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Use and Misuse of Oxytocin During Delivery

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Abstract

Obstetric malpractice claims, concerning delivery during a period of eight years, were analysed for motives behind disciplinary actions, and for the frequency of inappropriate oxytocin use. Failure to respond to signs of foetal distress, injudicious use of oxytocin and a failure to effect a timely delivery were the recurrent problems that accounted for the majority of disciplinary actions. Inappropriate use of oxytocin was more frequent than reported in earlier studies. (Paper I)

In a case-control study, differences in the obstetric management in neonates born with and without acidemia (umbilical artery pH < 7.05), was evaluated. Out of 28,486 deliveries during 1994–2004, 305 neonates were born with acidemia. Uterine hyperactivity and oxytocin use were independently associated to acidemia at birth. The increased uterine activity was related to oxytocin treatment in 75% of cases. Pathological cardiocatographic patterns occurred significantly more often in the case group. The results indicate that guidelines on oxytocin use and foetal surveillance are not followed. The duration of bearing down is less important when uterine contraction frequency has been considered. (Paper II)

In a subset of study II, cases with metabolic acidosis (umbilical artery pH < 7.05 and base deficit ≥12 mmol/L) and controls were audited for the occurrence of suboptimal intrapartum care, and the nature of such care. It was found that suboptimal care occurred in half (49%) of the cases, while it was less frequent but not uncommon among controls (13%). Suboptimal care consisted of injudicious use of oxytocin and a failure of appropriate action upon signs of foetal distress. A high rate of NICU admissions and diagnosis of encephalopathy in the case group confirms that metabolic acidosis should be avoided. We estimate that metabolic acidosis could probably have been prevented in 40-50% of the cases. (Paper III)

Women (n=103) scheduled for elective caesarean section in regional anaesthesia were randomised to 5 or 10 units oxytocin, given as an intravenous bolus (double blinded), and electrocardiograms were analysed for ST depressions as a sign of myocardial ischaemia. ST depressions were associated with oxytocin administration significantly more often in subjects receiving 10 compared with 5 units. A dose of 10 units resulted in a more marked decrease of the mean arterial blood pressure, but no difference in increase of the heart rate. There was no difference in estimated blood loss. (Paper IV)

Keywords: oxytocin, labour, malpractice, acidemia, metabolic acidosis, uterine contractions, second stage management, foetal surveillance, suboptimal care, caesarean section, heart, ischaemia, hypotension, electrocardiogram

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To my family

True knowledge exists in knowing that you know nothing

Sokrates

To my family
List of papers

This thesis is based on the following papers, which are referred to in the text by their Roman numerals.


I  Jonsson, M., Nordén Lindeberg, S. Östlund, I., Hanson, U. (2008) Acidemia at birth, related to obstetric characteristics and to oxytocin use, during the last two hours of labor. *Acta obstetricia et Gynecologica*, 87(7):745-750


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Abbreviations

AEM  Ambulatory electrocardiographic monitoring
BMI  Body mass index, kg/cm²
BMR  Board of Medical Responsibility
bpm  Beats per minute
CI   Confidence interval
CP   Cerebral palsy
CS   Caesarean section
CTG  Cardiotocography
ECG  Electrocardiogram
FBS  Fetal scalp blood sampling
FHR  Fetal heart rate
FIGO International Federation of Gynecology and Obstetrics
h    hour
HIE  Hypoxic ischaemic encephalopathy
HR   Heart rate
i.v. intravenous
MAP  Mean arterial blood pressure
NICU Neonatal intensive care unit
ns   Non significant
OCP  Occipito-posterior
OR   Odds ratio
SD   Standard deviation
SPSS Statistical Package for Social Sciences
UK   United Kingdom
VAS  Visual analogue scale
VE   Vacuum extraction
WHO  World Health Organisation
Introduction

Oxytocin is a commonly used drug in labour. It can be applied in all stages of labour: induction, including the latency phase, in stages one and two for augmentation and in stage three as a tool for bleeding prophylaxis. Oxytocin is also used in the caesarean section (CS) procedure to promote uterine contraction and prevent large blood losses. Cardiovascular effects of oxytocin are well known and are marked if administered as a bolus.

Oxytocin is of enormous benefit to women in labour with poor progress. This holds true for both nulliparous and parous women (1-3). In a study by Arulkumaran et al, almost 80% of nulliparous and 90% of parous with poor progress were delivered vaginally after eight hours of augmentation with oxytocin (1). Few side effects will occur if an oxytocin infusion is carefully controlled. Nevertheless, serious complications in the mother and foetus have been reported after infusion of oxytocin, and oxytocin is a frequent issue in obstetric malpractice claims (4-7). Approximately half of all paid obstetric litigation claims in the United States involve allegations of injudicious use of oxytocin (8). Recently oxytocin was added to the list of medications designated as high-alert by the Institute for Safe Medication, USA (9). Such drugs are defined as those bearing a heightened risk of harm when they are used in error. Violation of guidelines regarding use of oxytocin is probably one reason for adverse neonatal outcomes. The use of oxytocin is on the increase and it is estimated that about 50% of nulliparous and 20% of parous women receive oxytocin during delivery (10, 11).

The association between oxytocin use and acidaemia at birth has not been thoroughly investigated. In prospective studies of induced or augmented labour in which high- vs. low-dose protocols for oxytocin administration have been compared, no increased risk of acidaemia has been found (12-15). Higher doses resulted in increased rates of hyperstimulation in some studies, although none demonstrated any significant difference in neonatal outcomes (13, 15, 16). The study protocol limited the use of oxytocin in those studies, and the infusion was discontinued or decreased in situations of hyperstimulation, resulting in improvement of the foetal status. It was not the objective to study acidaemia and the rate of sampling of umbilical cord blood could be as low as 40 per cent. In a study of augmented labour, the condition of the neonate was assessed by cardiotocographic (CTG) tracings, umbilical artery blood gas monitoring and Apgar score at birth. The results indicated that oxytocin did not cause acidaemia (17). The same conclusion was drawn by
Nickelsen et al, who evaluated the umbilical acid-base status in relation to delivery mode and Apgar scores (18). In neither of these studies a description was found on how the oxytocin infusion was titrated in response to uterine contraction frequency. A few studies have shown an association between acidaemia at birth and oxytocin administration (19, 20). In a study by Herbst et al, oxytocin was found to be a risk factor for acidaemia at birth, with an odds ratio of (OR) 3.1, confidence interval (CI) 2.1- 4.6. Acidaemia was defined as a pH value < 7.05 and the study population consisted of 23,000 deliveries (20). Thus, studies regarding the association between oxytocin use and acidaemia have yielded conflicting results. A possible explanation is that on the one hand, when effects of the drug are being investigated in clinical trials, there are limitations to how to administrate the drug in study protocols, while on the other hand, in practice in the clinic, the use of the drug is less controlled.

The associations between oxytocin use, hyperstimulation, foetal distress and adverse neonatal outcome are well known (20-23). Foetal distress has usually been defined as abnormal cardiotocographic (CTG) patterns or occurrence of meconium stained amniotic fluid and adverse neonatal outcome as low Apgar scores (< 7 at five minutes), admission to neonatal intensive care unit (NICU) and/or a description of neonatal morbidity in terms of respiratory or neurological impairment.

Although too frequent uterine contractions generally are considered to be the cause of foetal distress in oxytocin-stimulated labours (24, 25), few studies have addressed the relation of uterine contraction frequency to acidaemia at birth. In studies of associations between neonatal outcome and different CTG patterns, the tocographic part of the CTG is rarely mentioned. Recently Bakker et al reported that increased uterine activity was associated with a higher incidence of foetal acidaemia at birth (26). The acidaemic group in that study had a significantly higher contraction frequency in the second stage of labour than the group with a normal umbilical artery pH.

Claims for malpractice and medical negligence are potentially important sources of information on causes of harm to patients. Analyses of obstetric claims have shown recurrent themes: misinterpretation of CTG tracings, an inappropriate or delayed personnel response to CTG findings, inappropriate use of oxytocin and record keeping and communication issues (4, 7, 27). These themes may represent the tip of a larger problem and may warrant further consideration and provide an opportunity for process improvement.

Confidential Inquiries into Stillbirths and Deaths in Infancy and into cases of neonatal encephalopathy, United Kingdom (UK), indicate that in 60% of labour cases there is a preventable element related to incorrect assessment of foetal monitoring, and episodes of suboptimal care have been identified in 64% of encephalopathy cases and in 75% of deaths (28, 29). According to a Scandinavian study, neonatal death due to suboptimal care is avoidable in 38.5% of non-malformed infants with a gestational age of 34 weeks or more.
Suboptimal care as a cause of harm or death has been reported repeatedly and efforts to determine the nature of such care with the aim of finding preventive tools are important. Most of the preventable complications arise from violation of a few basic principles of intrapartum care. Inappropriate use of oxytocin is one of the most common issues (31).

Definitions and important concepts in the management of delivery

Labour is a clinical diagnosis and the occurrence of three to five contractions in five minutes has been used to define adequate labour and is seen in approximately 95% of women in spontaneous labour at term (32-34). This frequency of contractions will allow adequate placental gas exchange and oxygenation of the foetus (35, 36). Uterine contractions can be monitored externally with a tocodynamometer, which gives a good indication of the onset, peak and end of a contraction. The frequency and the duration of contractions are displayed with the external method, but not the intensity. External tocography can provide adequate information on how contractions and the foetal heart rate (FHR) are related. To measure the intensity of contractions an intrauterine pressure monitoring device is required (37).

Although it is a continuous physiological process, labour is divided into three stages. The first and second stages are commented upon in the following paragraphs.

First stage of labour

The first stage of labour is established when there are regular painful contractions and there is progressive cervical dilatation from 3-4 cm to a fully dilated state. The length of the first stage varies between women and is influenced by parity. In the nulliparous the average length of the first stage is 8 hours with an upper limit of 18 hours and in the parous, the average length is 5 hours and the upper limit 12 hours. The upper limit corresponds to the 95th percentile or + 2 standard deviations (SD) and the above definitions are based on pooled findings from descriptive studies (38-41). During the first stage of normal labour there is only a slight decline in foetal pH, which is of no clinical significance (42-45), and the lactic acid concentration in the blood is unchanged (44).

Second stage of labour

The second stage refers to the interval between full cervical dilatation and delivery of the infant. Uterine activity increases progressively during delivery and the second stage of labour is characterised by uterine contractions
that are more frequent, intense and prolonged (32). The active phase of the second stage, the period when a maternal urge to bear down is superimposed on uterine activity, is considered critical to the foetus, since it can have an adverse impact on foetal oxygenation (46-48). During the active phase of the normal second stage there is a decline in foetal blood pH and an increase in lactic acid, with hypoxic effects on the foetus (49-51).

It is a common belief that foetal asphyxia develops during the second stage of labour, and several investigators have recommended a time limit from complete dilatation of the cervix to delivery, regardless of the urge to bear down, to ensure foetal well-being (49, 52, 53). However, subsequent research has yielded conflicting results on the effect of the duration of the second stage on foetal morbidity (54-57).

The normal duration (mean) of the second stage in the nulliparous is 54 minutes and the upper limit is 140 minutes (+ 2 SD), and in the parous 18 minutes with an upper limit of 60 minutes (38, 58, 59). With epidural anaesthesia one hour should be added.

Abnormal labour, dystocia

There is no universal consensus on definitions of abnormal labour, which makes it difficult to estimate the incidence of dystocia.

One way to categorise labour abnormalities is to divide them into protraction disorder (slower than normal) and arrest disorder (complete cessation of progress). To diagnose either of these disorders, the woman must be in the active phase of labour. The World Health Organisation (WHO) defines protraction disorder as less than 1 cm / h, cervical dilatation for a minimum of 4 hours (60). According to the Swedish ICD-10 classification, a protraction disorder is diagnosed if cervical dilatation is < 1 cm / h, and an arrest disorder if there is complete cessation of progress ≥ 2 hours (61).

Sokol et al reported that 25% of nulliparous and 15% of parous women had labour that was complicated by active phase abnormalities (62). In a Swedish retrospective study of 1480 deliveries, 21% were diagnosed with labour dystocia. The study included nulliparous and parous women and covered both the first and second stages of labour (63).

Augmentation of labour

The goal of oxytocin administration is to effect augmentation of labour; that is, uterine activity sufficient to produce cervical change and foetal descent while avoiding uterine hyper-stimulation and foetal compromise. A wide variety of oxytocin regimens may be used for labour augmentation provided that proper precautions are met (clear guidelines and continuous CTG).

The uterus of a woman in labour is sensitive to oxytocin and treatment is best started at a low dose and should be administered at the lowest possible
effective dose (64). The half life of oxytocin is 10-15 minutes and a steady plasma concentration is reached 40-60 minutes after every increase in infusion rate (65). The recommended interval between dose increments is 30 minutes and a frequency of contractions of three to four in ten minutes with each contraction lasting > 40 seconds is associated with normal progress of labour (66-68). The period of augmentation should be limited to four hours unless there is progress but can be continued up to six to eight hours as long as there is evidence of some progress (69).

