ANAESTHETIC METHOD AND SHORT-TERM OUTCOMES OF PRETERM INFANTS DELIVERED BY CAESAREAN SECTION IN A TERTIARY HOSPITAL IN SOUTH AFRICA

By

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Declaration

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General Declaration

This dissertation is a presentation of my original research work. The research reported is based on independent work performed by myself. Neither the whole work nor any part of it has been, is being, or is to be submitted for another degree to any other university.

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Acknowledgements, format and contributions

This minor dissertation is submitted in the "already published" format according to the mostrecent UCT guidelines. The research was published in the South African Journal of Child Health (SAJCH) in Volume 13, Number 3, pp125-129. 2019

Following examination, the dissertation now contains minor grammatical corrections and improvements to the text and tables, which are not present in the version published in the SAJCH.

Working on this dissertation has been a very rewarding and gratifying experience. The data collection and analyses were completed before the expiration of the ethics approval date.

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Abbreviations

APH	antepartum haemorrhage
CPR	cardiopulmonary resuscitation
CS	caesarean section
CTG	cardiotocograph
ETT	endotracheal tube
GA	general anaesthesia
GSH	Groote Schuur Hospital
GPH	gestational proteinuric hypertension
IUGR	intrauterine growth restriction
IOL	induction of labour
IQR	inter-quartile range
IVH	intraventricular haemorrhage
Med	median
MgSO4	magnesium sulphate
NEC	necrotizing enterocolitis
cPVL	cystic periventricular leukomalacia
preg	pregnancy
RA	regional anaesthesia
SA	spinal anaesthesia
VON	Vermont Oxford Network Database

Abstract

Background. There are inconsistent published data describing the influence of anaesthetic type during caesarean section (CS), on outcomes of preterm neonates.

Objectives. To describe indications and type of anaesthesia in preterm neonates and to describe short-term outcomes, comparing spinal anaesthesia (SA) to general anaesthesia (GA).

Methods. Data were collected retrospectively on preterm babies born at 28 – 35 weeks' gestation by CS, between 1 January and 30 Sep 2014 at Groote Schuur Hospital, Cape Town, South Africa. Babies with missing data were excluded. The largest group of babies with similar indications for delivery were identified from the theatre register. Baseline characteristics and short-term outcomes for this group were extracted from an existing prospective data base, and compared between those delivered under SA and GA.

Results. Data were available for 226 deliveries, having excluded 23 with incomplete data. Most babies (75%) were delivered under SA. The most common indication for CS was 'cardiotocograph abnormalities,' in 139 deliveries. Within this group, SA was more frequent (81.7% vs. 12.9%) while GA was associated with lower Apgar scores ($p < 0.001$) and more intubation at birth ($p = 0.004$). There was no difference in mortality when comparing SA with GA.

Conclusion. Our data suggest a sedative effect of maternal GA on preterm babies delivered by CS, and the need for staff with advanced resuscitation skills. This study provides novel baseline data in our setting, but these data need to be validated in a prospective study.

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Cover Page

Anaesthetic method and short-term outcomes of preterm infants delivered by caesarean section in a tertiary hospital in South Africa

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None of the authors have any competing interests.

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Abstract

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Introduction

Prematurity is a leading cause of morbidity and mortality globally, particularly in developing countries. [1] Caesarean section (CS) of preterm neonates implies increased risk due to the indications for operative delivery, such as intra-partum emergencies, fetal hypoxia, maternal illness, and maternal medication. The influence of the type of anaesthesia on outcomes in this group may assist with appropriate assignment of medical staff, but current data are conflicting. [2,3]

The effect of general anaesthesia (GA) and regional anaesthesia (RA) on short-term outcomes of neonates after CS was studied in a Cochrane review that was updated in 2012. [2] Regional anaesthesia included both epidural and spinal anaesthesia (SA). The authors found no difference in 1-minute and 5-minute Apgar scores, but most of the included studies either compared outcomes in term babies only, or they did not analyse data from preterm babies separately. A more recent study in Nigeria, found that GA was an independent risk factor for low Apgar scores in neonates of <36 weeks' gestation. [3] A low Apgar score indicates the need for skilled medical personnel to be present at the delivery, [4,5] and is strongly associated with neonatal and infant death in both preterm and term neonates, when compared with other predictable variables. [6–8]

At Groote Schuur Hospital (GSH), a tertiary hospital in South Africa, both GA and SA are performed for preterm caesarean delivery. We designed a descriptive study to obtain baseline data in our setting, comparing SA to GA. The objectives of this study were: i) to describe the indications for CS and the type of anaesthesia in a cohort of preterm neonates; ii) to identify a subgroup of babies defined by a common indication for CS; and iii) to describe the need for resuscitation and related short-term outcomes in the uniform subgroup, comparing SA to GA.

Methods

Study design and ethics approval

A retrospective study was conducted on a cohort of preterm CS deliveries from 1 January to 30 September 2014. The study was a descriptive one, to generate novel baseline data in our setting. A 9-month period of study was identified as being the most accessible and recent period with complete data at the time of data collection. In addition, this period was expected to generate a sample of ~ 200 neonates.

