# Oxytocin administration for induction and augmentation of labour in Polish maternity units– an observational study

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# Abstract

Background

There is not enough data regarding practices and protocols that healthcare personnel follow and the amount of oxytocin that women receive during labour. Empirical evidence indicates that compliance with the guidelines improves the quality of healthcare and reduces adverse effects. The aim of the study was to evaluate oxytocin supply practices of oxytocin for labour induction and augmentation in Polish maternity units.

Methods

The article presents a prospective observational study. Data collection took place in two selected maternity units between January 15 and July 31, 2019 (n=545). Inclusion criteria were women in term pregnancies, undergoing oxytocin induction or augmentation of labour. Exclusion criteria were women who were in preterm labour, aged less than 18 years, and women whose baby was known to have a malformation.

Results

The average total amount of oxytocin administrated to women before birth was 7,329μg following labour induction and 3.952μg following labour augmentation. The actual administration of oxytocin deviated both from the unit and national guidelines in 93,6% of all observed labours. We found no statistically significant correlation between the amount of oxytocin administered and mode of delivery, immediate postpartum blood loss or Apgar scores. There was no observed effect of total oxytocin on short-term perinatal outcomes. Hospitals with similar protocols did not differ significantly in terms of total oxytocin amount, induction to stimulation ratio—the only observed difference was the mode of delivery.

Conclusions

There is a need for a thorough analysis to find out the reasons for the observed discrepancies between protocols and practice.


# Background

The number of women who have their labour induced or augmented with synthetic oxytocin is increasing in high-income countries throughout the world [1, 2]. At the same time, there are considerable differences in the intrapartum oxytocin administration regimens between and within countries, regions and hospitals in Europe [3]. In Poland, there is no official data regarding oxytocin administration. Surveys of postpartum women revealed that between 43% and 63% of all births are induced or stimulated with synthetic oxytocin [4]. However, there is not enough data regarding practices and protocols that healthcare personnel follow and the amount of oxytocin that women receive during labour. Observed differences in the practice of oxytocin use should stimulate efforts to standardize the procedures. Following a strict protocol may face

resistance from those responsible for labour care [5]. Empirical evidence indicates that compliance with the guidelines improves the quality of healthcare and reduces adverse effects [6].

The effect that endogenous oxytocin and its receptor have in reproduction, and social and emotional behaviours, has been researched extensively [7]. During labour, the mechanism by which exogenous (synthetic) oxytocin works differs from the natural pulsating secretion of endogenous oxytocin [8]. Synthetic oxytocin may result in desensitization of oxytocin receptors which may inhibit calming and analgesic effects of endogenous oxytocin [9, 10]. Despite its widespread use during labour, and its effectiveness in labour induction and augmentation [11], there is still little research on the short and long-term consequences of synthetic oxytocin on both the woman and child [12]. However, the immediate adverse effects may include hypertonic uterine contractions, uterine rupture, cardiac arrhythmia, hypotension, extensive bleeding and pulmonary oedema in the woman, hypoxia and retinal haemorrhage in the baby [13, 14].

Literature reviews show that the use of synthetic oxytocin in cases of hypotonic uterine contractions lowers the risk of a caesarean section. Routine Oxytocin use presents no benefits when there are no medical indications for labour augmentation [15, 16]. In nulliparous women, the active labour management, early amniotomy and Oxytocin infusion result in a decrease of caesarean sections [17]. Some recent studies show that, compared to expectant management, induction of labour at 39 weeks' gestation may have benefits for the woman and baby [11, 18].

Endogenous Oxytocin promotes good mood and regulates maternal behaviour. The use of synthetic oxytocin impairs the natural secretion of endogenous oxytocin which may result in a shorter breastfeeding duration [19] and a higher risk of symptoms of anxiety and depression in women [20]. Moreover, some studies suggest that there may be a link between the use of synthetic oxytocin in labour and autism in children, but links to behavioural disorders remain unclear [21, 22].