Uterine hyperactivity

Adverse perinatal outcomes, related to foetal hypoxia due to impairment of gas exchange between contractions, may occur in the presence of uterine hyperactivity (24, 25). The condition can occur spontaneously or be of iatrogenic origin (oxytocin administration). As a general guideline, hyperactivity may be defined as a persistent pattern of more than five contractions in ten minutes, contractions lasting more than two minutes or more, or elevated basal tone, or contractions of normal duration occurring within 1 minute of each other and accompanied or not by reassuring CTG patterns (70). The frequency of contractions is considered more important with regard to placental perfusion and foetal hypoxia than are the duration and amplitude of contractions (22).

Studies have shown that the greatest drop in foetal oxygen saturation (SpO₂) occurs approximately 90 seconds after a contraction and an additional 90 seconds are needed for the foetus to recover (10, 35). During normal labour, foetal SpO₂ can decrease to a minimum level of 42.9 % (35, 71, 72), whereas during a hyperstimulation, a value as low as 23 – 36 % has been seen (24, 72). If hyperstimulation occurs during oxytocin administration the infusion rate should be decreased or discontinued. Discontinuation is effective on account of the short half-life of oxytocin.

Acidaemia at birth

An umbilical artery pH < 7.20 has traditionally been used to define acidaemia and at this level less severe neonatal outcome events, as admission to the NICU, Apgar score < 7 at five minutes, and assisted ventilation will occur. With worsening acidosis a progression of risk for these adverse outcomes has been described (73-76). A statistically significant increase in the incidence of serious neonatal morbidity (neonatal encephalopathy and demise) is not seen until the pH level is < 7.00 (73, 77, 78). The risk of complications in the newborn increases with umbilical artery blood gas values reflecting metabolic acidaemia with a base deficit ≥ 12 mmol/L (77-79). An umbilical arterial pH < 7.00 and base deficit ≥ 12 mmol/L occur in 3-4 / 1000 deliver-
ies (73, 80, 81). Of neonates with this degree of acidosis, 23.1% suffered from neonatal neurological morbidity or mortality (81).

Asphyxia occurs when placental gas exchange is impaired to an extent sufficient to cause metabolic acidosis, and if it is not relieved, the foetus will lose the ability to protect vital organs, resulting in cellular death, tissue damage, organ and system failure, and ultimately foetal death. The diagnosis requires a blood gas and acid–base assessment (82).

In situations where foetal compromise is suspected at birth, umbilical blood gas sampling is recommended, as it may assist with clinical management and excludes a diagnosis of birth asphyxia in approximately 80% of depressed newborns at term (82, 83). Obtaining umbilical artery blood gas in all deliveries gives an opportunity to evaluate intrapartum care objectively. With routine sampling care-givers receive immediate feedback and can learn from that information. Normal cord pH at birth provides evidence that the management of labour has not harmed the foetus and it will exclude oxygen deficiency during the final stage of labour. Abnormal values indicate that the foetus was in a state of biochemical decompensation at the time of birth which should stimulate care-givers to evaluate their care during labour critically (84).

The mean umbilical artery pH in newborns is 7.26-7.28 ± SD 0.05-0.07 (85-88). In a Swedish population of 23,000 neonates the mean umbilical artery pH was ± SD 7.28 ± 0.09 (20).

CTG patterns and association with neonatal acidaemia

Although intrapartum CTG monitoring has a low sensitivity for prediction of asphyxia, it serves as a screening method for predicting foetal asphyxial exposure in most modern delivery units. The sensitivity of the method with respect to the detection of foetal distress is high, but the specificity is low (89). This means that the method results in a high rate of false positive signals, and a concomitantly large number of interventions, especially if used in a group of low risk pregnant women (90). The low specificity of CTG for detection of foetal distress can be increased if it is combined with analysis of blood pH retrieved from the foetal scalp (fetal scalp blood sampling, FBS) (91). Compared to intermittent auscultation, FBS as a test adjuvant to CTG monitoring in the assessment of foetal well being, has been shown to reduce neonatal seizures (89, 92). If the scalp blood pH is < 7.20 intervention is appropriate (93).

A normal (reassuring) CTG is characterised by: a normal baseline frequency, normal variability, accelerations and no decelerations (94). A foetus with an initially normal CTG pattern will not fail to respond with CTG changes during hypoxic periods during delivery. With evolving patterns, acidaemia develops over a reasonable long period of time, of the order of at least one hour, which suggests that there is time for decision making and
appropriate intervention before serious acidaemia sufficient to damage the foetus has occurred (95). The interpretation of CTGs is difficult and highly subjective. The tracings are often interpreted differently by different caregivers, and even by the same people at different times (96-98).

In observational studies, different CTG patterns have been correlated to neonatal acidaemia, usually defined as pH < 7.15 or < 7.20 in the umbilical artery (95, 99-101). In general, there was agreement amongst these studies on the following: presence of variability is associated with absence of acidaemia, whereas a reduction in variability, particularly when combined with other abnormalities, is associated with acidaemia. In a review by Parer et al, it was emphasised that it is important to pay attention to the progress of loss of variability or deepening of decelerations, since evolution of a deteriorating CTG patterns indicates a risk of acidaemia (95).

The use of CTG patterns to identify foetuses with serious metabolic acidosis (pH < 7.00 and base deficit ≥ 12 mmol/L) and hypoxic ischaemic encephalopathy (HIE) has been studied by Larma et al., who found an association with CTG abnormalities, but the predictive values for these outcomes were low (102). Cases with metabolic acidosis had a significant increase in late and prolonged decelerations and late decelerations/contractions the last hour before delivery whereas cases with HIE had a significant increase in bradycardia, decreased variability and non-reactivity.

In studies of associations between neonatal outcome and different CTG patterns, the tocographic part of the CTG is rarely mentioned. Likewise, in guidelines on CTG monitorings, usually no information concerning uterine activity is provided (103).

**Neonatal outcome measures**

The goals of intrapartum foetal surveillance are to reduce the incidence of intrapartum foetal asphyxia and to prevent foetal asphyxia, thereby reducing perinatal mortality and to some extent cerebral palsy (CP). The outcome measures of interest when evaluating the effectiveness of foetal surveillance are perinatal mortality, CP and neonatal encephalopathy. The prevalence of these conditions is low, which means there is a need for large studies and long-term follow-up.

The incidence of neonatal encephalopathy (all grades) in term liveborn infants is estimated to be 2.5/ 1000 live born infants in developed countries (104). In Sweden the estimated incidence is 1.8/1000 live born infants (105). The incidence of neonatal encephalopathy attributable to intrapartum hypoxia is approximately 1.6/10,000 (106). In a recent review it was estimated that 14.5% of cases of CP in non-anomalous term infants were associated with intrapartum hypoxia-ischemia (81).
By reason of these low figures, intermediate measures that occur more often, such as different degrees of acidaemia, metabolic acidosis at birth, low Apgar scores and convulsions, are commonly used as outcomes (93).

Abnormal CTG → intermediate measures → absolute outcome measures

One essential criterium for defining an intrapartum hypoxic event as sufficient to cause CP is evidence of metabolic acidosis in foetal umbilical cord arterial blood obtained at delivery, see box below (107). Neonates with neurological morbidity and neonates who die of intrapartum asphyxia are recruited from the group of neonates born with metabolic acidosis, for which reason metabolic acidosis at birth should be avoided (108).

Admission to the NICU, Apgar score < 7 at five minutes and assisted ventilation are other outcome measures that are often used to evaluate neonatal morbidity.

Box 1.

Criteria for defining an acute intrapartum hypoxic event as sufficient to cause cerebral palsy:

1. Evidence of a metabolic acidosis in foetal umbilical cord arterial blood obtained at delivery (pH < 7.00 and base deficit ≥ 12 mmol/L).
2. Early onset of severe or moderate neonatal encephalopathy in infants born at ≥ 34 weeks of gestation
3. CP of the spastic quadriplegic or dyskinetic type.
4. Exclusion of other identifiable aetiologies, such as trauma, coagulation disorders, infectious conditions or genetic disorders.

Oxytocin in the third stage of caesarean delivery

Oxytocin stimulates the contraction of uterine smooth muscle and is recommended in the third stage of labour to reduce postpartum haemorrhage (109, 110). The value of routine oxytocin for prevention of excessive bleeding after vaginal delivery is well established and appears to reduce the risk of postpartum haemorrhage (> 500 ml) by about 40 % (111). It is assumed that routine oxytocin given in the third stage of labour at CS is also beneficial, although the doses appear to be empirical and to be extrapolated from studies on vaginal delivery (111-113).
Practice regarding administration of oxytocin at CS varies widely, reflecting the limited knowledge in this area (114, 115). In the UK, as in Sweden, an intravenous (i.v.) bolus is common, while in the United States an infusion is practice (114, 115). In 2004, a questionnaire was sent to 33 of the 47 obstetric units in Sweden and it was found that 70% administered an i.v bolus of 10 units, and 21% a bolus of 5 units, and that infusions were rare (unpublished data, M.J).

In a survey of the use of oxytocin at CS in the United Kingdom (UK) in 2001, it was found that 87% of obstetric anaesthetists used 10 units, and 50% administered the drug by rapid bolus (114). After the report of the Confidential Enquiries into Maternal Deaths in the UK 2001, which highlighted the risks of oxytocin given by rapid injection, The National Institute of Excellence, UK, recommended the use of 5 units of oxytocin given by slow i.v. injection, after delivery by CS (110, 116). The report prompted discussions within the obstetric anaesthesia community about the correct dose of oxytocin and its method of administration during CS, and in a follow up survey, a marked change in practice was found; then only 15% still administered 10 units (114).

Cardiovascular effects of oxytocin during caesarean delivery under regional anaesthesia

Oxytocin, given as an i.v. bolus, causes transient hypotension, a reflex tachycardia and an increase in cardiac output, in healthy women undergoing CS under spinal anaesthesia (117-119). The magnitude of these effects is dose-related (117, 119).

It is assumed that the primary haemodynamic effect of oxytocin is vasodilatation via receptors on vascular endothelium that trigger the nitric oxide pathway (120). The vascular effects of oxytocin occur shortly after an injection and are of short duration (117, 118, 121). Pinder et al compared 5 and 10 units of oxytocin administered as rapid boluses and found a significant decrease in mean arterial blood pressure (MAP) 30 seconds after injection of 10 units but not after 5 units, a significant increase in heart rate (HR) from 30 to 60 seconds after injection of 5 units and from 30 to 120 seconds after 10 units. The stroke volume increased significantly 60 seconds after 10 but not after 5 units (117).

Electrocardiographic changes during caesarean section

Electrocardiographic (ECG) changes, suggestive of myocardial ischaemia, have been observed in healthy women during elective CS under regional anaesthesia, and the reported incidence has varied from 25% to 60% (122-126). It has been suggested that the haemodynamic stress at CS delivery may
produce a situation in which myocardial oxygen demand outstrips the supply resulting in subendocardial ischaemia with consequent symptoms and ECG changes (123). An association of tachycardia and hypotension with ST depressions occurring during CS has been observed (123-125, 127, 128). The exact aetiology of ST segment depression is unknown and a number of explanatory theories have been proposed and are described below.

Delivery, whether vaginal or caesarean, increases venous return through the relief of aortocaval compression and an autotransfusion of uterine blood, with a resultant increase in cardiac output (129). In the presence of sympathetic blockade (regional anaesthesia) the acute hypervolaemia induced by prehydration and auto-transfusion from the uterus may place excessive demands on the myocardium, causing a transient increase in the left ventricular end diastolic volume and a consequent increase in myocardial oxygen demand (130).

A sympathectomy-induced decrease in diastolic arterial pressure decreases coronary perfusion pressure and impairs the myocardial oxygen supply (130).

Ephedrine is widely used in obstetrics to prevent and treat hypotension during regional anaesthesia. Both the systolic and diastolic blood pressures are elevated, mainly through cardiac stimulation (131, 132). The heart rate, myocardial contractility, and cardiac output increase, and it has been suggested that the myocardial oxygen demand increases (133), but no significant association between the peroperative use of ephedrine and subsequent ST-segment changes has been found during CS (122, 124, 126). Other vasopressor agents such as phenylephrine are also commonly used during caesarean delivery, but have not been subject to investigations with regard to ST depressions.