The study was approved by the University of Cape Town Health Sciences Faculty Human Research Ethics Committee (ref. no. 598/2015) and conforms to the principles of the 2013 Declaration of Helsinki. [9]

Study setting

Groote Schuur Hospital is a tertiary academic hospital in Cape Town, South Africa. Obstetric services include a dedicated obstetric theatre for both elective and emergency caesarean sections with 24-hour coverage. Neonatal services include a 75-bed neonatal unit with intensive care facilities and ~ 200 admissions per month. At GSH, the type of anaesthesia for CS (SA or GA) is decided by the attending anaesthesiologist and may be determined by the clinical and physical condition of mother and/or fetus. The anaesthetic is usually performed by an anaesthetic registrar, supported by an on-site consultant or senior registrar. Neonatal resuscitation is provided by an intern or medical officer, supported by an on-site paediatric registrar. A senior medical officer or registrar is expected to attend if intrapartum hypoxia or a birth weight of < 1 200 g is expected.

Population

All preterm babies born at 28 - 35 weeks' gestational age with a birth weight of < 1 500 g and delivered by CS under GA or SA (not epidural anaesthesia) were included. Neonates with missing data regarding indication for CS or method of anaesthesia were excluded.

Data collection and analysis

The type of anaesthesia utilized and the indications for CS were obtained from the obstetric theatre register. The largest subgroup of neonates with similar indications for delivery were identified; baseline characteristics and outcome data for this subgroup were extracted from a prospectively maintained data base of very low birth weight neonates (< 1 500 g) admitted in GSH. The database forms part of the Vermont Oxford Network Database (VON). Neonatal units from around the world submit data to the VON, through clinical review of medical records according to common definitions, to facilitate anonymous data comparison. [10]

The main indication for caesarean section was determined – where more than one indication was listed, that based on preserving fetal well-being was noted as the primary one. Cardiotocograph (CTG) abnormalities described as 'fetaldistress', 'pathological CTG', and 'non-reassuring CTG' were grouped in a single category called 'CTG Abnormalities'. All data were derived from the theatre register and the VON database. CTGs were not available for review. When sentinel events (acute fetal emergencies) such as abruptio placentae, cord prolapse and fetal bradycardia were present, these were listed as the primary indication.

Neonatal baseline characteristics included birth weight, gestational age and gender. Maternal characteristics included antenatal care, treatment with antenatal steroids, treatment with magnesium sulphate, maternal hypertension, gestational proteinuric hypertension (GPH) and multiple gestation. The neonatal outcomes included 1-minute and 5-minute Apgar scores, oxygen administration during resuscitation, intubation in the delivery room, cardiac compression in the delivery room, surfactant administration, oxygen administration on day 28, severe intraventricular haemorrhage,cystic periventricular leukomalacia, necrotizing enterocolitis, pneumothorax and mortality.

The data from the theatre register were captured into an Excel (Microsoft, USA) spreadsheet and matched to data extracted from the GSH portion of the VON using folder numbers.

Stata version 12 (StataCorp, USA) was used for statistical analysis. Indications for CS were described using frequency distributions and compared according to mode of anaesthesia. A relatively uniform subgroup of neonates with similar indications for CS was identified – maternal and neonatal characteristics, and short-term perinatal outcomes, were compared by mode of anaesthesia. Categorical variables were compared using the Fisher's exact test or Chi-squared, depending on the expected values. Continuous variables were compared using Student's t-test for parametric variables and Wilcoxon Ranksum test for non-parametric variables, respectively. All tests were two-sided with significance set at $p < 0.05$.

Results

There were 249 preterm CS deliveries during the 9-month study period. Data describing the method of anaesthesia and/or the indication for CS were incomplete or missing for 23 deliveries. Of the remaining 226 CS deliveries, 24.8% (n=56) were delivered under GA and 75.2% (n=170) under SA.

The indications for CS are shown in Table 1. The most common indication for CS was, 'CTG Abnormalities,' irrespective of the method of anaesthesia. General anaesthetic was used relatively more frequently when acute fetal emergencies such as abruptio placentae or cord prolapse were present.

The 139 CS deliveries performed due to 'CTG abnormalities' formed the largest, relatively uniform subgroup for which we could most reasonably compare outcomes of SA with GA. The majority of deliveries in this subgroup (87.1%) were done under SA. General anaesthesia was used significantly more frequently in deliveries due to abruptio placentae, GPH and placenta praevia. There was a trend towards increased frequency of GA in deliveries due to cord prolapse andextra-uterine pregnancy. The baseline characteristics of the 'CTG abnormalities' subgroup are shown in Table 2. The only significant difference was that antenatal magnesium sulphate was used more frequently in the neonates delivered by GA. There was a trend towards a marginally higher gestational age at birth in the neonatesdelivered by SA.

Resuscitation requirements, Apgar scores and other short-term outcomes of the 'CTG abnormalities' group are shown in Table 3. Both the 1-minute and the 5-minute Apgar scores were significantly lower in the GA group. Oxygen administration and intubation during resuscitation also both occurred significantly more frequently in the GA group. There was a trend towards increased oxygen requirement on day 28 in the GA group, but there were no significant differences in mortality or any of the other outcome variables.

A box plot showing the distribution of Apgar scores at 1 minute in the GA and SA groups is shown in Fig 1. The box plot shows that 25% of the neonates in the GA group had a 1-minute Apgar of 1, which was also the lowest recorded Apgar.