While an increasing number of studies suggest possible adverse effects of intrapartum synthetic oxytocin, there is no data on the impact of the total amount of synthetic oxytocin administered during labour. Several studies have compared the results of high and low-dose oxytocin administration regimens [15, 23]. Still, few have focused on the duration of the oxytocin infusion and total amount administrated, dose-escalation and intervals and outcomes for women and babies [24–27]. Studying these aspects is particularly crucial in the light of the latest reports on the longer than the previously believed half-life of oxytocin that can lead to high accumulation and unnecessary exposure in women and children [28].

This study aimed to assess administration practices of oxytocin for labour induction and augmentation in maternity units. The assessment included calculation of total amounts of oxytocin, accordance with national guidelines and analysis of maternal and neonatal outcomes.

# Methods

## Study design and setting

The study was conducted between January 1 and July 31 2019, in Warsaw, Poland. In 2018 Poland's population was 37.9 million [31], and there were 388,178 live births. In the same year, Poland had a fertility rate of 1.46, slightly lower than the EU 28 average of 1.56 [30, 31]. Currently, there are 378 maternity units in Poland, organized on a three-level referral system, with tertiary hospitals providing the most specialist care [32]. Sixteen of these maternity units are in Warsaw, catering for approximately 21,000 births per annum [33]. In 2018, the caesarean section (CS) rate was 43.85%, and labour induction and augmentation rates were 43% and 61%, respectively [4, 34].

In 2017, the Polish Society of Gynaecologists and Obstetricians (PSOGO https://www.ptgin.pl/) issued national guidelines on the use of synthetic oxytocin for labour induction and augmentation [35]. The guidelines outline indications and contraindications (including specific criteria for women with previous CS, twin pregnancy, or hypertension). They recommend two oxytocin administration regimens: (i) low dose (start dose 0.5-2 milliUnits per minute (mU/min), escalating at 1–2 mU/min at 15–40 min intervals) and (ii) high dose (start dose 6 mU/min, escalating at 3–6 mU/min at 15–40 min intervals). The guidelines also state that there are no apparent benefits to continuing oxytocin infusion after established labour has been achieved.

# Data collection

All 16 maternity units were invited to participate in the study. The inclusion criteria for maternity units was consent for participation and implemented internal written protocols compatible with the national guidelines for oxytocin administration during labour. Five hospitals did not consent to participation in the study. Eight hospitals did not have a written protocol. One hospital had a written protocol, but it did not adhere to the national guidelines. Two hospitals fulfilled the established inclusion criteria (unit A and B). Both of these units were tertiary hospitals. In those units, contemporaneous observation of labour assessing oxytocin use was performed by trained volunteer midwives between January 15 and July 31 2019. Midwives working in labour and delivery wards in both units were invited to volunteer their participation in the study. Volunteer midwives were trained on how to record intrapartum oxytocin administration and complete the data collection form [see Additional file 1]. Convenience sampling was used to collect the data. Trained midwives observed and filled the data collection forms of induced or augmented labours during their planned shifts. The inclusion criteria were women in term pregnancies, women > 18 years of age, no known fetal abnormalities. The exclusion criteria were women who were in preterm labour, i.e., before 36 completed weeks' gestation, aged less than 18 years, and pregnancies with an identified fetal abnormality.

Data were collected on maternal age, parity, gestational age, indication(s) for induction or augmentation of labour, type and volume of infusion solution (ml), amount of oxytocin in the infusion (International Units - IU), start dose (ml/min), maximum dose (IU), escalation rate and exact time of each escalation (ml/min), use of epidural anaesthesia, Apgar scores and blood loss (ml). The amount of oxytocin administrated during labour was calculated in micrograms (μg).

In cases of emergency CS, the amount of oxytocin administered after birth was excluded from the calculation. The total time of oxytocin administration was calculated from the start of the infusion until the baby's birth. The time during which the infusion was stopped/disconnected (e.g., for the administration of epidural anaesthesia) was deducted from the administration time. The protocols in the studied units are presented in Table 1.