In previous studies, most of the ST depressions have occurred after delivery, which is the time period when oxytocics are given (122, 123, 126). Nevertheless, oxytocin as a causative agent of ST depressions has not been discussed in detail and has sometimes not been mentioned at all (122, 124). Recently, in a randomised double blind study comparing 10 units oxytocin with 0.2 mg methylergometrine, an association between oxytocin administration and ST depression was found during CS (134). A group of non-pregnant women receiving 10 units oxytocin was included for comparison in that study and it was concluded that signs of myocardial ischaemia were associated to oxytocin administration and not to pregnancy, spinal anaesthesia, surgical procedure or delivery.
Aims

The general aim of the thesis was to study adverse effects of oxytocin on foetal outcome when used in labour and maternal cardiac effects when used during caesarean section to prevent excessive bleeding

The specific aims were to:

- To analyse motives behind disciplinary actions in obstetric malpractice cases concerning delivery and to evaluate the frequency of inappropriate oxytocin use in these cases (study I)

- To find possible differences in the obstetric management during the last two hours of labour, especially with regard to uterine contraction frequency and to oxytocin use, in deliveries resulting in neonates with and without acidaemia at birth (study II)

- To find out the frequency of occurrence of suboptimal intrapartum care, and the nature of such care, during the last two hours before delivery in cases of metabolic acidosis in the neonate at birth. Further to estimate the proportion of cases with metabolic acidosis that possibly could have been prevented (study III)

- To investigate whether there is a difference in occurrence of electrocardiographic changes suggestive of cardiac ischaemia after injection of 5 or 10 units of oxytocin in healthy patients delivered by caesarean section under regional anaesthesia (study IV)
Material and methods

Study populations and study designs

Study I
A descriptive study of obstetric malpractice claims in Sweden, 1996-2003, concerning delivery cases that resulted in disciplinary action. During this period 369 malpractice claims involving pregnancy and delivery were filed with the Board of Medical Responsibility (BMR), 77 of which resulted in disciplinary action against physicians, midwives or both. Sixty cases concerned women in labour. Protocols were provided by the BMR.

Studies II and III
Retrospective case-control studies conducted in the period 1994-2004 at the delivery departments of Örebro and Uppsala University Hospitals in Sweden. The delivery departments maintain computerized databases containing data entered prospectively from the medical charts, delivery records and neonatal records by nursing personnel.

In study II the databases were searched for all newborns with a gestational age of ≥ 34 weeks’ and an umbilical artery pH < 7.05. Controls consisted of the first two newborns delivered after each study case with the same parity as the index case, a cord artery pH ≥ 7.05 and an Apgar score ≥ 7 at five minutes.

Deliveries by elective CS and cases of obstetric catastrophes (placental abruption, cord prolapse and eclampsia) and multiple pregnancies were excluded. Out of 28,486 deliveries, 305 cases and 610 controls were included in the study.

Study III compromised a subset of study II and consisted of cases with metabolic acidosis together with their two controls selected as described above. Metabolic acidosis was defined as pH < 7.05 and base deficit as ≥ 12 mmol / L. and 161 such cases were found.

Studies I – III were approved by the regional ethics committee in Uppsala.
Study IV
A randomised controlled study. All healthy term parturients scheduled to undergo elective CS under spinal anaesthesia at the Department of Obstetrics and Gynecology at the University Hospital in Uppsala, Sweden and who were ≥ 18 years old, were candidates for inclusion in the study.

Exclusion criteria were: multiple pregnancies, obesity (body mass index, BMI, > 35), pregnancy complications and non-proficiency in the Swedish language. Participants were recruited from November 2005 to July 2008. A total of 123 women were randomised, 61 of them to receive 5 units and 62 to receive 10 units of oxytocin, of whom 52 and 51 underwent the allocated intervention in the two groups respectively.

The study was approved by the regional ethics committee in Uppsala and the Medical Products Agency. Verbal and written consent was obtained from each participant.

Methods
Study I
In all cases, the investigations by and decisions of the BMR were reviewed with special focus on the use of oxytocin. Cases in which oxytocin was used were classified into high risk and low risk groups. The high risk group comprised pregnancies complicated by preeclampsia, preterm delivery (< 37 weeks), post term delivery, breech presentation, intrauterine growth restriction, and multiple pregnancies. Those assigned to the low risk group were singleton pregnancies with cephalic presentation, entering labour spontaneously at term after a normal pregnancy.

Factors analysed were parity, events during labour, mode of delivery, oxytocin use, perinatal outcome, and the assessment and decision made by the BMR, all of which were extracted from each protocol.

Study II
The delivery records were reviewed and the maternal information extracted for this study included maternal age, parity, length of gestation at delivery, pregnancy complications, use of intrapartum analgesia, mode of delivery and duration of bearing down. The complications of pregnancy or intercurrent disease retrieved were hypertension disorders, diabetes, autoimmune disease and asthma. Neonatal factors registered included gender, birth weight, Apgar score, umbilical artery blood gas analysis, cord entanglement and admission to the NICU.
**Umbilical artery blood gas**

The hospital policy at the centres includes obtaining umbilical artery blood samples for blood gas analyses in all deliveries. To identify foetuses adjusting to hypoxia and based on previous demonstrations of associations with neonatal complications, a pH value of < 7.05 in the umbilical artery was used as a definition of acidaemia, and metabolic acidosis was defined as pH < 7.05 with a base deficit of ≥ 12 mmol/L.

Of the blood gas samples in which paired pH and pCO$_2$ results were available, a venous-arterial pH difference of < 0.03 and a pCO$_2$ difference of < 1.0 kPa were considered to originate from the same vessel.

**Cardiotocography tracings**

The CTGs during the last 2 hours before delivery were reviewed in a blinded fashion and in accordance with the International Federation of Gynaecology and Obstetrics (FIGO) classification (94) by the authors M.J. and S.N.L. The FIGO categorisation defines a pathological CTG as a baseline of < 100 beats per minute (bpm), > 170 bpm, baseline variability < 5 bpm for > 40 minutes, severe variable decelerations, prolonged decelerations, late decelerations, or a sinusoidal pattern.

A hyperactive contraction pattern was defined as six or more contractions/10 minutes for at least 20 minutes. If there was no tracing, if the trace was too short (< 20 minutes) to allow interpretation, or if intermittent auscultation was used, the tracing was regarded as missing.

To evaluate interobserver agreement in the assessment of CTG tracings, a number of registrations were interpreted by both authors (n=25).

**Oxytocin**

Oxytocin treatment during labour, total duration of treatment and maximum infusion rates were recorded. The labour ward departmental protocol for oxytocin use was available at both units, with guidelines on how to control the effect of oxytocin infusion and how to avoid hyperstimulation, and it also required continuous CTG tracings during oxytocin treatment.

**Second stage**

Onset of the second stage of labour is usually defined as the time of full dilatation of the cervix. It is not possible to determine the precise moment of full dilatation. In the present study the last 2 hours of labour were studied in an attempt to analyse the second stage or the last part of the second stage of labour. Different labour strategies are used during the second stage and recommendations on when to push vary. At the delivery departments in the present study a tradition of delayed pushing is practised, i.e. awaiting the urge to push. Since the second stage or the last part of labour is considered the most dangerous to the foetus other intrapartum variables were not included in the present study.
Study III

Additional information from maternity and delivery records was retrieved for cases and controls. Maternal demographic variables added were: height (cm), BMI, and smoking during pregnancy. Additional variables related to delivery were: induction or spontaneous onset, prolonged rupture of membranes (> 24 h), oligohydramnios, meconium-stained fluid, intrapartum temperature > 38°C and duration of labour (stages I and II). A diagnosis of HIE (grade II and III) in the neonatal chart was recorded. The assessments (reassuring or nonreassuring) of admission CTGs performed by the attending midwives were retrieved.

Cases and controls were audited to evaluate the occurrence of suboptimal obstetric care. The audit was performed by the author M.J. with the same protocol for cases and controls without blinding as to groups.

The CTG interpretations made previously (study II) were used. Admission testing is routine and the delivery wards hold protocols for CTG interpretation and for guidelines on what action is to be taken in the event of abnormality. A normal (reassuring) CTG was defined as a normal CTG according to the FIGO criteria (94).

Study criteria for suboptimal care were predefined and cases and controls were assessed with respect to the categories described below. The criteria for suboptimal care used in this study can be regarded as the threshold below which, by consensus, the care is not acceptable to most practising obstetricians.

CTG patterns and suboptimal care

This category concerns the assessments of CTG recordings made during the last two hours before delivery and the CTG assessments made at the time when an oxytocin infusion was started.

In this category care was considered suboptimal if:

- there was failure to respond within the specified time limit to a pathological CTG pattern of ≥ 40 minutes’ duration (with the exception of bradycardia), by: decreasing or stopping an oxytocin infusion, taking a foetal scalp blood sample, or by delivery.

- there was failure to perform a CTG despite indications, or if there were poor quality tracings.

In the literature, we have found no specific time limit for action in the event of a pathological CTG pattern. We chose ≥ 40 minutes since this duration of pathological CTG resulted in marked neonatal morbidity (NICU stay > 2 days) in the present study.
Indications for continuous CTG recording during labour were: induction of labour, a non reassuring admission test, hypertensive disorders, oligohydramnios, gestational length ≥ 42 weeks, prolonged rupture of membranes, meconium – stained amniotic fluid, abnormal bleeding, raised intrapartum temperature > 38°C, and oxytocin administration.

**Oxytocin administration and suboptimal care**

In this category care was considered suboptimal if:

- oxytocin was administered without indication.
- oxytocin infusion was started or increased despite a pathologic CTG pattern
- oxytocin infusion was started despite uterine hyperactivity
- short increment intervals were applied (< 15 minutes).
- uterine contractions were hyperstimulated (≥ 6 contractions / 10 minutes > 20 minutes).
- a CTG tracing was not used continuously or if there was no or only a low quality tracing of uterine contractions.

When the oxytocin infusion was started, an assessment of the CTG was made (by author M.J). To decide whether there was an indication for oxytocin treatment, partograms were scrutinised and protraction or arrest disorders were diagnosed if the following criteria were met:

<table>
<thead>
<tr>
<th></th>
<th>Protraction disorder</th>
<th>Arrest disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First stage</strong></td>
<td>Cervical dilatation: &lt; 1 cm/hour</td>
<td>Arrest of cervical dilatation: ≥ 2 h</td>
</tr>
<tr>
<td><strong>Second stage</strong></td>
<td>Nulliparous: &gt; 2 h (epidural &gt; 3h)</td>
<td>Nulliparous: descent (epidural &gt; 2h)</td>
</tr>
<tr>
<td></td>
<td>Parous: &gt; 1 h (epidural &gt; 2h)</td>
<td>Parous: descent &lt; 2 cm/h</td>
</tr>
</tbody>
</table>

A combined disorder was designated a protraction disorder. Care was recorded as suboptimal if the patient did not fulfil the criteria (no indication) but was treated with oxytocin. The criteria used for protracted labour in the first stage were chosen, in the audit perspective, to avoid overestimation of cases without indication for oxytocin treatment.
Vacuum delivery and suboptimal care

Vacuum extractions (VE) exceeding 20 minutes, more than seven pulls, or with more than two detachments were regarded as suboptimal care (94, 135, 136).

Caesarean section and suboptimal care

In this category care was considered suboptimal if a CS for asphyxia was not started within 30 minutes from the decision.

After the systematic review of the events during labour and delivery, care was designated as optimal or suboptimal.

Precipitate labour was diagnosed if the active stage of labour was completed in three hours or less and on the assumption that it (from 3 – 4 cm of cervical dilatation) was displayed on the partogram, i.e. the diagnosis was not given if duration of labour was unknown (137, 138).

Study IV

In this double-blind randomised controlled study, participants were randomised to receive either 5 or 10 units of oxytocin (Syntocinon®, Novartis, Täby, Sweden) during CS under regional anaesthesia.

Primary endpoint: depression of the ST segment on ECGs during caesarean section.

Secondary outcomes: symptoms such as chest pain, shortness of breath or a feeling of heaviness on the chest; Troponin I levels 12 hours postoperatively; MAP; HR; and blood loss.

The anaesthetic technique used was the same in all subjects. Oxytocin was given in one minute as an i.v. bolus dose immediately after clamping of the umbilical cord.

Electrocardiographic recordings

Electrocardiograms were recorded by continuous ambulatory ECG (Holter) monitoring (SEER/MARS ® 10109; GE Medical systems, UK) during the peroperative period using a chest modified V5 (CM 5) lead and a modified inferior lead. ST segment depressions of 1 mm (0.1 mV), starting 60 ms after the J-point and lasting for a minimum of 1 minute, were considered significant if horizontal or downward sloping (139, 140). Holter tapes were analysed for significant changes by a cardiologist blinded to patient data.

The ST segment information obtained on ambulatory ECG monitoring has been validated and is similar to that obtained from the 12-lead ECG and can accurately reproduce ischaemic changes (140, 141). For identification of ischaemic ST segment deviation only two leads are required. The CM₅ is the single lead with the highest sensitivity (89%) in detecting myocardial ischaemia. With the addition of CM₃ or an inferior lead, the sensitivity can be increased to 94 % (142).
**Haemodynamic monitoring**

Noninvasive blood pressure (systolic, diastolic, and mean arterial (MAP)) and heart rate were monitored every 2 minutes, throughout surgery, using an automated blood pressure device.