Figure 1: One-minute Apgar scores after general and spinal anaesthetic

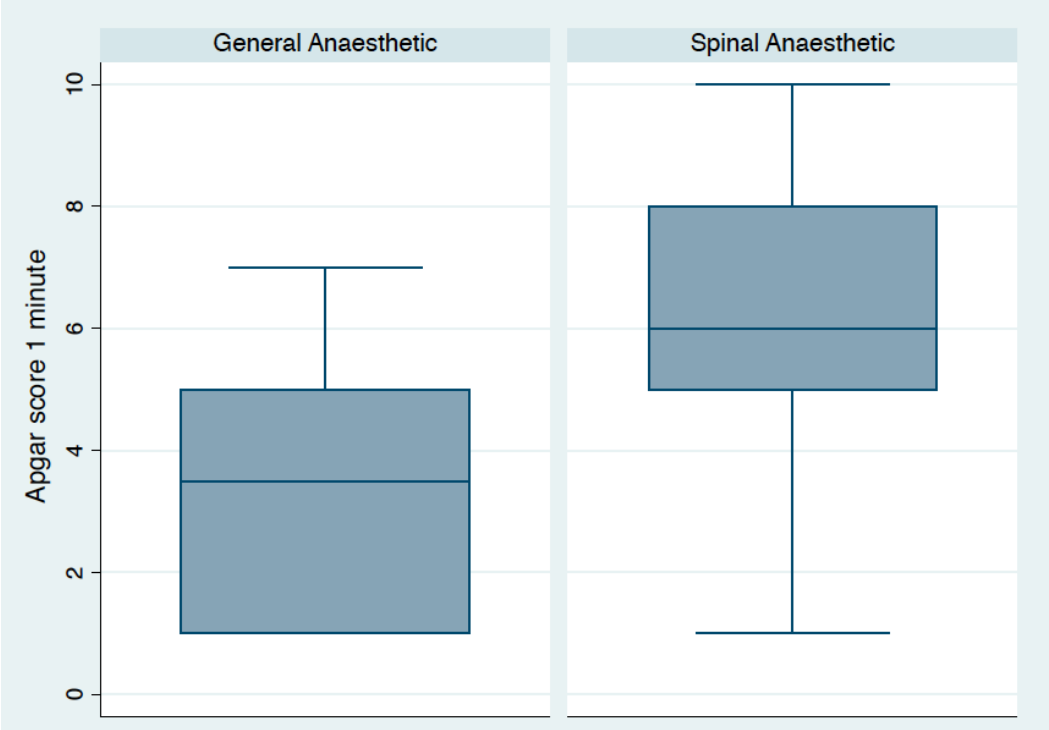

Table 1: Indication for caesarean section in preterm delivery

Primary Indications	Total deliveries (N=226), n (%)	General anaesthesia (n=56), n (%)	Spinal anaesthesia (n=170), n (%)
CTG Abnormalities*	139 (61.5)	18 (32.1)	121 (71.2)
Abruptio Placenta	7 (3.1)	5 (8.9)	2 (1.2)
Cord Prolapse	2 (0.9)	2 (3.6)	0 (0)
Fetal bradycardia (<100bpm)	2 (0.9)	1 (1.8)	1 (0.6)
Previous CS	8 (3.5)	2 (3.6)	6 (3.5)
GPH	26 (11.5)	13 (23.2)	13 (7.6)
IUGR	3 (1.3)	0 (0)	3 (1.8)
Abnormal lie	16 (7.1)	2 (3.6)	14 (8.2)
APH	2 (0.9)	0 (0)	2 (1.2)
Maternal cardiac/pulmonary oedema	1 (0.4)	1 (1.8)	0 (0)
Extra-uterine preg.	2 (0.9)	2 (3.6)	0 (0)
Multiple preg.	9 (4.0)	2 (3.6)	7 (4.1)
Placenta previa	7 (3.1)	7 (12.5)	0 (0)
Failed IOL	2 (0.9)	1 (1.8)	1 (0.6)

*APH= antepartum haemorrhage; CS = caesarean section; CTG = cardiotocography; GPH= gestational protienuric hypertension; IOL= induction of labour; IUGR= intrauterine growth restriction; preg: pregnancy. * CTG abnormalities excluded abruptio placentae, cord prolapse and fetal bradycardia and included fetal distress, pathological CTG and non-reassuring CTG.*

Table 2: Baseline characteristics in the cohort with CTG abnormalities (N=139)			
Characteristics	**GA (n=18), n (%)***	**SA (n=121), n (%)***	**p-value**
CTG description			
Fetal distress	17 (94.4)	95 (78.5)	0.197
Pathological CTG	1 (5.6)	14 (11.6)	0.692
Non-reassuring CTG	0 (0)	12 (9.9)	0.365
Neonatal characteristics			
Birth weight (grams), median (IQR)	1 215 (1 000 -1 310)	1 200 (1 040 - 1 360)	0.880
Gestational age (weeks), median (IQR)	30 (28 - 32)	31 (30 - 32)	0.056
Male sex	8 (44.4)	58 (47.9)	0.782
Maternal characteristics			
Antenatal care	15 (83.3)	106 (87.6)	0.705
Antenatal steroids	17 (94.4)	109 (90.1)	1.000
Antenatal MgS04	13 (72.2)	45 (37.2)	0.009
Maternal HPT	15(83.3)	85 (70.2)	0.399
Maternal GPH	6 (33.3)	24 (19.8)	0.222

CTG=cardiotocograph, GA=general anaesthesia, GPH=gestational protienuric hypertension, HPT= hypertension, IQR=Inter-quartile range, MgSO4=magnesium sulphate, SA=spinal anaesthesia