Table 1
Protocols on oxytocin administration for induction and augmentation of labour (n = 2)

| | Unit A | Unit B |
|---|---|---|
| Infusion fluid | 5 IU oxytocin in 0.9% NaCl 50 ml | 5 IU oxytocin in Glucose 50 ml |
| Starting dose | 1 ml/min | 0.6–1.2 ml/min |
| Maximum dose | 6 IU | 18 IU |
| Escalation rate | 1 ml every 10–15 min | 0.6–1.2 ml every 30 min |
| Contraindication to use | None stated | None stated |

The sample size was achieved through convenience sampling over a limited time, as described above (244 births in unit A and 301 in unit B). There was no prespecified sample size calculated because no comparisons regarding outcome and interventions were made between the studied units.

# Data analysis

All analysis was conducted using statistical program R with statistical significance set at $p = < 0.05$ for all analysis [36]. Correlations between the amount of oxytocin administered and maternal age, parity, and duration of pregnancy were analyzed using Spearman test. Correlations with variables such as blood loss, epidural use and Apgar scores were calculated using a linear model. Correlations with induction or augmentation of labour and mode of birth were calculated using Wilcoxon rank-sum test with continuity correlation.

# Ethical issues

The Bio-ethical Commission approved the study of the Medical University of Warsaw (reference number AKB/226/2018). According to Polish law, non-interventional observational studies do not require patient consent.

# Results

The data on 545 births were analyzed, 244 births in unit A and 301 in unit B (Table 2). Women's average age was 31 years [range 19 to 44 years, SD = 4.48], 68.81% (n = 375) were nulliparous. The rate of augmentation of labour was 33.39% (n = 182), while the rate of induction was 66.61% (n = 363). The most common indications for labour induction were maternal gestational diabetes mellitus, pregnancy-induced hypertension, small for gestational age (fetal growth ≤ 10th percentile for gestational weight) and

prelabour rupture of membranes. The only indication for labour augmentation was hypotonic uterine action.

Table 2
Induction and augmentation rates in observed labours (n = 545)

| | Unit A (n = 244) | Unit B (n = 301) | Total (N = 545) |
|---|---|---|---|
| Induction | 161 (65.98%) | 202 (67.11%) | 363 (66.61%) |
| Augmentation | 83 (34.02%) | 99 (32.89%) | 182 (33.39%) |

In the studied group, after induction of labour (n = 295), 81% of women delivered vaginaly. Primiparas had higher rates of cesarean sections than multiparas (Table 3). In the group with augmented labour (n = 182), 88% delivered vaginally (n = 161). Still, among primiparas, the cesarean rate was 4%, versus 14% among multiparas (there were no statistical differences between the groups regarding the mode of delivery) - Table 3.

Table 3
The mode of delivery after induction in the groups of primiparas and multiparas (n = 363)

| | Vaginal delivery (n = 295) | Cesarean section (n = 68) | Total (N = 363) | Test |
|---|---|---|---|---|
| Nulliparous | 182 (75%) | 61 (25%) | 243 | chi2 = 18,34 p = 0,00002 |
| Multiparous | 113 (94%) | 7(6%) | 120 | |

In both units, the amount of oxytocin administered until childbirth was considerably higher when labour was induced (p = 2.513e-16**[1]). Women whose labour was induced received, on average, 7.329 µg (± 5,841) of oxytocin, while women in augmented labours received 3.952 µg (± 3,296). The total amount of oxytocin administered until childbirth and after birth to women during labour was 17.5 µg (± 7,593) for induction of labour and 14.76 µg (± 6,616) for augmentation of labour, a statistically significant difference (p = 2.209e-06***[2]).

[1] p-value is less than 0.01

[2] p-value is less than 0.001

Without exception, the oxytocin infusion was continued after 5 cm cervical dilatation following induction of labour and discontinued only after the baby's birth.