**Measurements of Troponin I**

Troponin I, as a marker of ischaemic myocardial damage, was measured with a chemiluminescent microparticle immunoassay (Architect® STAT Troponin-I: ABOTT Laboratories, USA) in blood sampled 12 hours postoperatively. The reference ranges and cut-offs that we used were based upon results from population studies (143, 144) and the experiences of our Biochemistry Department and were as follows: lower limit of detection: < 0.022 μg/L; possible ischaemia or myocyte damage: > 0.030 μg/L; and acute myocardial infarction: > 0.30 μg/L. A dichotomous variable was used: values > 0.030 μg/L were considered elevated, while those < 0.030 μg/L were not.

Troponin I is considered the most useful biochemical marker for monitoring pregnant women for myocardial injury (145). In a study on healthy women at term, Shivers et al found that Troponin I levels remained undetectable and were not affected by obstetric anaesthesia, prolonged labour, or operative delivery (145). After myocardial damage Troponin I increases after four hours, peaks at around 12 h, and remains elevated for at least 4 days (146). In addition to conditions related to cardiac disease, elevated Troponin I levels can follow pulmonary embolism, renal failure and sepsis (147).

**Measurement of blood loss**

Blood loss during surgery was estimated by visual assessment of suction bottles and drapes. Preoperative haemoglobin values obtained at the latest antenatal visit (i.e. after 36 weeks of gestation) were recorded and 12 hours postoperatively, a full blood count was taken.

**Symptoms**

During surgery, any spontaneous complaints by the women of symptoms such as chest pain, shortness of breath or a feeling of heaviness on the chest were recorded, as well as the duration of these symptoms. Episodes of chest pain were assessed with a visual analogue scale (VAS).
Statistical analysis

For analysis of the data, the Statistical Package for Social Sciences (SPSS) for Windows, version 15.0, was used (SPSS, Inc., Chicago, IL, USA). A p value < 0.05 was considered to indicate a statistically significant difference.

Study I

Frequency distributions presented as percentages were used to describe variables.

Study II

To compare group distributions the chi-square test or Fisher’s exact test was applied. For comparing continuous variables, the Mann-Whitney U-test or t-test was used. Multivariate logistic regression was used to test for associations between different intrapartum factors and pH < 7.05 in the umbilical artery at birth. The 95% confidence intervals were calculated for the odds ratios. Interrater agreement in interpretation of CTG recordings was assessed by computing Cohen’s kappa (κ).

Study III

To compare group distributions the chi-square test or Fisher’s exact test was applied and the Mann-Whitney U-test or t-test was used for continuous variables.

Study IV

To compare group distributions the chi-square test or Fisher’s exact test was applied, while the Mann-Whitney U-test or t-test was used for continuous variables.
Results

Study I

During the study period 60 cases of malpractice claims concerned women in labour, and of these, oxytocin was used in 54 (90%). Cardiotocograms were normal at the beginning of labour in 87 % of the 54 cases, indicating a non-asphyxiated foetus (Table 1). As labour progressed the situation changed, in most cases with development of abnormal CTG patterns.

Table 1. Data on parity, delivery and neonatal outcome among the 54 cases in whom oxytocin was used.

<table>
<thead>
<tr>
<th></th>
<th>Low risk group</th>
<th>High risk group</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( n = 31 )</td>
<td>( n = 23 )</td>
<td>( n = 54 )</td>
</tr>
<tr>
<td><strong>Parity</strong>*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>nullipara</td>
<td>15 (48)</td>
<td>10 (43)</td>
<td>25 (46)</td>
</tr>
<tr>
<td>multipara</td>
<td>10 (32)</td>
<td></td>
<td>16 (29)</td>
</tr>
<tr>
<td><strong>Labour started</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>spontaneously</td>
<td>29 (93.5)</td>
<td>13 (56.5)</td>
<td>42 (78)</td>
</tr>
<tr>
<td>induced</td>
<td>2 (6.5)</td>
<td>10 (43.5)</td>
<td>12 (22)</td>
</tr>
<tr>
<td><strong>Door test</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>normal</td>
<td>28 (90.3)</td>
<td>19 (83)</td>
<td>47 (87)</td>
</tr>
<tr>
<td>abnormal</td>
<td>3 (9.6)</td>
<td>4 (17)</td>
<td>7 (13)</td>
</tr>
<tr>
<td><strong>Operative delivery</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VE or VE trial</td>
<td>20 (64.5)</td>
<td>14 (61)</td>
<td>34 (63)</td>
</tr>
<tr>
<td>Caesarean section</td>
<td>7 (22.5)</td>
<td>6 (26)</td>
<td>13 (24)</td>
</tr>
<tr>
<td><strong>Neonatal outcome</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>good/probably good</td>
<td>9 (29)</td>
<td>6 (26)</td>
<td>15 (28)</td>
</tr>
<tr>
<td>brain damage / CP</td>
<td>8 (26)</td>
<td>8 (35)</td>
<td>16 (30)</td>
</tr>
<tr>
<td>death</td>
<td>14 (45)</td>
<td>9 (39)</td>
<td>23 (42.6)</td>
</tr>
</tbody>
</table>

*not known in 13 cases.

VE= vacuum extraction

Table 2 summarizes the statements of the BMR and the different reasons underlying disciplinary action. More than one factor could contribute to reprimand in each case and more than one physician or midwife could be involved in the same case.
Table 2. The most frequent reasons for disciplinary action. Women in labour (n=60), subdivided according to use of oxytocin (n=54) or not (n=6). More than one reason was possible in each case.

<table>
<thead>
<tr>
<th>Reasons for reprimand</th>
<th>Oxytocin in labour n (%)</th>
<th>No oxytocin in labour n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Physicians</strong> (no. of cases)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Signs of compromised foetus, physician did not respond</td>
<td>27 (69)</td>
<td>6 (100)</td>
</tr>
<tr>
<td>Increased oxytocin infusion despite non reassuring CTG tracing or overstimulated labour</td>
<td>21 (54)</td>
<td>-</td>
</tr>
<tr>
<td>Misjudgement of the clinical situation</td>
<td>7 (18)</td>
<td>-</td>
</tr>
<tr>
<td>Inadequate CTG monitoring</td>
<td>4 (4.5)</td>
<td>1 (16.6)</td>
</tr>
<tr>
<td><strong>Midwives</strong> (no. of cases)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Signs of compromised foetus, did not call for the physician</td>
<td>17 (81)</td>
<td>-</td>
</tr>
<tr>
<td>Failure in responsibilities related to oxytocin administration</td>
<td>18 (86)</td>
<td>-</td>
</tr>
<tr>
<td>Inadequate CTG monitoring</td>
<td>3 (14)</td>
<td>1 (16.6)</td>
</tr>
<tr>
<td><strong>Physicians and midwives</strong> (no. of cases)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Signs of compromised foetus, physician or midwife did not respond</td>
<td>41 (76)</td>
<td>6 (100)</td>
</tr>
<tr>
<td>Injudicious use of oxytocin</td>
<td>37 (68.5)</td>
<td>-</td>
</tr>
<tr>
<td>Unclear roles of responsibility/ communication failure</td>
<td>4 (4.5)</td>
<td>1 (16.6)</td>
</tr>
</tbody>
</table>

FHR = foetal heart rate

Incorrect use of oxytocin was obvious in 68.5% of the 54 cases and was one of the main reasons for disciplinary action in 33%. When cases involving the use of oxytocin were categorised as high or low risk, physicians were found to be involved in the high risk group to a much higher degree (23/23) than midwives (4/23). Out of 22 disciplined midwives 18 midwives were involved in the low risk group.
Study II

Umbilical artery blood gas sampling was performed in 83% of all deliveries. The majority of neonates born with acidaemia had a normal Apgar score, 252/305 (82.6%). Among cases, the acidaemia had a metabolic component in 52.8%. Of the samples of paired pH and pCO2 results, it was estimated that 4.6% of samples were taken from the same vessel. A difference in age and post-term pregnancy was observed (Table 3).

Table 3. Obstetric and neonatal characteristics in the case and control group.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Cases n = 305</th>
<th>Controls n = 610</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parity nullipara</td>
<td>180 (59.0)</td>
<td>360 (59.0)</td>
<td></td>
</tr>
<tr>
<td>multipara</td>
<td>125 (41.0)</td>
<td>250 (41.0)</td>
<td></td>
</tr>
<tr>
<td>Age, yrs</td>
<td>30.7 ± 5.0</td>
<td>29.3 ± 5.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gestational length, wks</td>
<td>39.8 ± 1.4</td>
<td>39.6 ± 1.4</td>
<td>ns</td>
</tr>
<tr>
<td>Post-term pregnancy, ≥ 42 wks</td>
<td>33 (10.8)</td>
<td>32 (5.2)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Pregnancy complication or intercurrent disease</td>
<td>51 (16.7)</td>
<td>75 (12.3)</td>
<td>ns</td>
</tr>
<tr>
<td>Birth weight, g</td>
<td>3568 ± 506</td>
<td>3571 ± 518</td>
<td>ns</td>
</tr>
<tr>
<td>SGA &lt; mean – 2 SD</td>
<td>6 (2.0)</td>
<td>10 (1.6)</td>
<td>ns</td>
</tr>
<tr>
<td>LGA ≥ mean +2 SD</td>
<td>11 (3.6)</td>
<td>16 (2.6)</td>
<td>ns</td>
</tr>
<tr>
<td>Male gender in neonates</td>
<td>163 (53.4)</td>
<td>305 (50.0)</td>
<td>Ns</td>
</tr>
</tbody>
</table>

Values are given as n (%) or means ± standard deviation (SD).
LGA = large for gestational age; SGA = small for gestational age
ns = non - significant

The duration of bearing down was longer and cord entanglement at delivery was more common, in the case group. Cases were significantly more often delivered by vacuum extraction and in the occiptio-posterior (OCP) position (Table 4).
The proportions of newborns admitted to the NICU differed between cases (31.9 %) and controls (2.6 %). Among the cases, 13.8 % and among controls, 1.0 % stayed in the NICU for > 2 days (p< 0.001).

Table 3. Methods of delivery and of analgesia, and other intrapartum variables among cases and controls.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Cases n = 305</th>
<th>Controls n = 610</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bearing down efforts, minutes</td>
<td>53.0 ± 47</td>
<td>38.8 ±38</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Vacuum extraction</td>
<td>85 (27.9)</td>
<td>54 (8.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Caesarean delivery</td>
<td>31 (10.2)</td>
<td>48 (7.9)</td>
<td>ns</td>
</tr>
<tr>
<td>Breech presentation</td>
<td>5 (1.6)</td>
<td>6 (1.0)</td>
<td>ns</td>
</tr>
<tr>
<td>Occipito-posterior</td>
<td>23 (7.5)</td>
<td>22 (3.6)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Cord entanglement</td>
<td>86 (28.2)</td>
<td>79 (13.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Epidural anaesthesia</td>
<td>104 (34.1)</td>
<td>234 (38.4)</td>
<td>ns</td>
</tr>
<tr>
<td>Pethidine</td>
<td>16 (5.2)</td>
<td>21 (3.4)</td>
<td>ns</td>
</tr>
<tr>
<td>PCB</td>
<td>7 (2.3)</td>
<td>5 (0.8)</td>
<td>ns</td>
</tr>
</tbody>
</table>

Values are given as n (%) or means ± standard deviation (SD). PCB = paracervical blockade.

The use of oxytocin infusion during the last 2 hours of labour was more common among cases (Table 5). In women with hyperactive labour in the case group, 75% (63/84) were treated with oxytocin. The median (quartiles) duration of oxytocin treatment (total time) was 120 (60 - 300) minutes in the case and 180 (63 - 332) minutes in the control group (ns). The mean maximal oxytocin infusion rate was 18 ± 13 mU/min and 16 ± 13 mU/min respectively (ns).
Table 4. Use of oxytocin and frequency of contractions during the last 2 hours preceding delivery. Four or more contractions overlapping with 6 contractions/10 minutes.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Cases n = 305</th>
<th>Controls n = 610</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxytocin use during the last 2 hours of labour</td>
<td>186 (61.0)</td>
<td>254 (41.6)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>≥ 4 contractions /10 minutes*</td>
<td>195 (90.3)</td>
<td>303 (80.1)</td>
<td>0.001</td>
</tr>
<tr>
<td>≥ 6 contractions /10 minutes*</td>
<td>84 (38.9)</td>
<td>43 (11.3)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>≥ 6 contractions /10 minutes and oxytocin treatment*</td>
<td>63 (28.3)</td>
<td>29 (7.4)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

* in cases and controls in whom tocography was performed.