**Unless otherwise specified*

Table 3: Short term outcomes in the cohort with CTG abnormalities (N=139)			
Outcomes	**GA (n=18), n (%)***	**SA (n=121), n (%)***	**p-value**
One-minute Apgar, median (IQR)	3.5 (1-5)	6 (5-8)	< 0.001
Five-minute Apgar, median (IQR)	7 (6-8)	9 (8-10)	< 0.001
Oxygen during resuscitation	18 (100)	93 (76.9)	0.024
ETT Delivery room	5 (27.8)	5 (4.1)	0.004
Adrenaline delivery room	0 (0)	1 (0.8)	1.000
CPR delivery room	3 (16.8)	10 (8.3)	0.376
Surfactant any time	7 (38.9)	30 (24.8)	0.253
Oxygen on D28 (n=56)	4 (22.2)	6 (5)	0.080
Pneumothorax	0 (0)	2 (1.7)	1.000
NEC	2 (11.1)	7 (5.8)	0.329
Severe IVH (N=113)	0 (0)	7 (7)	1.000
cPVL (N=113)	0 (0)	3 (3)	1.000
Deaths	2 (11.1)	11 (9.1)	0.676

CPR=cardiopulmonary resuscitation; D28= day 28; ETT=endotracheal tube; GA=general anaesthesia; IQR=inter-quartile range; IVH=intraventricular haemorrhage; NEC=necrotising enterocolitis; cPVL= cystic periventricular leukomalacia; SA=spinal anaesthesia
**Unless otherwise specified*

Discussion

The most frequent primary indication for preterm caesarean delivery in the entire cohort was 'CTG abnormalities.' Spinal anaesthesia was used almost three times more often than GA in the entire cohort and more than five times more frequently in the subgroup of neonates delivered due to 'CTG abnormalities'. The neonates in this subgroup who were delivered using SA had higher 1- and 5-minute Apgar scores and required less resuscitation in the delivery room than those delivered using GA. Our findings are in keeping with global trends, including countries with similar health economics – there is a shift towards the use of SA for CS, with the aim of avoiding both maternal and fetal complications. [3,11]

Mothers with acute sentinel events, such as abruptio placenta and cord prolapse were almost exclusively delivered by GA – this may have been because some experts

consider GA to be the preferred method in fetal and maternal emergency scenarios due to a fast and reliable induction. [12] The potential poorer outcomes in these neonates could be expected to skew the GA group towards poorer outcomes, but these neonates were not included in the 'CTG abnormalities' group. The rationale for the preference for GA when performing CS for fetal emergencies was challenged in the retrospective observational study of preterm neonates in Nigeria by Nwafor et al. [3] – in this study, preterm neonates delivered by emergency CS under GA had significantly lower Apgar scores than those where SA was used.

There are significant challenges in interpreting Apgar scores. Population-based cohort studies have determined that 95.2% of preterm neonates have a 5-minute Apgar score of ≥ 7,[6] and 98.8% of neonates have a 5-minute Apgar score of ≥ 7 after normal vertex delivery.[8] The potential association between a low 5-minute Apgar score, fetal hypoxia and mortality [8] makes it difficult to ascertain whether a low 5-minute Apgar score is a consequence of the GA or the underlying fetal state. Most of the data comparing mode of anaesthesia and neonatal outcomes, includes term neonates, but Apgar scores in preterm neonates are usually lower than term neonates and so should be considered separately. [2,13]

A large Australian study had a similar approach and similar findings to those of our study. Algert et al. [7] showed that GA was associated with increased frequency of intubation and lower Apgar scores, in both term and preterm neonates. They similarly controlled for confounding factors by specifying pregnancy risk and indications for CS, and they found that the neonatal benefits from the use of RA (spinal and epidural anaesthesia were analysed as single group) for CS persisted across a range of delivery indications, i.e. planned repeat CS, failure to progress and fetal distress. The authors suggest a sedative anaesthetic effect. [7]

The level of experience and skill of practitioners attending newborns after CS delivery varies depending on the delivery circumstances and the available resources, but the attendance of an experienced midwife is the norm for uncomplicated vaginal deliveries. [14] A prospective South African study at GSH in 2010 found that complicated deliveries that included multiple pregnancy, low birthweight, prematurity, general anaesthetic, abnormal lie or known congenital

abnormality, had a higher resuscitation rate (45%). [14] Similarly, an observational study in 2005 found that after both emergency and elective CS, significantly more infants required resuscitation when GA was used. [15] Our findings concur with these studies, which recommend that skilled practitioners are present for all caesarean sections under GA because of the association with low Apgar score and need for resuscitation. [14,15]

The Cochrane database analyses showed a similar proportion of neonates with Apgar scores <6, in both term and preterm neonates delivered by CS when comparing GA with RA. However, the indications for delivery varied from uncomplicated pregnancies delivered electively at term to emergency caesarean sections, so the data interpretation is limited by heterogeneity. [2]

We considered the possibility that the significantly higher use of antenatal magnesium sulphate in the GA subgroup in our study may have confounded the difference in the Apgar scores. Magnesium sulphate is currently recommended for use in woman at risk of imminent preterm birth, as it has neuroprotective properties for the fetus in this setting and is associated with a reduced risk of cerebral palsy. [16] The beneficial effect of magnesium sulphate might therefore be thought to be associated with higher Apgar scores, but high fetal Magnesium levels might also be expected to cause respiratory depression at birth. A systematic review and meta-analysis of five studies published in 2017, found no difference in the frequency of low Apgar scores at 5 minutes, and no difference in the need for resuscitation at birth. [17]

With respect to mortality, we found no difference between the two anaesthetic methods – in keeping with findings from an observational study in a Nigerian Teaching hospital,[3] but in contrast to a large population-based cohort study of very preterm neonates (the EPIPAGE cohort), where mortality was increased in the SA group. [13] The authors postulated that associated hypotension and placental hypoperfusion could account for poorer outcomes, and that term neonates may tolerate placental hypoperfusion better. [13] In our study, the strong association between GA and decreased Apgar scores, in the face of no significant difference in deaths, suggests the presence of a sedative effect of GA on the neonates.

