7
No response	3.2

We used the responses to question 1 (elective CS) to compare data between central hospitals with peripheral hospitals (figure 3), and to compare responses between the different types of clinician (figure 4). Oxytocin doses are higher in peripheral hospitals than central. Nurse Anaesthetists were more likely to give a higher dose of oxytocin than physician anaesthetists: Chi-square statistic is 16.5176 and a p-value of 0.000259. For the patient in labour the chi-square statistic is 9.6244. The p-value is 0.00813.

Figure 3

Comparison between clinicians in central and peripheral hospitals in oxytocin use for elective Caesarean section

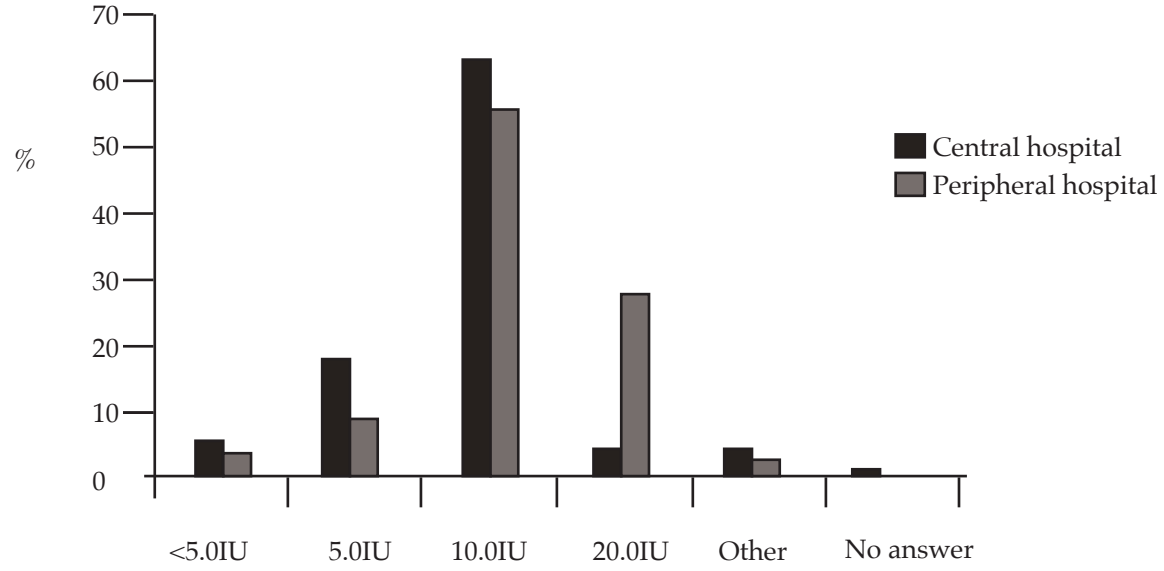
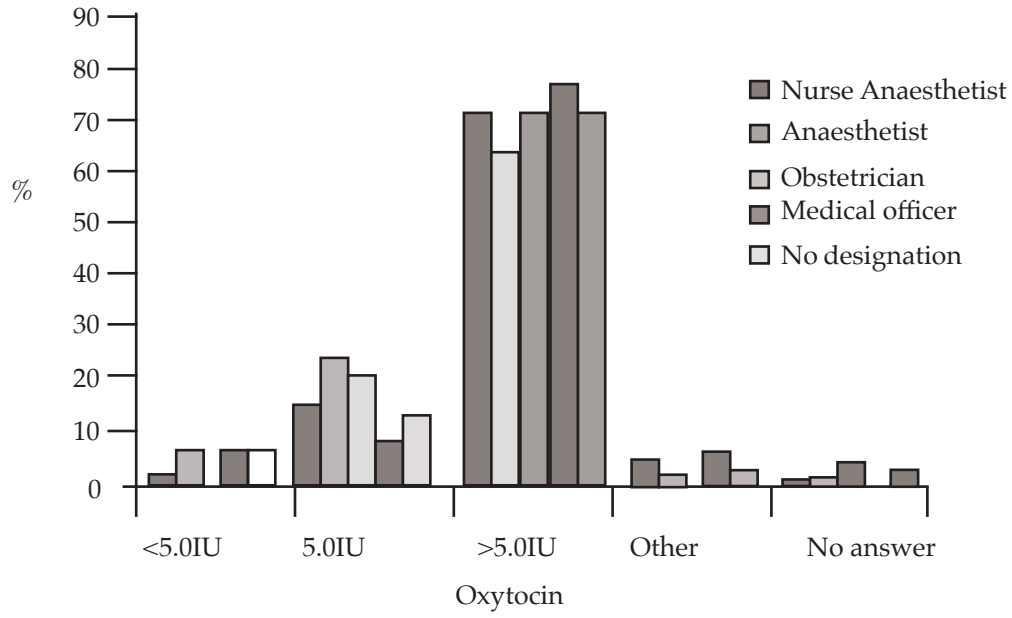


Figure 4

Who gives what? Type of clinician [%] giving which dose of oxytocin for elective CS



DISCUSSION

Post-partum haemorrhage is the leading cause of death in many low income countries. The use of oxytocin in high doses is potentially harmful as described in maternal mortality reports of several countries (1,3).

Current practice in Zimbabwe does not meet changing recommended international standards, and this could be mirrored in other developing countries. Specialist anaesthetists and obstetricians, nurse anaesthetists and other doctors providing obstetric surgical service give more than 5.0IU oxytocin intravenous bolus for all presentations of CS. In this survey only 4.5% and 18% of the respondents would give a dose of <5.0IU and 5.0IU respectively, which is compliant with previously recommended practice guidelines for elective CS. A significant number give doses of up to 20 IU bolus.