Pathological CTG patterns occurred in 68.8% of the cases and in 26.1% of the controls (p< 0.001). The duration of pathological patterns during the last two hours differed, being 55 ± 40 minutes (mean ± SD) vs. 44 ± 36 minutes in the case and control group respectively (p < 0.05). About 16 % of the CTG tracings were missing, in 12.1% of the cases and 20.3% of the controls (p < 0.05). The interobserver agreement in the interpretation of CTGs was good (κ = 0.66).

Table 6 gives the odds ratios and 95% confidence intervals for some intrapartum factors, including contraction frequency and oxytocin use.

Table 5. Logistic regression analysis of intrapartum factors associated with pH < 7.05. Age and post-term pregnancy are included in the analysis

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Univariate analysis OR (95% CI)</th>
<th>Multivariate analysis OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 6 contractions / 10 min</td>
<td>4.94 (3.25 - 7.49)</td>
<td>5.36 (3.32 - 8.65)</td>
</tr>
<tr>
<td>Oxytocin infusion during the last 2 hours of labour</td>
<td>2.20 (1.66 - 2.92)</td>
<td>1.89 (1.21 - 2.97)</td>
</tr>
<tr>
<td>Cord entanglement</td>
<td>2.65 (1.88 - 3.73)</td>
<td>4.08 (2.49 - 6.67)</td>
</tr>
<tr>
<td>Occipito-posterior position</td>
<td>2.18 (1.19 - 3.98)</td>
<td>1.59 (0.60 - 4.18)</td>
</tr>
<tr>
<td>Bearing down for ≥ 45 min</td>
<td>1.77 (1.31 - 2.38)</td>
<td>1.42 (0.91 - 2.22)</td>
</tr>
</tbody>
</table>

OR = odds ratio; CI = confidence interval.
The results of the multivariate analysis showed that significant risk factors associated with pH < 7.05 were six or more contractions/10 minutes, oxytocin use and cord entanglement (Table 6). Duration of bearing down and OCP position were significant in the univariate analysis but reduced and not significant in the multivariate analysis.

**Study III**

Seventy-nine cases (49.1 %) and 42 controls (13.0 %) were assessed as having had suboptimal care (p < 0.001). Labour started spontaneously in 134 cases (83.2 %) and 283 controls (87.9 %) (ns), and the admission test was reassuring in 140 (86.9 %) and 303 (94.1 %) respectively (p< 0.05). There was a difference in maternal age, 31 ± 5 vs. 29 ± 5 years, and maternal height, 166 ± 6 vs. 167 ± 6 cm, between the case and control groups respectively. There was no difference in BMI, smoking during pregnancy, gestational length, complications of pregnancy or intercurrent disease.

Table 6. Duration of labour and oxytocin administration during the last two hours preceding delivery.

<table>
<thead>
<tr>
<th></th>
<th>Cases n = 161</th>
<th>Controls n = 322</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of labour, total time(hours)*</td>
<td>6.3 (3.7 - 9.8)</td>
<td>5 (3.1 -7.6)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>First stage, h*</td>
<td>4.9 (2.5 – 8.0)</td>
<td>4 (2.5 – 6.6)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Second stage, min *</td>
<td>60 (30 – 105)</td>
<td>45 (19 – 90)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Bearing down effort, min ( mean ± SD)</td>
<td>60 (± 52)</td>
<td>44 (± 40)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Protraction or arrest disorder</td>
<td>48 (29.8)</td>
<td>105 (32.6)</td>
<td>ns</td>
</tr>
<tr>
<td></td>
<td>42 (87.5)</td>
<td>91 (86.7)</td>
<td></td>
</tr>
<tr>
<td>First stage</td>
<td>6 (12.5)</td>
<td>14 (13.3)</td>
<td></td>
</tr>
<tr>
<td>Second stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Precipitate labour</td>
<td>28 (17.4)</td>
<td>33 (10.2)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Oxytocin administration in the last 2 hours before delivery</td>
<td>99 (61.5)</td>
<td>135 (41.9)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Duration of oxytocin treatment, min (total time)</td>
<td>130 (65-328)</td>
<td>195 (68 – 360)</td>
<td>ns</td>
</tr>
<tr>
<td>Maximum infusion rate mU/min</td>
<td>12 (7-20)</td>
<td>15 (8-20)</td>
<td>ns</td>
</tr>
</tbody>
</table>

Values are given as n(%), or median (quartiles), Chi-square test or Mann-Whitney test.
* Vaginal delivery
The duration of labour was longer in the case group, but no difference in diagnosis of protraction or arrest disorders was found (Table 7). There was no difference in occurrence of prolonged rupture of membranes, oligohydramnios, or increased intrapartum temperature. Meconium stained water occurred more often among cases than among controls (56 cases, 35.0 %; 60 controls 18.8 %) p < 0.001. The mode of delivery differed; 24 cases (14.9 %) and 22 controls (6.8 %) were delivered by a CS (p < 0.01), whereas 44 cases (27.3 %) and 26 controls (8.1 %) were delivered by vacuum extraction (p < 0.001).

Tables 8 and 9 show the nature of suboptimal care with regard to the use of oxytocin and pathological CTG patterns, during the last two hours before delivery. Hyperactive labour occurred in 42 of the cases (26.1 %) vs. 22 of the controls (6.8 %). In cases with hyperactive labour 71.4 % (30/42) were treated with oxytocin. Injudicious use of oxytocin mainly consisted of a lack of indication in the control group, whereas in the case group there was a distribution amongst all criteria for suboptimal care.

Table 7. Suboptimal care regarding oxytocin use during the last two hours preceding delivery in the case and control group. There is overlapping within groups.

<table>
<thead>
<tr>
<th></th>
<th>Cases, n= 161</th>
<th>Controls, n = 322</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxytocin administration in last 2 hours before delivery</td>
<td>99 (61.5)</td>
<td>135 (41.9)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Injudicious use of oxytocin</td>
<td>75 (46.6)</td>
<td>42 (13.0)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>No indication was found</td>
<td>41 (25.4)</td>
<td>35 (10.8)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Infusion was started despite a pathological CTG</td>
<td>31 (19.4)</td>
<td>5 (1.6)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Infusion rate was increased despite a pathological CTG ≥ 40 min</td>
<td>44 (27.3)</td>
<td>8 (2.5)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Short increment interval (&lt; 15 min)</td>
<td>31 (19.3)</td>
<td>12 (3.7)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Contractions ≥ 6/10 min and oxytocin treatment</td>
<td>30 (18.6)</td>
<td>10 (3.1)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Precipitate labour</td>
<td>6 (3.7)</td>
<td>4 (1.2)</td>
<td>ns</td>
</tr>
</tbody>
</table>
In a sub analysis of the oxytocin stimulated labours, care was considered suboptimal in 75/99 (75.8 %) of cases and in 42/135 (31.1 %) of controls. The most prominent finding was the difference in increase of an oxytocin infusion and/or overstimulation of labour despite a pathological CTG ≥ 40 min which was found in 44/99 (44.4 %) of cases compared to 8/135 (5.9 %) of controls and in 15/47 (31.2 %) compared to 1 /27 (3.7 %) respectively.

Pathological CTG patterns occurred significantly more often in the case group (Table 9). The types of pathological CTG patterns that differed most between cases and controls were: decreased variability (42.4 vs. 7.3%), bradycardia (31.5 vs. 6.1%) and variable decelerations (69.2 vs. 36.0 %). In a subanalysis of cases, subjects with pH < 7.00 differed with regard to type of CTG pattern compared to those with pH > 7.00 (decreased variability 51.6 vs. 26.4%; and complicated variable decelerations 54.7 vs. 37.3 %), whereas cases with HIE differed from those without HIE with regard to decreased variability (91.7 vs. 38.2 %). The duration of a pathological CTG pattern in the last two hours before labour did not differ between cases and controls, (mean ± SD) 58 ± 42 vs. 50 ± 39 minutes or between cases with pH < 7.00 and those with pH > 7.00 (61 ± 42 vs. 53 ± 40 minutes) or between cases with and without HIE (71 ± 49 vs. 56 ± 40 minutes).

Table 8. Occurrence of pathological CTG patterns during the last two hours before delivery among cases and controls. Types of suboptimal care that were identified, overlap within groups.

<table>
<thead>
<tr>
<th></th>
<th>Cases, n = 161 n (%)</th>
<th>Controls, n = 322 n (%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CTG recordings missing</td>
<td>17 (10.6)</td>
<td>52 (16.1)</td>
<td>ns</td>
</tr>
<tr>
<td>Pathological CTG pattern</td>
<td>109 (67.7)</td>
<td>71 (22.1)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Pathological CTG pattern ≥ 40 min</td>
<td>65 (40.4)</td>
<td>37 (11.5)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>No response to pathological CTG pattern ≥ 40 min</td>
<td>32 (19.9)</td>
<td>4 (1.2)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Injudicious use of oxytocin and pathological CTG pattern ≥ 40 min</td>
<td>39 (24.2)</td>
<td>7 (2.2)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>No CTG performed despite indications, or poor CTG quality</td>
<td>8 (5.0)</td>
<td>26 (8.1)</td>
<td>ns</td>
</tr>
</tbody>
</table>

Newborns were admitted to the NICU more often from the case group: 78 (48.4 %), compared to 15 (4.6 %) in the control group (p < 0.001). Among
the cases, 47 (29.2 %) stayed in the NICU for > 2 days, compared to 7 (2.2 %) among the controls (p < 0.001). There was no difference in birth weight or gender of the neonate between the case and control group.

The neonatal outcome in the case group, sorted into subgroups with a reassuring and non reassuring admission test, is presented in Table 10.

Table 9. Neonatal outcome in the case-group according to the admission test.

<table>
<thead>
<tr>
<th></th>
<th>Reassuring admission test n (%), n = 140</th>
<th>Non- reassuring admission test n (%), n = 20</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH &lt; 7.00</td>
<td>78 (55.7)</td>
<td>13 (65.0)</td>
<td>ns</td>
</tr>
<tr>
<td>Apgar &lt; 7 at five minutes</td>
<td>26 (18.5)</td>
<td>10 (50.0)</td>
<td>0.002</td>
</tr>
<tr>
<td>Apgar &lt; 4 at five minutes</td>
<td>6 (4.3)</td>
<td>1 (5.0)</td>
<td>ns</td>
</tr>
<tr>
<td>NICU &gt; 2 days</td>
<td>39 (27.8)</td>
<td>8 (40.0)</td>
<td>ns</td>
</tr>
<tr>
<td>HIE grade II</td>
<td>8 (5.7)</td>
<td>6 (30.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>grade III</td>
<td>5</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>grade III</td>
<td>3</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

NICU: neonatal intensive care unit. HIE: hypoxic ischaemic encephalopathy.

Table 11 shows the neonatal outcome in relation to the admission test and assessment of care. Three cases with encephalopathy were found in the group where the care had been assessed as optimal and the admission test was normal. One had precipitate labour, one was admitted with a cervical dilatation of 10 cm and was delivered by VE because of fetal distress and one neonate was born with unexpected asphyxia after a delivery with intermittent foetal surveillance.
Table 10. Neonatal outcome in the case-group according to the admission test and assessment of intrapartum care.

<table>
<thead>
<tr>
<th></th>
<th>Reassuring admission test</th>
<th>Non-reassuring admission test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Suboptimal care, n (%)</td>
<td>Optimal care, n(%)</td>
</tr>
<tr>
<td>n = 81</td>
<td>n = 57</td>
<td></td>
</tr>
<tr>
<td>pH &lt; 7.0, umb artery</td>
<td>47 (58.0)</td>
<td>30 (52.6)</td>
</tr>
<tr>
<td>Apgar &lt; 7 at five minutes</td>
<td>19 (23.5)</td>
<td>7 (12.3)</td>
</tr>
<tr>
<td>Apgar &lt; 4 at five minutes</td>
<td>4 (4.9)</td>
<td>2 (3.5)</td>
</tr>
<tr>
<td>NICU &gt; 2 days</td>
<td>27 (33.3)</td>
<td>12 (21.1)</td>
</tr>
<tr>
<td>HIE grade II</td>
<td>5 (6.3)</td>
<td>3 (5.3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Suboptimal care, n (%)</td>
<td>Optimal care, n(%)</td>
</tr>
<tr>
<td>n = 8</td>
<td>n = 12</td>
<td></td>
</tr>
<tr>
<td>pH &lt; 7.0, umb artery</td>
<td>5 (62.5)</td>
<td>8 (66.6)</td>
</tr>
<tr>
<td>Apgar &lt; 7 at five minutes</td>
<td>4 (50.0)</td>
<td>6 (50.0)</td>
</tr>
<tr>
<td>Apgar &lt; 4 at five minutes</td>
<td>0</td>
<td>1 (8.3)</td>
</tr>
<tr>
<td>NICU &gt; 2 days</td>
<td>3 (37.5)</td>
<td>5 (41.7)</td>
</tr>
<tr>
<td>HIE grade II</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>HIE grade III</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

NICU=neonatal intensive care unit. HIE = hypoxic ischaemic encephalopathy.