The minimum escalation rate was 1 mililiter per hour (ml/h) and maximum was 35 ml/h [median 5.6 ml/h, average 6.2176 ml/h]. The minimum interval was 2 min, and a maximum of 480 min (median 43.3333 min, average 54,1363 min).

A negative correlation was observed between the amount of oxytocin administered during labour and parity (R Spearman = -0.4087, p = 1.465e-14), and a weak correlation with duration of pregnancy (R Spearman = -0.138, p = 0.03367). No statistically significant correlation was found between the amount of oxytocin administered and maternal age (p = 0.2669).

The use of epidural anaesthesia increased slightly with the increasing dose of Oxytocin (Estimate = 0.04908, Pr(> |z|) = 0.005876). In the studied group most deliveries were vaginal (83,67%; n = 456), and only 16,33% (n = 89) ended up in a cesarean section.

In Unit, A cesarean section were 12,7%, and in Unit B 19,93%. No, statistically significant correlation was found between the amount of oxytocin administered and the rate of emergency CS (p = 0.05926), forceps-assisted (p = 0.3884) or vacuum-assisted births (p = 0.7281), immediate postpartum blood loss (p = 0.7609) or Apgar scores (p = 0.8908). There were no statistically significant differences between the units in the total amount of oxytocin administrated to women.

In most instances (93,6%), the actual administration of oxytocin did not comply with the PSOG guidelines, mainly because the infusion was continued after established labour was achieved (Table 4). In regard of the start dose, escalation dose and interval the protocol was followed in 18.9% (n = 103) of labours: 18.35% (n = 100) followed the low-dose protocol (start dose 0.5-2 mU/min, escalation rate 1–2 mU/min, interval 15–40 min) and only 0.55% (n = 3) followed the high-dose protocol (start dose 6 mU/min, escalation rate 3–6 mU/min, interval 15–40 min). In cases of inconsistencies in escalation rates and intervals, most often the escalation rate increased, and intervals extended.

Table 4
Accordance with oxytocin national administration protocol (N = 545).

| | VARIABLES OF ACCORDANCE WITH NATIONAL PROTOCOL | | | | | |
|---|---|---|---|---|---|---|
| | Medium (n = 545) | Start dose* (n = 509) | Escalation rate (n = 545) | Interval (n = 545) | Continuation of infusion after established labour was achieved** (n = 363) | All variables of accordance present (n = 545) |
| In accordance | n = 545 (100%) | n = 130 (26%) | n = 131 (24%) | n = 192 (35%) | n = 4 (1%) | n = 35 (6,4%) |
| Discordant | n = 0 (0%) | n = 379 (74%) | n = 414 (76%) | n = 353 (65%) | n = 541 (99%) | n = 510 (93,6%) |
| *36 patients had previously administered oxytocin – start dose not available | | | | | | |
| ** only induced labours | | | | | | |

# Discussion

The mean total amount of oxytocin administrated to women in our study was 3.95 µg following augmentation and 7.329 µg following induction of labour. We found no other research assessing these two values. Selin *et al.* (2019) reported on the total amount of oxytocin administrated to women in low and high-dose oxytocin augmentation schemes [37]. In low-dose regimens, women received 5.74 µg and while women in high-dose regimens received 7.98 µg [37], higher than the total amount found in our study. Similar to our findings, Frey *et al.* (2015) found that induction was associated with higher maximum oxytocin doses [38]. The fact that higher amounts of oxytocin were administrated to women following induction of labour is understandable, given that the infusion is likely to be continued for a more extended period.

Furthermore, there was a correlation between the total amount of oxytocin infused, parity and duration of pregnancy. Multiparous women, on average, received lower total amounts of oxytocin compared to nulliparous women. A longer duration of pregnancy was associated with a smaller amount of oxytocin being administered, i.e., women whose labours were induced at 40 weeks' gestation, on average, received less oxytocin than women whose labours were induced at 39 weeks' gestation. Similar correlations between parity were reported by Oscarssona *et al*. (2006). Multiparous women were less likely than nulliparous women to receive intrapartum oxytocin [25].