Oxytocin is the most widely used uterotonic agent in Zimbabwe. Ergometrine and syntometrine are available but not as commonly used. Intra-muscular oxytocin (10.0IU) is given by nurses at clinic level for vaginal deliveries. Misoprostol (prostaglandin E1) [Cytotec] is increasingly part of routine prophylaxis for uterine haemorrhage. None reported the use of carboprost (prostaglandin F2α).

The majority of CS in Zimbabwe are performed in peripheral hospitals, with a national CS rate averaging 4.8% (12,13).This is lower than the CS rate expected by the WHO/UNICEF which lies between 10 and 15% (14).

The strongest evidence and guidelines for low-dose oxytocin in CS applies to elective cases (3,4). Increased doses of oxytocin administered increase the demand for vasopressors, and in clinical scenarios where haemodynamic instability is present, this might be fatal (1,3). Data from several African countries confirms that most patients have CS in the non-elective setting, following a period of labour and failed delivery [maternal indications] or foetal indications (15,16). In this setting a higher dose of intravenous oxytocin bolus is indicated. Studies suggest oxytocin dose in the non-elective patient is about 3.0IU, possibly followed by infusion, as the risk of post-partum haemorrhage increases and oxytocin receptor sensitivity decreases (6,17,18). Tsen *et al* have emphasised the need for considering risk/benefit ratio while designing oxytocin protocols during Caesarean delivery (19). They suggest a rule of '3' for dosing oxytocin: 3.0 IU followed by 3 minutes delay, if needed repeat 3.0 IU and consider infusion of 3.0IU in a litre of crystalloid at 100.0mls/hr. Finally consider 3 other pharmacological options (ergometrine, carboprost and misoprostol). It was argued that use of alternatives, speed of administration and previous exposure should be considered.

The survey showed that in Zimbabwe the use of infusion was not consistent. There is a range of doses and durations of infusion given, and no international consensus on the matter. Research from Canada indicated that infusion doses of 0.4IU per minute may be up to 30% higher than the minimum effective dose required to prevent uterine haemorrhage and post-partum uterine atony in low risk patients undergoing elective CS. Administration of oxytocin at lower infusion rates of 0.29 IU per minute (15 IU in 1 litre of IV fluid over a one hour period) may provide sufficient uterine contractility while reducing maternal side-effects including hypotension (20). Oxytocin infusion in itself is not without problems, particularly when a large fluid volume is given, with fluid retention and hyponatraemia reported as complications due to the antiduretic effect of oxytocin (21). In addition high dose oxytocin infusion during labour has also been implicated in causing post-partum haemorrhage (22,23).

The response rate from medical officers who perform the majority of CS was low at 16.5%. The doses of oxytocin used were consistently high across all types of clinicians (specialists, nurse anaesthetists and medical officers) who responded, reflecting the teachings to lower cadres of clinicians by specialists in the central hospitals.

Both the national guidelines and current teaching should be aligned with the best available current evidence. The practicalities of low-dose infusion are debatable and national guidelines, when developed should be applicable to all levels of hospitals. Several studies advocated the combined use of oxytocin with other uterotonics like misoprostol and/or ergometrine, although not all studies are as promising (24-26).New national guidelines have been proposed for South Africa. These include 2.5 IU initial slow (30s) bolus, with the remaining 7.5 IU of a 10.0 IU ampule given into the remaining intravenous infusion. This is followed by 20.0 IU in 1.0L crystalloid for 8.0 hrs (125mls/hr: 42 drops per minute with a 20 drop/min giving set). This regime is best performed with an infusion pump. When pump not available intramuscular oxytocin is recommended at 10.0 IU repeated at 4.0 hrs, with an infusion of 20.0 IU in 1.0L crystalloid for 8hrs. Where uterine atony is present at three minutes, a repeat dose of 2.5 IU and infusion plus an additional oxytocic drug is recommended. (27)

One of the difficulties with this study was communication with the peripheral hospitals. Despite access to mobile phones and emails, contact details change frequently and get out of date. A number of questionnaires were not returned despite reminders and prompts from the active point person, resulting in a response rate of only 61%. This is a common problem with self-administered questionnaire-based surveys. It is unlikely that the missing forms would have changed results significantly, since there was

considerable alignment in response. In addition the anaesthesia providers in the peripheral hospitals are principally NAs. In this survey we were able to reach 69% [42/71] of NA in peripheral hospitals surveyed. In addition the hospitals surveyed, especially the peripheral hospitals, were very widely distributed across the country. The practice of clinicians in peripheral hospitals reflected that in the central hospitals (Fig 3). A higher proportion in the central hospital would give a lower dose of oxytocin [5.0IU] and this may be a factor of the study and general awareness of the literature. In the peripheral hospitals there is a tendency towards higher doses. Patients presenting for emergency CS may already be potentially hypovolaemic, may have a spinal anaesthetic and may bleed or have bled. The above combination may be compounded by high dose oxytocin. The shift from high dose (10.0IU) to intermediate dose (5.0IU) has been slow to occur but needs to proceed further to the low dose (1.0 – 3.0IU) and possibly combination with other uterotonics (27,28).

In conclusion, oxytocin is an important drug in prevention and treatment of obstetric haemorrhage but has side effects that may be life threatening. Changes in the literature towards low dose oxytocin have not translated into clinical practice in many countries. In the low resource setting where maternal mortality from haemorrhage is a leading cause of death, there is greater urgency to act.

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