Suboptimal care related to complicated VE was found in 5 /42 in the case group and in 1/29 among the controls. The indication for vacuum delivery was mainly foetal distress among cases (80%), whereas dystocia or maternal exhaustion were the main indications among controls (69 %).

When CS was performed because of fetal distress, a delay in time between decision and delivery occurred twice in the case group, and once in the control group. The indications for CS differed, foetal distress being the indication in 17 subjects (70.8 %) in the case group compared to 3 (13.6 %) in the control group.

**Study IV**

There was no difference in baseline demographic or clinical characteristics, or in indication for CS, between groups. A significant difference between groups in the occurrence of ST depressions associated with oxytocin administration was found (Table 12). The relative risk reduction with the lower dose was 64.4 % for this outcome measure, while the absolute risk reduction was 13.9 % (95% CI, 0.5 – 27.3). When all ST depressions were considered, 68 % showed a temporal relationship with oxytocin administration i.e., they occurred within 3 minutes after the injection.
Table 11. ST depression on the electrocardiogram (ECG), symptoms and Troponin I.

<table>
<thead>
<tr>
<th>ST depression associated with oxytocin bolus</th>
<th>5 units, n = 52</th>
<th>10 units, n = 51</th>
<th>Difference % (95 % CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ST depression not associated with oxytocin bolus</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ST depression, total number</td>
<td>4 (7.7)</td>
<td>11 (21.6)</td>
<td>13.9 (0.5 – 27.3)</td>
<td>0.046</td>
</tr>
<tr>
<td>Duration of ST depression, minutes</td>
<td>3 (5.8)</td>
<td>4 (7.8)</td>
<td>-</td>
<td>ns</td>
</tr>
<tr>
<td>Symptom*</td>
<td>2 (3.8)</td>
<td>7 (13.7)</td>
<td>-</td>
<td>0.09</td>
</tr>
<tr>
<td>Troponin I elevated</td>
<td>2 (4.3)</td>
<td>2 (4.5)</td>
<td>-</td>
<td>ns</td>
</tr>
</tbody>
</table>

Values are given as n (%) or as medians with percentile range (25th – 75th). CI = confidence interval. ns = non significant.
*Chest pain, feeling of heaviness in the chest, shortness of breath.
Troponin I elevated if > 0.030 μg/L. Blood samples missing in 12 patients (5 units, n = 5 and 10 units, n = 7).

Figure 1 shows the mean MAP after oxytocin bolus injection. The difference in decrease in mean MAP from baseline to 2 minutes between groups was significant (p < 0.01).

Figure 1. Mean arterial pressure (MAP): mean ± SD, time from drug administration.

In six of the seven subjects with an ST depression not associated with oxytocin administration, a decrease in MAP comparable to that occurring
with ST depression after an oxytocin bolus was found. In one of the six subjects, a hypertensive episode with tachycardia was recorded.

Figure 2 shows that both regimens produced a statistically significant increase in mean HR from baseline to 2 minutes (p < 0.001); the difference between groups was not significant.

Symptoms such as chest pain (n = 2), shortness of breath, or a feeling of heaviness in the chest (n = 7) occurred in nine patients, two in the group that received 5 units of oxytocin, and seven in the 10 unit group (ns).

ST depression occurred in 6 (67 %) of the patients with symptoms (all of whom were in the 10 unit group), while 27 % of patients with ST depression had symptoms.

The Troponin I level was increased in four subjects (3.9%), two in each dosage group. There were no differences in blood loss or pre- or postoperative haemoglobin values between the 5 and 10 unit group (Table 13).

Table 12. Estimated blood loss and haemoglobin values.

<table>
<thead>
<tr>
<th></th>
<th>5 units oxytocin mean ± SD</th>
<th>10 units oxytocin mean ± SD</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin (g/L), preoperative</td>
<td>124 ± 9.0</td>
<td>124 ± 9.4</td>
<td>ns</td>
</tr>
<tr>
<td>Haemoglobin (g/L), postoperative</td>
<td>111 ± 9.9</td>
<td>111 ± 9.3</td>
<td>ns</td>
</tr>
<tr>
<td>Estimated blood loss, mL</td>
<td>585 ± 434</td>
<td>540 ± 363</td>
<td>ns</td>
</tr>
</tbody>
</table>

ns = non significant
SD = standard deviation
Discussion

Study I

In the material presented here, disciplinary action due to negligence was, with few exceptions related to misjudgement of CTG patterns. The most common shortcoming was that physicians failed to act in a timely and appropriate manner when CTG patterns indicated a compromised foetus. Injudicious use of oxytocin was obvious in most cases, with a frequency higher than has been reported from earlier studies and close to the level found with failure to respond to an abnormal CTG pattern. A common negligence pattern was violation of unit guidelines regarding oxytocin use and CTG patterns, and despite objective evidence of foetal distress there was failure to perform investigation (FBS) and timely delivery. The physicians were generally considered too passive in their management of the woman in labour.

The majority was classified as low risk, which is in agreement with results of similar studies but also with observational studies (6, 148, 149). In a study by Westgate et al on infants born with moderate or severe neonatal encephalopathy, none were associated with high risk pregnancies (149). It was suggested that improvements in obstetric care have been effective in the high risk population and that obstetricians should be aware that encephalopathy in term infants now derives primarily from low and medium risk pregnancies.

Analyses of obstetric claims of medical negligence during the last two decades have shown recurrent themes and the findings are in accordance with the present results (4, 7, 27). In a Swedish study on complaints filed to the BMR published in 1992 (6), the percentages of failure to respond appropriately to CTG abnormalities were almost identical to our results, and since the frequency of obstetric complaints filed to the BMR resulting in disciplinary action has not decreased, it has to be questioned whether this source has been used to increase knowledge.

Although the generalisability of analyses of this kind is weak they may help to identify opportunities to improve quality of care and also to form the basis of research hypotheses (150-152).

In summary, most of the preventable complications that lead to claims of medical malpractice in labour arise from violation of a few basic principles of intrapartum care. Many, if not most, involve the misuse of oxytocin.
Study II

In this study, the strong association between acidaemia and a hyperactive uterine contraction pattern during the last two hours before delivery implies a difference in labour management in neonates with and without acidaemia at birth. In the majority of cases with hyperactive labour, oxytocin was administered, indicating that its use was inappropriate and the acidaemia iatrogenic and probably avoidable.

Oxytocin remained as an independent risk factor for acidaemia after adjustment for uterine contraction frequency in the analyses. This finding is in agreement with the results from a study by Herbst et al, who like us defined acidaemia as an umbilical artery pH < 7.05 (20). The present study and the study by Herbst et al were data based from clinical practice and were not conducted as prospective studies of the drug. By contrast, several prospective studies on oxytocin-induced or augmented labour have failed to show an increased risk of acidaemia in association with oxytocin treatment (12-15). An explanation for the conflicting results may be that if strict guidelines for oxytocin administration are followed, regarding supervision of the contraction frequency and CTG pattern, the risk of acidaemia at birth for this reason could be avoided.

There was no difference in maximum infusion rate or duration of oxytocin administration between cases and controls, which supports the assumption that the responses of the uterus and the foetus are more important than the infusion rate or duration of oxytocin administration.

The higher frequency of pathological CTGs and the longer duration of such patterns in the case group imply that a failure of adherence to guidelines on CTGs occurred more often among cases.

After adjustment for uterine contraction frequency, duration of bearing down efforts of ≥ 45 minutes had no impact on the occurrence of acidaemia in the present study. This underlines the importance of avoiding uterine hyperactivity during the bearing down period. This finding is in contrast to the results of other studies, where progressive acidaemia or lactacidaemia with increased duration of bearing down efforts has been reported (49, 51, 153). None of these reports included uterine contraction frequency or the use of oxytocin, which could explain the conflicting results. Thus, in studies on the second stage and in particular the active second stage (bearing down period), the uterine contraction frequency is an important variable to consider.

An OCP position is associated with a prolonged second stage of labour and increased oxytocin augmentation (154, 155). Findings on the association between an OCP position and adverse neonatal outcomes are contradictory (155-157). In a large retrospective cohort study, Cheng et al found an association between acidaemia and an OCP position (157). In that study, length of labour, but not oxytocin use or uterine activity, was taken into account in
the multivariate analysis, which could explain why the reported results contradict the results of the present study.

The risk of morbidity associated with acidaemia increases progressively with decreasing pH levels (73-76). According to a study by Victory et al, the risk of neonatal morbidity begins at pH 7.20 with a less severe neonatal outcomes such as low Apgar score (< 7 at 5 minutes), admission to the NICU and a need for assisted ventilation (76). The risk increased with worsening acidosis. In accordance with those findings, the cases in our study were more often admitted for neonatal care than were controls, and newborns with metabolic acidosis were in even greater need of neonatal care at birth. Nevertheless, most infants with acidaemia at birth are healthy, and it is important to recognise the difficulty in anticipating the ability of the individual foetus to cope with the stress of labour in a given situation.

To avoid acidaemia in the newborn, close attention to the uterine contraction frequency and CTG patterns is important, particularly so in labours in which contractions are stimulated pharmacologically. To obtain umbilical arterial pH values in the depressed neonate is important and in the vigorous newborn it appears to be a valuable tool in the assessment of the quality of intrapartum care.

Study III

In this study, we found that suboptimal intrapartum care occurred in half of the cases with metabolic acidosis at birth, while it was less frequent, but not uncommon among controls. Among the cases, suboptimal care consisted of injudicious use of oxytocin and failure to take appropriate action upon signs of foetal distress. The high rate of NICU admission and diagnosis of encephalopathy in the case group confirms that metabolic acidosis should be avoided. We estimate that metabolic acidosis could probably have been prevented in half of the cases with a reassuring admission test.

Most alarmingly, in many cases, oxytocin infusions were started and increased despite a pathological CTG pattern without confirming foetal well-being, and uterine contractions were frequently overstimulated among cases. Probably, oxytocin was given to an already compromised foetus with the aim of delivering promptly. It appears that the relationship between oxytocin administration and pathological CTG patterns has been overlooked and that appropriate attention to uterine contraction patterns, which is a prerequisite for proper reading and interpretation of cardiotocograms, has not been paid. Such incorrect management was less frequent in the control group.

Pathological CTG patterns occurred in both groups but were more frequent among cases. The difference in the response to abnormal patterns of this duration was pronounced and is an important finding in the present study. Failure to respond to foetal distress was uncommon in the control group, whereas non-responsiveness was frequent in the case group. Thus,
CTG interpretation and responsiveness to abnormalities constitute an important area for improvement.

In agreement with the results by Larma et al, we found a CTG pattern with decreased variability in the last two hours of labour to be associated with serious neonatal morbidity (102).

As in study II, there was no difference in the occurrence of intercurrent disease or complications during the pregnancy between cases and controls, although there was a tendency to more complications among cases (p value = 0.06). The majority of the cases group derived from a low risk group: women with an uncomplicated pregnancy and a spontaneous start of delivery. This finding is consistent with previous reports that serious neurological morbidity in term neonates almost entirely derives from low and medium risk pregnancies (148, 149).

An unexpected finding was that a significant number of cases had precipitate labour. The possibility of an association of this condition with metabolic acidosis has not, to our knowledge, been investigated and our results indicate that precipitate labour is not always favourable and could be a risk factor.

Overall, suboptimal care related to complicated vacuum extractions and a delay in decision-to-delivery time for caesarean section or vacuum delivery was not so frequent in the present study. This result is in accordance with findings in a case-control study by Gaffney et al, who also investigated suboptimal intrapartum care (158), whereas the results are contradictory to reports from malpractice studies (159, 160). Malpractice analyses are biased towards more serious injuries and this issue does not seem to be applicable in a large population.

A high incidence of abnormal admission CTGs has been reported among neonates with encephalopathy and neurologically impaired infants, implying an antenatal event beyond the control of the obstetrician (161-163). Accordingly, we found the highest rate of low Apgar scores, NICU stay > 2 days and encephalopathy in this group. Failure to respond appropriately to pathological CTG tracings was the most frequent form of suboptimal care in this group. These foetuses may be more vulnerable and labour might aggravate the risk of neonatal morbidity (164). The possibility of preventing neonatal morbidity in this group is difficult to evaluate, since the duration of foetal compromise is not known.

The question to what extent metabolic acidosis, neonatal morbidity and encephalopathy can be prevented is difficult to assess (86, 158, 165). A reassuring admission test reflects normal foetal behaviour and absence of hypoxia at the beginning of labour (166, 167) and was found in a great majority of our cases and controls. This group is important, as here, the probability of delivering a healthy infant is the greatest and preventive measures could be successful. Nevertheless it is obvious from the present study that in a number of cases with a normal admission test, metabolic acidosis is probably not avoidable despite appropriate intervention.
The incidence of metabolic acidosis in this study was low, 0.68 %. Nevertheless, we estimate that metabolic acidosis at birth could probably have been avoided in 40-50 % of cases.