We also found a correlation between the total amount of oxytocin administrated during labour and the use of epidural anaesthesia. Other studies have reported similar findings, both in terms of more frequent use of oxytocin administration after the epidural anaesthesia commenced [39,40] and in the more frequent use of epidural anaesthesia following oxytocin augmentation of labour. [41,42]. This may be explained, in part, by the more painful nature of oxytocin-stimulated contractions and restrictions in movement that many women face when continuous electronic fetal monitoring is required during labour induction or augmentation [43].

Although some studies have reported negative associations between intrapartum oxytocin administration and neonatal outcomes [25,44], we did not find any correlation between the total amounts of oxytocin administrated and Apgar scores. However, using a more sensitive indicator of neonatal wellbeing, such as pH values in neonates, may lead to different results. In our study, 84% of women birthed vaginally following labour augmentation, similar to the proportion of 87% found in a Danish study [44] but considerable higher than the 51% reported in Bugg *et al*.'s (2005) study with nulliparous women [45].

We did not find any correlation between the total amount of oxytocin administrated to women before birth and the mode of delivery. In other words, women who received large amounts of oxytocin during labour were as likely as women who received small quantities to have an emergency CS. Similar findings were reported in studies comparing the high, and low-dose augmentation, where the higher doses of oxytocin administrated did not lower the risk of CS [37]. A systematic review concluded that early administration of oxytocin did not affect the mode of birth [16]. However, some studies have demonstrated a correlation between oxytocin administration and mode of delivery, including a lower risk

of CS when compared to expectant management [42] but overall higher risk of intrapartum interventions [25,41,45]. We were unable to find any other study reporting on the correlation between the total amount of oxytocin administered and mode of birth.

Multiparous women whose labour was induced were less likely to have an emergency CS than nulliparous women. Similar findings were reported in a study using the Ten-Group Classification system [46], which compared outcomes for women birthing in three hospitals in Norway, Ireland and Slovenian. The CS rate in group 2 (nulliparous women at term gestation, cephalic presentation, induction of labour) was 25.7% in Norway, 34.4% in Ireland and 30.4% in Slovenia. In group 4a (multiparous women at term gestation, cephalic presentation, induction of labour), the CS rates were 6.4%, 5.8% and 4.2% respectively. However, the study included data on all methods of induction of labour, oxytocin infusion being just one possible option.

Findings show that the majority of hospitals did not have written protocols on intrapartum oxytocin administration for induction or augmentation of labour. Even in units where protocols were available and compliant with the national guidelines, the actual administration of oxytocin did not follow the recommended regimen in 93.60% of labours.

While one study conducted in Germany found that 69% of participating units had protocols on oxytocin administration [3], they did not explore actual adherence to the protocol. In a study by Jackson establishing of a collaboration to build a consensus-driven, evidence-based approach to the use of oxytocin resulted within seven years in accordance with the guidelines in 73% to 100% [5]. Studies show that the use of oxytocin in accordance with guidelines was associated with several significant clinical outcomes, including a decrease in cesarean births for fetal distress based on electronic fetal monitoring, decreases in length of first stage labour, and decreases in maximum dose of oxytocin. [47].

With few exceptions, the oxytocin infusion was continued in all the observed labours, despite the national guidelines,[35] and information in Summary of Product Characteristics for Oxytocin,[14] stating that the infusion may be discontinued when labour becomes established, i.e., when cervical dilatation reaches 5 cm. In the light of the latest reports that show the benefit of discontinuing the infusion once established labour is achieved [48,49], observed practices require further analysis.