The labour ward register did not have data on uterine incision to delivery time, so we are not able to comment on a potential effect that may have had on neonatal outcomes. However, a prospective 2-year cohort study of 812 in-labour caesarean sections of non-anomalous term neonates did not find an association between incision to delivery time and hypoxia-associated morbidities. [18] A secondary analysis of a prospective cohort of 793 caesarean sections, including both term and preterm neonates, compared outcomes of neonates who had an incision to delivery interval of ≥ 2 minutes to those with shorter intervals, and found that gestational age was the only variable independently associated with neonatal morbidity. [19]

Study strengths and limitations

Our study has several limitations. It is a retrospective study with some missing data and the potential for selection bias. The theatre register did not include data regarding pre- or intra-operative maternal complications which could have affected Apgar scores. but the primary indication for delivery was neonatal in all cases. Although maternal hypotension can be more frequent in spinal anaesthesia, this group had better outcomes so it is unlikely to have played a role. The study is observational and not powered for a specific outcome. The "CTG abnormalities group" may not be entirely homogenous but the criteria for inclusion in this group were defined and babies with acute fetal emergencies were excluded. The generalizability of the findings is limited both to the setting and the population - it is a single hospital-based study at a tertiary referral centre, with a high-risk population of mothers and very low birth weight preterm neonates.

The study also has significant strengths; first, it identified a group of neonates with relatively uniform indications for operative delivery; second, the exclusion of term neonates further enhanced homogeneity; and third, important maternal and neonatal variables that could affect outcome were included.

Conclusion

CTG abnormalities constituted the most frequent indication for CS delivery of preterm neonates, and SA was the most frequently used method of anaesthesia. General anaesthesia was strongly associated with lower Apgar scores compared with SA and this study provides novel baseline data in our setting. Our data suggest a sedative effect of maternal GA on preterm babies, but prospective, matched, case-control studies are needed to provide more robust results. Our data could be used to inform the design and power of such studies. Irrespective of the cause of the low Apgar scores, our data suggest that staff with advanced resuscitation skills should be present at all preterm deliveries where GA is used.

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Appendices

Appendix I: Ethics approval

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room E53-46 Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6626
Email: shuretta.thomas@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

30 June 2017

HREC REF: 598/2015

A/Prof A Horn
Neonatology
H46.63, OMB

Dear A/Prof Horn

PROJECT TITLE: THE INFLUENCE OF ANAESTHETIC METHOD ON OUTCOMES OF PRETERM INFANTS DELIVERED BY CAESAREAN SECTION IN A TERTIARY HOSPITAL IN SOUTH AFRICA: A PILOT REVIEW (MMED CANDIDATE - DR R STANDER)

Thank you for submitting your request to the Faculty of Health Sciences Human Research Ethics Committee.

The HREC acknowledge that the MMed candidate Dr Raphaella Stander will also be involved in this study.

Please quote the HREC reference number in all your correspondence.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE

Appendix II: Hospital approval

GROOTE SCHUUR HOSPITAL
Enquiries: Dr Bernadette Eick
E-mail : Bernadette.Eick@westerncape.gov.za

Professor Alan Horn
Division of Paediatrics
H-Floor - OMB

E-mail: Alan.Horn@uct.ac.za

Dear Professor Horn

RESEARCH PROJECT EXTENSION: The Influence Of Anaesthetic Method On Outcomes Of Preterm Infants Delivered By Caesarean Section In A Tertiary Hospital In South Africa (A Pilot Review (Dr Raphella Stander)

Your recent communication to the hospital refers.

The extension of your research has been approved in accordance with UCT Ethics clearance, until **24 April 2018**.

As previously mentioned:

a) Your research may not interfere with normal patient care.
b) Hospital staff may not be asked to assist with the research.
c) No hospital consumables and stationary may be used.
d) **No patient folders may be removed from the premises or be inaccessible.**
e) Please provide the research assistant/field worker with a copy of this letter as verification of approval.
f) Confidentiality must be maintained at all times.
g) Once the research is complete, please submit a copy of the publication or report.

I would like to wish you every success with the project.

Yours sincerely

DR BERNADETTE EICK
CHIEF OPERATIONAL OFFICER
Date: 12 May 2017
BE/vms

C.C. Mr L. Naidoo, Professor E. Weimann, Professor M. Harrison

G46 Management Suite, Old Main Building,
Observatory 7925

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www.capegateway.go.v.za

Appendix III: Instructions to Authors

Author Guidelines

Please view the Author Tutorial for guidance on how to submit on Editorial Manager.

To submit a manuscript, please proceed to the *SAJCH* Editorial Manager website: Editorial Manager

To access and submit an article already in production, please see the guidelines here.

Author Guidelines
Please take the time to familiarise yourself with the policies and processes below. If you still have any questions, please do not hesitate to ask our editorial staff (tel.: +27 (0)21 532 1281, email: submissions@hmpg.co.za).

Authorship

Named authors must consent to publication. Authorship should be based on: (*i*) substantial contribution to conceptualisation, design, analysis and interpretation of data; (*ii*) drafting or critical revision of important scientific content; or (*iii*) approval of the version to be published. These conditions must all be met for an individual to be included as an author (uniform requirements for manuscripts submitted to biomedical journals; refer to www.icmje.org)

If authors' names are added or deleted after submission of an article, or the order of the names is changed, all authors must agree to this in writing.

Please note that co-authors will be requested to verify their contribution upon submission. Non-verification may lead to delays in the processing of submissions.