General discussion studies I - III
Suboptimal CTG monitoring practice and injudicious use of oxytocin are persistent findings in obstetric malpractice analyses and observational studies concerning HIE and CP (29, 159, 160, 168, 169). Analyses of this kind are limited, as they concern series of highly selected cases from which it is difficult to generalise. Our studies on cases with acidaemia in the neonate at birth and controls from a large population confirm that incorrect assessment of CTGs and the misuse of oxytocin are issues of concern not only in seriously damaged infants.

Oxytocin is the drug most commonly associated with preventable adverse events during delivery (170). The mistakes regarding oxytocin use in clinical practice need to be emphasised, not least in view of the fact that the use of oxytocin is liberal, widespread and is on the increase. It is estimated that about 50 % of nulliparous and 20 % of parous women receive oxytocin during delivery (10, 11). The delivery units evaluated in these studies have guidelines on how to use oxytocin, as well as on interpretation of CTG tracings, and how to act in event of abnormality. These guidelines are apparently not always followed. It is unlikely that there is a lack of awareness of their existence and their contents. A possible reason is that non-adherence only uncommonly results in an adverse neonatal outcome experienced by the individual midwife or physician, since many foetuses have the ability to tolerate hyperstimulation without becoming seriously affected (171).

The high rate of oxytocin administration despite a lack of indication found in study III is in agreement with a recently published Swedish study, in which 40% of augmented labours had no diagnosis of dystocia(63). This implies that the adherence to definitions of adequate and inadequate labour is vague or that the ability to define abnormal labour fails.

In a Swedish survey on policies for labour management performed in 2005, including all delivery units and with a high percentage of responders (98%), it was found that the majority (73%) of the labour wards in Sweden did not have written criteria for diagnosing dystocia (172). It was also found that a written policy for oxytocin use existed in 92 %. The majority (81%) had a written policy on initial and maximum doses, but there was a wide variation with respect to administration of the drug (172).

Thus, there appears to be a lack of uniformity regarding oxytocin administration and a gap between evidence-based knowledge and clinical practice that needs to be closed. The existence and availability of guidelines are obviously insufficient.
Checklists and standardised protocols for the use of oxytocin have recently been tested and recommended by several authors with the aim of reducing adverse neonatal outcomes (173, 174). Clark et al implemented a checklist-based protocol for oxytocin infusion, based on the uterine and foetal response (CTG) to the drug, and found a significant reduction in maximum infusion rates of oxytocin without lengthening of labour or an increase in operative interventions (173). Furthermore the caesarean delivery rate declined and the newborn outcome also appeared to be improved in that study. An aim of the protocol was to achieve uniform practice patterns, since uniformity will generally result in outcome improvement compared to processes that are highly variable (175).

In addition to such measures, it needs to be emphasised that adherence to checklists and guidelines regarding oxytocin and interpretation of CTG tracings has to be supervised as does the maintenance of knowledge on these issues at an organisational and individual level. Routine cord blood gas measurement in all deliveries could be used to assess the result of the management of labour (84, 85, 176-178). Implementation of such routines would seem appropriate in a culture increasingly focused on patient safety.

In infants born at term, neonatal encephalopathy following asphyxia is considered an important cause of later major neurodevelopmental impairment, mainly CP and mental retardation (Figure 3). Milder impairments such as cognitive and behavioural difficulties at school age possibly also have an association with encephalopathy if moderate or severe (179).

Reports on the long-term outcome after acidaemia without encephalopathy at birth are contradictory (180-183). Most studies have shown no association, but in the majority of studies a follow-up from 1-4 years and not from school age was described. According to a Swedish study, infants with acidaemia at birth, even without encephalopathy, may be at risk for more subtle developmental problems later on, such as speech/language problems (183).

Figure 3. Neonatal encephalopathy has to be present in the pathway from intrapartum asphyxia to subsequent CP (108).
The extent to which asphyxia may be preventable is controversial. From single departments a decline in asphyxia-related morbidity and mortality has been reported (170, 184-186). Becher et al suggested that a significant proportion of cases of intrapartum asphyxia may be preventable (186). A marked reduction in asphyxia-related mortality and morbidity over a 12-year period in term non-anomalous infants was shown in that study. There was a decrease of HIE (all grades), from 2.41/1000 to 0.77/1000 live births during that time period. No reasons for the decline were suggested. In a case control study by Gaffeney et al, the relation between suboptimal care and CP or death was investigated (158). Their findings suggested an association between suboptimal care and CP, but this seemed to have a role in only a small proportion of all cases of CP (6.8 %). Our results are in agreement with this finding, since only a few cases with HIE were in the group in which asphyxia could possibly have been prevented (reassuring admission test and suboptimal care). Thus, the challenge for the clinician is the small group of children with CP with apparently potentially avoidable intrapartum hypoxia.

The possibility of preventing CP associated with intrapartum asphyxia has been questioned by Clark et al, who argued that CP is an unpreventable event given our current methods of foetal surveillance (187). The rate of CP in term neonates has not decreased over the past 30 years despite the widespread use of CTGs and the increase in caesarean section rates, and if possible, according to Clark, a decrease in the incidence of CP would have manifested itself during the last decades.

The occurrence of birth asphyxia in the etiology of CP is nevertheless considered an important reason for the continued efforts to avoid intrapartum asphyxia. Suboptimal care as a cause of neonatal morbidity or mortality must be prevented. In view of the low incidence of neonatal encephalopathy and CP associated to intrapartum asphyxia however, it will probably be difficult to demonstrate a decrease on these outcome measures despite improved intrapartum care. Admission to the NICU due to intrapartum foetal asphyxia is a less serious and more common outcome that could be useful.

Further improvements in obstetric care will require greater vigilance in low risk pregnancies and improved practice with regard to foetal monitoring and oxytocin use.

Study IV

In this double-blind, randomised controlled trial we demonstrated that ST segment changes suggestive of myocardial ischaemia occurred and had an association with oxytocin administration significantly more often in subjects receiving 10 units compared with 5 units during elective CS under regional anesthesia. The decrease in MAP following the oxytocin bolus was more pronounced in the 10 unit group and could be an explanation for the ECG
changes. Myocardial ischaemia was quantified by Troponin I levels and a few of the ST segment depressions observed were associated with increased levels, indicating myocardial damage. Estimated blood loss during the surgical procedure did not differ between the two dosage groups.

The decrease in mean MAP after a bolus injection differed between doses, which is in agreement with a study by Pinder et al (117). In subjects with ST depression the decrease in mean MAP was even more pronounced compared with that in subjects without ST depression. In contradiction to the findings of Pinder et al, we observed no difference in increase in HR between the two doses or between cases with and without ST depression. These results indicate that the hypotensive episode that occurs after administration of an oxytocin bolus may lead to a relative myocardial hypoperfusion with resultant myocardial ischaemia and appearance of ST depression on the ECG. Oxytocin is also known to produce vasoconstriction of coronary arteries (188, 189) and this mechanism has been discussed as a possible cause of myocardial ischaemia in case reports (190, 191), but was not investigated in the present study.

In one-fifth of the subjects with ST depression, no association with oxytocin administration was found, but in the majority there was a connection to a hypotensive episode.

ST changes can occur for reasons other than myocardial ischaemia and it is important to be aware of the possibility of these false positive changes. These include hyperventilation, hypertension, tachyarrhythmia, postural changes, drugs, electrolyte abnormalities, left ventricular hypertrophy or dysfunction, and sympathetic nervous system influences (140). In patients with no evidence of ischaemia during exercise testing, ST segment changes indicative of myocardial ischaemia are infrequent.

Overall, the occurrence of symptoms was much lower than the frequencies reported from previous studies. Palmer et al reported all complaints, and in the study by Moran et al patients were asked about symptoms experienced peroperatively, which could explain differences apart from the discrepancies in doses and in the way the drug was administered (123, 126). There was a relation in time between symptoms and oxytocin administration, but there are several other occurrences that could be attributable to the symptoms during this eventful time of a CS, for example; fundal pressure to effectuate delivery, intra-abdominal leakage of amniotic fluid and blood, uterine massage, and exteriorisation of the uterus. Nevertheless, symptoms implied a risk of ST depression, which is in agreement with earlier reports (123, 126).

In spite of the fact that the participants were healthy, a few of them had elevated Troponin I levels indicating myocardial damage. This finding is in agreement with the report by Moran et al. and although there might be false positive values, the finding is difficult to ignore (126). The estimated blood loss during the surgical procedure did not differ between the two dosage
groups, nor did the postoperative haemoglobin values, indicating that 5 units probably should be the clinical preference, since the purpose of giving oxytocin is to prevent excessive blood loss. A repeated dose of oxytocin was needed among subjects receiving the lower dose but in > 80 % a single dose was sufficient. It seems prudent to use the lowest effective dose and the result of this study underlines that 5 units is clinically preferable to 10 units since there was no differences in blood loss, and there were fewer side-effects with the lower dose, which is also less costly.

The results of the present study apply to healthy women during elective CS and the clinical importance of the findings may be questioned, since only a few patients had symptoms and the ECG changes suggestive of myocardial ischaemia resolved after a short period of time. A bolus of 10 units of oxytocin is still administered in clinical practice and is possibly more common in intrapartum caesareans. Excessive blood loss is more likely during intrapartum CS and oxytocin could be detrimental to women who are hypovolemic (116, 191-193). It is reasonable to believe that ST depressions are as common during intrapartum caesareans and the clinical importance of our results could be more important in such circumstances.

Recent studies suggest that the oxytocin dose given during elective caesarean section could be reduced and that an infusion gives haemodynamic advantages (121, 194). It is possible that the majority of ST depressions could be prevented by a slow infusion of oxytocin since the haemodynamic side-effects will be less marked with this method (121, 195).

In conclusion, ST depressions during caesarean delivery of healthy women are probably a consequence of hypotension following oxytocin bolus administration or hypotension of other causes. In our subjects receiving 10 units of oxytocin, ST depressions showed an association with oxytocin administration significantly more often than in those who were given 5 units. Interventions to prevent hypotension and to preserve haemodynamic stability during caesarean section may reduce the occurrence of ST depressions on ECGs.
Conclusions

- Disciplinary actions resulting from negligence were with few exceptions related to misjudgement of CTG patterns, and the majority involved inappropriate use of oxytocin. Passiveness was noticeable and the outcome could possibly have been prevented if proper action had been taken.

- There is a strong association between acidaemia at birth and a pattern of hyperactive uterine contractions in the last two hours before delivery. In the majority of cases with hyperactive labour, oxytocin had been given, which together with the higher rate of abnormal CTG patterns indicates that suboptimal care contributes to acidaemia at birth.

- The duration of bearing down is less important and not associated to acidaemia when the uterine contraction frequency has been taken into consideration.

- Metabolic acidosis at birth is associated with suboptimal intrapartum care in half of the cases. The high rate of suboptimal care with regard to oxytocin use and foetal surveillance illustrates a gap between guidelines and clinical practice. Metabolic acidosis and the related neonatal morbidity can probably be prevented in 40-50% of the cases. The adherence to guidelines needs to be checked continuously.

- ST depressions are associated with oxytocin administration significantly more often in healthy women receiving 10 units compared with 5 units during elective CS in regional anaesthesia. Interventions to prevent hypotension during CS may reduce the occurrence of ST depressions on electrocardiograms.
Aims for the future

To facilitate and improve adherence to guidelines, a checklist for oxytocin-stimulated labour with focus on the foetal response to uterine activity has been developed (Appendix 1a & b). This checklist will be implemented and its effect on neonatal outcomes such as metabolic acidosis at birth and admission for neonatal care will be evaluated.

The question whether an association exists between precipitate labour and increased neonatal morbidity and mortality has not been fully investigated. After precipitate labour, slightly more than 25 % of the neonates in the case group were admitted to the NICU in our study (study III). Two of these neonates suffered from neonatal encephalopathy. To further evaluate precipitate labour as a possible risk factor for metabolic acidosis, a prospective case-control study would be desirable.

The haemodynamic effects of a bolus dose of oxytocin are pronounced. By administering oxytocin as an infusion over five minutes, these effects can be reduced in patients undergoing caesarean section (121). We concluded that ST depressions were probably associated with a hypotensive episode and it would be of interest to determine whether an infusion would reduce the occurrence of ST depressions compared with a bolus oxytocin dose.

Pre-eclampsia is a syndrome of pregnancy that affects 3-5 % of first pregnancies and is defined by the onset of hypertension and proteinuria. Pre-eclampsia is characterised by widespread dysfunction of the endothelium (196, 197). It is possible that pre-eclampsia is the initial point of expression of an inherent adverse phenotype associated with the early development of cardiovascular disease (198).