The guidelines for the supply of oxytocin proposed by PSOGO do not apply to particular situations such as twin pregnancies, pregnancies with previous caesarean section, pregnancies in ob.ese women. They also lack information on the dose of oxytocin that should be set after disruption of infusion for the time epidural anaesthesia provision.

Even assuming that there were situations in our study group that required non-standard behaviour, it seems unlikely that this would apply to over 90% of those surveyed.

Jackson et al. showed that the lack of oxytocin protocols was primarily due insufficient consensus between those taking care of the mother (midwives and doctors), between providers and the relevant

literature regarding specific, restrictive dosing of oxytocin. When midwives and doctors work together to write a guideline, it has a higher likelihood of being successfully followed [50]. This was not our case, because national guidelines for oxytocin administration in Poland were formed by a group of expert obstetricians.

Typically, deviations from the protocol for stimulation have been associated with increasing time interval to dose escalation. This may be due to the burden being placed on staff when caring for several labouring women at a time and the inability to increase the dose at an exact interval. Investigating the cause of this condition, however, requires detailed research.

The Jackson study found that increasing compliance was associated with a statistically significant reduction in the amount of oxytocin used during labour and a reduction in the time between initiating oxytocin administration and the birth of the child. [5].

The two maternity units selected for this study, despite having similar protocols on oxytocin administration, differed considerably in the rates of labour induction and augmentation, as well as the rates of vaginal births after labour induction. Similar discrepancies among units were reported in studies from Sweden and the UK, suggesting that care offered in different units is based on clinicians' attitudes and preferences rather than on scientific research [25,42]. As stated previously, the oxytocin administration regimens were not followed in 510 (93,6%) of the labours observed during our study. Although there is no scientific consensus on the optimal oxytocin administration dose or regimen, clinicians should follow their unit's guidelines unless exceptional circumstances are present.

### Limitations

One of the limitations of our study was the inability to access and analyze data from all women whose labours were induced or augmented with oxytocin. This was because some midwives practising in the units declined to take part, and we acknowledge that the analysis of data from all women may have resulted in different outcomes.

Our study was conducted in tertiary-level urban units providing specialist care to some women who may have had complicated medical and obstetric health needs. This may have affected the rates of therapeutic interventions, including induction and augmentation rates, and it would be beneficial to conduct a similar study in units catering mostly for healthy women.

## Conclusions

No effect of total oxytocin on short-term perinatal outcomes was observed. It is worth assessing the effect of oxytocin on long-term effects. Oxytocin supply in most deliveries was incompatible with oxytocin supply protocols proposed by national experts. A thorough analysis should be performed to find out the reasons why the oxytocin infusion was continued after established labour was achieved. This should also be an essential part of the labour ward staff training. Hospitals with similar protocols did not

differ significantly in terms of total oxytocin, induction to stimulation ratio. Still, they differed in mode of the delivery - qualitative research explaining what makes this difference would be significant. The observations from our study can be subject to several generalizations. Following guidelines improves the quality of care and increases the safety of those giving birth. In countries with low compliance of practices with standards, measures should be taken to investigate the reasons for such a situation, as well as measures to support their implementation.

# Abbreviations

CS – Caesarean section

mU – milliUnits

IU – International Units

mU/min – milliUnits per minute

ml/min - Mililiter per minute

ml/h – Mililiter per hour

# Declarations

### Ethics approval and consent to participate

The Bio-ethical Commission approved the study of the Medical University of Warsaw (reference number AKB/226/2018). According to Polish law, non-interventional observational studies do not require patient consent.

### Consent for publication

Not applicable

### Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

### Competing interests

The authors have no conflicts of interest to disclose.

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### Authors' Contributions

Barbara Baranowska: Conceptualization, Data curation, Formal analysis, Methodology, Project administration; Funding acquisition, Writing- original draft, Writing- review&editing;

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Maria Węgrzynowska; Conceptualization, Formal analysis, Writing- original draft

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# Additional Files

Additional file 1.docx

“Observation chart for recording oxytocin administration”

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