Author contributions should be listed/described in the manuscript.

Conflicts of interest

Conflicts of interest can derive from any kind of relationship or association that may influence authors' or reviewers' opinions about the subject matter of a paper. The existence of a conflict – whether actual, perceived or potential – does not preclude publication of an article. However, we aim to ensure that, in such cases, readers have all the information they need to enable them to make an informed assessment about a publication's message and conclusions. We require that both authors and reviewers declare all sources of support for their research, any personal or financial relationships (including honoraria, speaking fees, gifts received, etc) with relevant individuals or organisations connected to the topic of the paper, and any association with a product or subject that may constitute a real, perceived or potential conflict of interest. If you are unsure whether a specific relationship constitutes a conflict, please contact the editorial team for advice. If a conflict remains undisclosed and is later brought to the attention of the editorial team, it will be considered a serious issue prompting an investigation with the possibility of retraction.

Research ethics committee approval

Authors must provide evidence of Research Ethics Committee approval of the research where relevant. Ensure the correct, full ethics committee name and reference number is included in the manuscript.
If the study was carried out using data from provincial healthcare facilities, or required active data collection through facility visits or staff interviews, approval should be sought from the relevant provincial authorities. For South African authors, please refer to the guidelines for submission to the National Health Research Database. Research involving human subjects must be conducted according to the principles outlined in the Declaration of Helsinki. Please refer to the National Department of Health's guideline on Ethics in Health research: principles, processes and structures to ensure that the appropriate requirements for conducting research have been met, and that the HPCSA's Researchers have been adhered to.

Clinical trials

Since 1st December 2005, all clinical trials conducted in South Africa have been required to be registered in the South African National Clinical Trials Register. The *SAJCH* therefore requires that clinical trials be registered in the relevant public trials registry at or before the time of first patient enrolment as a condition for publication. The trial registry name and registration number must be included in the manuscript.

Protection of rights to privacy

Patient

Information that would enable identification of individual patients should not be published in written descriptions, photographs, radiographs and pedigrees unless the information is essential for scientific purposes and the patient (or parent or guardian) has given informed written consent for publication and distribution. We further recommend that the published article is disseminated not only to the involved researchers but also to the patients/participants from whom the data was drawn. Refer to Protection of Research Participants. The signed consent form should be submitted with the manuscript to enable verification by the editorial team.

Other individuals

Any individual who is identifiable in an image must provide written agreement that the image may be used in that context in the *SAJCH.*

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Ethnic/race classification

Use of racial or ethnicity classifications in research is fraught with problems. If you choose to use a research design that involves classification of participants based on race or ethnicity, or discuss issues with reference to such classifications, please ensure that you include a detailed rationale for doing so, ensure that the categories you describe are carefully defined, and that socioeconomic, cultural and lifestyle variables that may underlie perceived racial disparities are appropriately controlled for. Please also clearly specify whether race or ethnicity is classified as reported by the patient (self-identifying) or as perceived by the investigators. Please note that it is not appropriate to use self-reported or investigator-assigned racial or ethnic categories for genetic studies.

Continuing Professional Development (CPD)

SAJCH is an HPCSA-accredited service provider of CPD materials. Principal authors can earn up to 15 CPD continuing education units (CEUs) for publishing an article; co-authors are eligible to earn up to 5 CEUs; and reviewers of articles can earn 3 CEUs. Each month, *SAJCH* also publishes a CPD-accredited questionnaire relating to the academic content of the journal. Successful completion of the questionnaire with a pass rate of 70% will earn the reader 3 CEUs. Administration of our CPD programme is managed by Medical Practice Consulting. To complete questionnaires and obtain certificates, please visit MRP Consulting

Manuscript preparation

Preparing an article for anonymous review

To ensure a fair and unbiased review process, all submissions are to include an anonymised version of the manuscript. The exceptions to this requirement are Editorials, Correspondence, Book reviews and Obituary submissions.

Submitting a manuscript that needs additional blinding can slow down your review process, so please be sure to follow these simple guidelines as much as possible:

- An anonymous version should not contain any author, affiliation or particular institutional details that will enable identification.

- Please remove title page, acknowledgements, contact details, funding grants to a named person, and any running headers of author names.
- Mask self-citations by referring to your own work in third person.

General article format/layout

Submitted manuscripts that are not in the correct format specified in these guidelines will be returned to the author(s) for correction prior to being sent for review, which will delay publication.

General:

- Manuscripts must be written in UK English (this includes spelling).
- The manuscript must be in Microsoft Word or RTF document format. Text must be 1.5 line spaced, in 12-point Times New Roman font, and contain no unnecessary formatting (such as text in boxes). Pages and lines should be numbered consecutively.
- Please make your article concise, even if it is below the word limit.
- Qualifications, ***full*** affiliation (department, school/faculty, institution, city, country) and contact details of ALL authors must be provided in the manuscript and in the online submission process.
- Abbreviations should be spelt out when first used and thereafter used consistently, e.g. 'intravenous (IV)' or 'Department of Health (DoH)'.
- Scientific measurements must be expressed in SI units except: blood pressure (mmHg) and haemoglobin (g/dL).
- Litres is denoted with an uppercase L e.g. 'mL' for millilitres).
- Units should be preceded by a space (except for % and ºC), e.g. '40 kg' and '20 cm' but '50%' and '19ºC'.
- Please be sure to insert proper symbols e.g. µ not u for micro, a not a for alpha, b not B for beta, etc.
- Numbers should be written as grouped per thousand-units, i.e. 4 000, 22 160.
- Quotes should be placed in single quotation marks: i.e. The respondent stated: '...'
- Round brackets (parentheses) should be used, as opposed to square brackets, which are reserved for denoting concentrations or insertions in direct quotes.