It would be of value to investigate the frequency of ST depressions in pre-eclamptic patients delivered by CS under regional anaesthesia. Also important would be to determine whether there is a difference in occurrence of ST depressions after injection of 5 and 10 units of oxytocin in pre-eclamptic patients delivered by CS under regional anaesthesia.
Oxytocin stimulerar värkarbetet under förlossning men har också effekt på många andra organ och organsystem i kroppen. Det är väl känt att oxytocin orsakar blodtryckssökning och hjärtfrekvensökning om det ges i injektionsform. Administration av oxytocin är mycket vanligt under förlossning, dels för igångsättning av förlossningar, dels i vävköstarkande syfte då förlossningen går för långsamt (värkrubbning) och dels för att förebygga blödning efter förlossning.

I de flesta fall går det att korrigera värkrubbningar med hjälp av oxytocin och eftersom värkrubbning är ett vanligt kliniskt problem är att läkemedlet till stor nyttja i förlossningsvården. Under förlossning tillförs oxytocin genom dropp (intravenös infusion). En risk med behandlingen är läkemedlet överdoseras så att värkarna kommer för tätt varvid fostrets tillgång på syre kan försämras och bli otillräcklig (syrebrist). Att oxytocin kan orsaka överstimulering av värkarbetet med risk för syrebrist för fostret är kunskap som funnits länge och i princip alla förlossningsavdelningar i Sverige har skriftliga riktlinjer för oxytocin administrering. Med hjälp av fosterövervakning (s.k. CTG registrering) kan fostrets reaktion på värkarbete och värkarnas frekvens övervakas och kontinuerlig fosterövervakning rekommenderas under behandling med oxytocin.

Genom att analysera syra-bas status i arteriellt blod från navelsträngen vid födseln går det att undersöka om barnet varit utsatt för en syrebristsituation under förlossningen. Ett lågt pH värde (acidemi) i provet talar för att syre tillgången varit otillräcklig. Vid en svår syrebrist måste fostret utnyttja s.k. anaerob metabolism (icke syrgaskrävande) för att klara energiomsättningen. I den processen bildas sura restprodukter som sänker pH och förbrukar s.k. buffert varvid en metabol acidos kan uppmätas i navelsträngsprovet. Om barnet föds med en svår metabol acidos finns risk för neurologiska skador och död.

Det finns ett fåtal studier som påvisat ett samband mellan oxytocin administration under förlossning och acidemi. Ungefär hälften av kvinnor som föder sitt första barn och en femtedel av kvinnor som fött barn tidigare, behandlas med oxytocin under förlossning i Sverige idag. Andelen som drabbas av värkrubbning beräknas till ca 20 % vilket betyder att en överanvändning av oxytocin föreligger.
Efter förlossningen ges vid såväl vaginal- som vid kejsarsnittsförlossning en stötdos av oxytocin för att åstadkomma en kontraktion av livmodern och på så sätt minkas risken för stor blödning hos den nyförlösta kvinnan. I flera studier har EKG förändringar talande för syrebrist i hjärtmuskeln (ST sänkning) påvisats hos friska kvinnor som genomgått planerat kejsarsnitt i ryggbedövning. Orsaken till dessa förändringar är oklara. Oxytocin som har påtagliga effekter på hjärta och kärl, speciellt då det ges i form av snabb injektion, har inte utförligt studerats som möjlig orsak till dessa EKG förändringar.

Studie I

I en analys av förlossningsärenden handlagda i ansvarsnämnden under en åtta års period och som lett till disciplin påföljd för läkare och/eller barnmorskor, fann vi återkommande problem vad gäller handläggning av förlossning. Dessa bestod i uteblivna åtgärder trots avvikelser vid fosterövervakning talande för syrebrist hos fostret (76 %) samt oskicklig användning av oxytocin (68.8%). I jämförelse med andra studier påvisades en hög andel fall med felaktig oxytocin hantering.

Studie II

I en fall-kontroll studie undersökte om det fanns skillnader i handläggningen, med speciellt focus på oxytocin användning, under de två sista timmarna av förlossningen om barnet föttes med (fall) eller utan (kontroller) acidemi i arteriellt navelsträngs blod definerat som pH < 7.05. Från två förlossningskliniker där navelsträngsprov tas rutinmässigt, under perioden 1994-2004, omfattande 28 486 förlossningar, hämtades fall (n=305) och kontroller (n=610). Majoriteten var friska graviditeter och det fanns ingen skillnad i graviditetskomplikationer mellan fall och kontroller.

Vi fann ett starkt samband mellan acidemi och överaktivt väkarbete (logistisk regressionsanalyse), odds ratio; 5.36 (95% konfidensintervall; 3.32-8.65). I majoriteten av fall med överaktivt väkarbete hade förlossningen stimulerats med oxytocin (75 %) vilket tyder på en felaktig användning av läkemedlet och följaktligen, att acidemi hos barnet vid födseln till stor del var iatrogent orsakad och troligen undvikbar. Det fanns också en stor skillnad i förekomst av onormala CTG registreringar mellan fall (68.8%) och kontroller (26.1%). Sammantaget indikerar dessa resultat att suboptimal handläggning förekommit oftare bland fallen.

Betydelsen av krystningstidens längd i förhållande till barnets pH-värde vid födseln har diskuterats mycket och en begränsning av tiden har rekommenderats för att undvika acidemi vid födseln. Efter att i analysen tagit hänsyn till värktätheten, fanns inget samband mellan krystningstidens duration och acidemi i den här studien.
Studie III

Studien är en subanalys av studie II. Fall med metabol acidos (n=161) har jämförts mot kontroller (n=322) med avseende på förekomst av suboptimal föllossningshandläggning samt i vad mån detta var undvikbart. Metabol acidos definierades som: pH < 7.05 och basedeficit ≥ 12 mmol/L i navelstrångs-artär vid födseln. Med hjälp av förutbestämda kriterier bedömdes om suboptimal handläggning förekommit eller ej. Vi fann att suboptimal handläggning förekom i hög grad i fallgruppen (49 %) jämfört med i kontrollgruppen (13 %). Skillnaden mellan fall och kontroller var avsevärd när det gäller oskickligt användande av oxytocin, vilket förekom hos 46.6 % av fallen jämfört med 13.0 % av kontroller (p < 0.001). Trots patologisk CTG ≥ 40 minuter vidtogs ej adekvat åtgärd hos 19.9 % av fallen jämfört med 1.2 % av kontroller (p < 0.001). Resultaten antyder att riktlinjer för oxytocinstimulering och fosterövervakning inte alltid följs.

Barn med metabol acidos vårdades i mycket högre utsträckning än kontrollbarnen på neonatal avdelning (48.8% jämfört med 4.6%) och andelen barn med hjärnsvikt under nyföddhetsperioden (neonatal encefalopati grad II och III) var hög (8.6%) i fallgruppen. Resultaten är i överensstämmelse med tidigare studier om ökad sjuklighet hos barn med syrebrist (metabol acidos) vid födseln och tillståndet bör därför undvikas.

Trots att incidensen av metabol acidos i studiepopulationen var låg (0.63 %) uppskattar vi att 40-50 % av dessa fall är potentiellt undvikbara. Studien visar också att trots optimal handläggning av försökning, så går det inte alltid att förhindra att barn födas med metabol acidos.

Sammanfattningsvis (studie I-III) fann vi att det inte bara är bland de svåraste fallen som brister vad gäller CTG tolkning och oxytocin hantering finns, utan också i en bakgrundspopulation. Riktlinjer finns men följs inte alltid vilket kan resultera i att fostret löper en risk att födas med syrebrist.

Studie IV

Friska kvinnor, planerade för kejsarsnitt i regional anestesi, randomiserades till 5 eller 10 enheter (IE) oxytocin och skillnad med avseende på förekomst av EKG förändringar av ischemi typ, ST sänkningar jämfördes (primärt utfalls mått). Sekundära utfallssätt var förekomst av skillnader i Troponin I nivå, blodtryck, puls, symtom förenliga med syrebrist i hjärtmuskeln och blödningsmängd.

Vi fann att frekvensen ST sänkningar som hade ett tidssamband med given oxytocin dos var signifikant högre bland kvinnor som fick 10 IE (21.6%) jämfört med de som fick 5 IE (7.7%) Den relativ risk reductionen med den lägre dosen var 64.4% medan den absoluta riskreduktionen var 13.9 %, (95% konfidensintervall; 0.5-27.3). Det fanns en signifikant skillnad mellan

Det fanns inga skillnader i övriga utfalls mått och av klinisk betydelse är att den lägre dosen gav mindre hjärteffekter och tycks vara tillräcklig för blödningskontroll.

Sammanfattningsvis förekom ST sänkningar oftare då 10 IE oxytocin gavs jämfört med 5IE bland friska kvinnor som genomgår kejarsnitt i spinal anestesi. Interventioner som förhindrar blodtrycksfall kan möjlichen förhindra att ST sänkningar uppkommer hos dessa kvinnor.
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References


171. Block KP WS. Normalize deviance at your peril: Do not let longtime incident free operation justify a design procedure that is not justifiable. Chemical Engineering 2004(May 1).


Checklista 1
-inför oxytocin administrering

Om följande checklista ej kan fyllas i fullständigt skall oxytocin inte ges.

Datum: ____________      Tid:   ____________    Signatur:  ___________

1. Anamnes och status har klarlagts och dokumenterats
2. Indikation finns dokumenterad
   - primär värksvaghet
   - sekundär värksvaghet
   - förlängt utdrivningsskede
   - induktion
3. Ansvarig läkare har informerats (undantaget situation då delegation gäller), dokumenterats
4. CTG har klassificerats normalt (registrering om minst 30 minuter) och detta dokumenterats.
   I vissa situationer kan läkare göra avsteg från protokollet vilket kan vara motiverat och kliniskt korrekt.
   Anledningen till avsteg dokumenteras i journalen.

Klassificera CTG enligt tabell:

Om > 1 avvikande parameter finns bedöms CTG som patologiskt.

<table>
<thead>
<tr>
<th>CTG klassificering</th>
<th>Hjärtfrekvens</th>
<th>Variabilitet/reaktivitet</th>
<th>Decelerationer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal CTG</td>
<td>110-150 spm</td>
<td>Accelerationer</td>
<td>- Tidiga uniforma</td>
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<tr>
<td></td>
<td></td>
<td>5-25 spm</td>
<td>- Ökomplikerade variabla med duration &lt; 60 s och slagförlust &lt; 60 slag</td>
</tr>
<tr>
<td>Avvikande CTG</td>
<td>- 100-110 spm</td>
<td>-25 spm – saltatoriskt mönster</td>
<td>- Ökomplikerade variabla decelerationer med duration &lt; 60 s men slagförlust &gt; 60 slag</td>
</tr>
<tr>
<td></td>
<td>- 150-170 spm</td>
<td>- &lt; 5 spm &gt; 40 min utan accelerationer</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Kortvarig bradykardi (&lt;100 spm &lt; 3 min)</td>
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<tr>
<td>Patologisk CTG</td>
<td>- 150-170 spm och nedsatt variabilitet</td>
<td>- &lt; 5 spm &gt; 60 min</td>
<td>- komplicerade variabla med duration &gt; 60 s</td>
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<tr>
<td></td>
<td>- &gt; 170 spm</td>
<td>- sinusoidalt mönster</td>
<td>- upprepade sena uniforma</td>
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<td></td>
<td>- Bestående bradykardi (&lt;100 spm &gt; 3 min)</td>
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<tr>
<td>Preterminalt CTG</td>
<td>Total avsaknad av variabilitet och reaktivitet med eller utan decelerationer eller bradykardi</td>
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Kommentarer __________________________________________________________________________
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2008-11-05 Maria Jonsson
Check lista 2
-oxytocin administrering under förlossning

- Checklistan går igenom före varje dosökning (även under utdrivnings skedet) och en gång i timmen vid uppnådd effektiv behandlingsdos. Signera varje gång bedömning görs i tabellen nedan.
- Oxytocin infusionen skall sänkas eller stängas av och läkare kontaktas om checklistan ej kan fyllas i fullständigt.
- Om droppet stängs av skall checklista 1 går igenom på nytt innan infusionen startas igen.
- Om yttre värkregistrering ej fungerar läggs en inre värk mätare (IUP).
- I vissa situationer kan läkare göra avsteg från protokollet vilket kan vara motiverat och kliniskt korrekt.

1. Fosterövervakning.
   - Kontinuerlig CTG
   - Normalt CTG eller ej avvikande >30 minuter
   - Ej mer än 2 sena decelerationer eller
   - Ej mer än 2 variabla decelerationer > 60 s duration eller mer än 2 varaibla decelerationer med slag förlust > 60.

2. Övervakning av kontraktioner.
   - ≤ 5 kontraktioner / 10 minuter
   - Kontraktioner < 120 sek duration
   - Uterus kan palperas relaxerad mellan kontraktioner. Om IUP är vilotonus < 25 mmHg.

Checklista. Ifylles i samband med dosökning och sedan en gång i timmen.

<table>
<thead>
<tr>
<th>Tillfälle</th>
<th>1</th>
<th>2</th>
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2008 11 20 Maria Jonsson

Person nr och namn:
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