If you wish material to be in a box, simply indicate this in the text. You may use the table format –this is the *only* exception. Please DO NOT use fill, format lines and so on.

SAJCH is a Journal on child health, therefore for articles involving genetics, it is the responsibility of authors to apply the following:

- Please ensure that all genes are in italics, and proteins/enzymes/hormones are not.
- Ensure that all genes are presented in the correct case e.g. TP53 not Tp53.

** NB: Copyeditors cannot be expected to pick up and correct errors wrt the above, although they will raise queries where concerned.

- Define all genes, proteins and related shorthand terms at first mention, e.g. ‘188del11’ can be glossed as ‘an 11 bp deletion at nucleotide 188.’
- Use the latest approved gene or protein symbol as appropriate:
  - Human Gene Mapping Workshop (HGMW): genetic notations and symbols
  - HUGO Gene Nomenclature Committee: approved gene symbols and nomenclature

- OMIM: Online Mendelian Inheritance in Man (MIM) nomenclature and instructions
- Bennet et al. Standardized human pedigree nomenclature: Update and assessment of the recommendations of the National Society of Genetic Counselors. J Genet Counsel 2008; 17:424-433: standard human pedigree nomenclature.

Preparation notes by article type

Research

Guideline word limit: 3 000 words (excluding abstract and bibliography)

Research articles describe the background, methods, results and conclusions of an original research study. The article should contain the following sections: introduction, methods, results, discussion and conclusion, and should include a structured abstract (see below). The introduction should be concise – no more than three paragraphs – on the background to the research question, and must include references to other relevant published studies that clearly lay out the rationale for conducting the study. Some common reasons for conducting a study are: to fill a gap in the literature, a logical extension of previous work, or to answer an important clinical question. If other papers related to the same study have been published previously, please make sure to refer to them specifically. Describe the study methods in as much detail as possible so that others would be able to replicate the study should they need to. Where appropriate, sample size calculations should be included to demonstrate that the study is not underpowered. Results should describe the study sample as well as the findings from the study itself, but all interpretation of findings must be kept in the discussion section, which should consider primary outcomes first before any secondary or tertiary findings or post-hoc analyses. The conclusion should briefly summarise the main message of the paper and provide recommendations for further study.

- May include up to 6 illustrations or tables.
- A max of 20 - 25references

Structured abstract

This should be no more than 250words, with the following recommended headings:

- **Background:** why the study is being done and how it relates to other published work.
- **Objectives:** what the study intends to find out
- **Methods:** must include study design, number of participants, description of the intervention, primary and secondary outcomes, any specific analyses that were done on the data.
- **Results:** first sentence must be brief population and sample description; outline the results according to the methods described. Primary outcomes must be described first, even if they are not the most significant findings of the study.
- **Conclusion:** must be supported by the data, include recommendations for further study/actions.
- Please ensure that the structured abstract is complete, accurate and clear and has been approved by all authors. It should be able to be intelligible to the reader without referral to the main body of the article.
- Do not include any references in the abstracts.

Here is an example of a good abstract.

***Scientific letters*/short reports**

These include case reports, side effects of drugs and brief or negative research findings.

Guideline word limit: 1500 words

- Abstract: unstructured, of about 100-150 words
- May include only one illustration or table
- A maximum of 6 references

Editorials

Guideline word limit: 1 000 words

These opinion or comment articles are usually commissioned but we are happy to consider and peer review unsolicited editorials. Editorials should be accessible and interesting to readers without specialist knowledge of the subject under discussion and should have an element of topicality (why is a comment on this issue relevant now?) There should be a clear message to the piece, supported by evidence.
Please make clear the type of evidence that supports each key statement, e.g.:

- expert opinion
- personal clinical experience
- observational studies
- trials
- systematic reviews.

Review articles

Review articles should always be discussed with the Editor prior to submission.

Guideline word limit: 4 000 words

These are welcome, but should be either commissioned or discussed with the Editor before submission. A review article should provide a clear, up-to-date account of the topic and be aimed at non-specialist hospital doctors and general practitioners. They should be aligned to practice in South and/or sub-Saharan Africa and not a precis of reviews published in the international literature
Please ensure that your article includes:

- Abstract: unstructured, of about 100-150 words, explaining the review and why it is important
- Methods: Outline the sources and selection methods, including search strategy and keywords used for identifying references from online bibliographic databases. Discuss the quality of evidence.
- When writing: clarify the evidence you used for key statements and the strength of the evidence. Do not present statements or opinions without such evidence, or if you have to, say that there is little or no evidence and that this

is opinion. Avoid specialist jargon and abbreviations, and provide advice specific to southern Africa.
- Personal details: Please supply your qualifications, position and affiliations and MP number (used for CPD points); address, telephone number and fax number, and your e-mail address; and a short personal profile (50 words) and a few words about your current fields of interest.

Correspondence (Letters to the Editor)
Guideline word limit: 400 words
Letters to the editor should relate either to a paper or article published by the SAJCH or to a topical issue of particular relevance to the journal's readership

- May include only one illustration or table
- Must include a correspondence address.

Obituaries
Guideline word limit: 400 words
Should be offered within the first year of the practitioner's death, and may be accompanied by a photograph.

Illustrations/photos/scans

- If illustrations submitted have been published elsewhere, the author(s) should provide evidence of consent to republication obtained from the copyright holder.
- Figures must be numbered in Arabic numerals and referred to in the text e.g. '(Fig. 1)'.
- Each figure must have a caption/legend: Fig. 1. Description (any abbreviations in full).
- All images must be of high enough resolution/quality for print.
- All illustrations (graphs, diagrams, charts, etc.) must be in PDF form.
- Ensure all graph axes are labelled appropriately, with a heading/description and units (as necessary) indicated. Do not include decimal places if not necessary e.g. 0; 1.0; 2.0; 3.0; 4.0 etc.
- Scans/photos showing a specific feature e.g. *Intermediate magnification micrograph of a low malignant potential (LMP) mucinous ovarian tumour. (H&E stain).* –include an arrow to show the tumour.
- Each image must be attached individually as a 'supplementary file' upon submission (not solely embedded in the accompanying manuscript) and named Fig. 1, Fig. 2, etc.

Tables

- Tables should be constructed carefully and simply for intelligible data representation. Unnecessarily complicated tables are strongly discouraged.
- Large tables will generally not be accepted for publication in their entirety. Please consider shortening and using the text to highlight specific important sections, or offer a large table as an addendum to the publication, but available in full on request from the author.
- Embed/include each table in the manuscript Word file - do not provide separately as supplementary files.

- Number each table in Arabic numerals (Table 1, Table 2, etc.) consecutively as they are referred to in the text.
- Tables must be cell-based (i.e. not constructed with text boxes or tabs) and editable.
- Ensure each table has a concise title and column headings, and include units where necessary.
- Footnotes must be indicated with consecutive use of the following symbols: * † ‡ § ¶ || then ** †† ‡‡ etc.

Do not: Use [Enter] within a row to make 'new rows':
Rather:
Each row of data must have its own proper row:

Do not: use separate columns for *n* and %:
Rather:
Combine into one column, *n* (%):

Do not: have overlapping categories, e.g.:
Rather:
Use <> symbols or numbers that don't overlap:

References

NB: *Only complete, correctly formatted reference lists in Vancouver style will be accepted. If reference manager software is used, the reference list and citations in text are to be unformatted to plain text before submitting..*

- Authors must verify references from original sources.
- Citations should be inserted in the text as superscript numbers between square brackets, e.g. These regulations are endorsed by the World Health Organization,[2] and others.[3,4-6]
- All references should be listed at the end of the article in numerical order of appearance in the Vancouver style (not alphabetical order).
- Approved abbreviations of journal titles must be used; see the List of Journals in Index Medicus.
- Names and initials of all authors should be given; if there are more than six authors, the first three names should be given followed by et al.
- Volume and issue numbers should be given.
- First and last page, in full, should be given e.g.: 1215-1217 **not** 1215-17.
- Wherever possible, references must be accompanied by a digital object identifier (DOI) link). Authors are encouraged to use the DOI lookup service offered by CrossRef:
- On the Crossref homepage, paste the article title into the 'Metadata search' box.
- Look for the correct, matching article in the list of results.
- Click Actions > Cite
- Alongside 'url =' copy the URL between { }.
- Provide as follows, e.g.: https://doi.org/10.7196/07294.937.98x

Some examples:

- *Journal references:* Price NC, Jacobs NN, Roberts DA, et al. Importance of asking about glaucoma. Stat Med 1998;289(1):350-355. http://dx/doi.org/10.1000/hgjr.182
- *Book references:* Jeffcoate N. Principles of Gynaecology. 4th ed. London: Butterworth, 1975:96-101.
- *Chapter/section in a book:* Weinstein L, Swartz MN. Pathogenic Properties of Invading Microorganisms. In: Sodeman WA, Sodeman WA, eds. Pathologic Physiology: Mechanisms of Disease. Philadelphia: WB Saunders, 1974:457-472.
- *Internet references:* World Health Organization. The World Health Report 2002 - Reducing Risks, Promoting Healthy Life. Geneva: WHO, 2002. http://www.who.int/whr/2002 (accessed 16 January 2010).
- Legal references
- Government Gazettes:
- National Department of Health, South Africa. National Policy for Health Act, 1990 (Act No. 116 of 1990). Free primary health care services. Government Gazette No. 17507:1514. 1996.
- In this example, 17507 is the Gazette Number. This is followed by :1514 - this is the notice number in this Gazette.
- Provincial Gazettes:
- Gauteng Province, South Africa; Department of Agriculture, Conservation, Environment and Land Affairs. Publication of the Gauteng health care waste management draft regulations. Gauteng Provincial Gazette No. 373:3003, 2003.
- Acts:

South Africa. National Health Act No. 61 of 2003.

- Regulations to an Act:

South Africa. National Health Act of 2003. Regulations: Rendering of clinical forensic medicine services. Government Gazette No. 35099, 2012. (Published under Government Notice R176).

- Bills:

South Africa. Traditional Health Practitioners Bill, No. B66B-2003, 2006.

- Green/white papers:

South Africa. Department of Health Green Paper: National Health Insurance in South Africa. 2011.

- Case law:

Rex v Jopp and Another 1949 (4) SA 11 (N)
Rex v Jopp and Another: Name of the parties concerned
1949: Date of decision (or when the case was heard)
(4): Volume number
SA: SA Law Reports
11: Page or section number
(N): In this case Natal - where the case was heard. Similarly, (C) woud indicate Cape, (G) Gauteng, and so on.
NOTE: no . after the v

- *Other references (e.g. reports) should follow the same format:* Author(s). Title. Publisher place: Publisher name, year; pages.
- Cited manuscripts that have been accepted but not yet published can be included as references followed by '(in press)'.

- Unpublished observations and personal communications in the text must **not** appear in the reference list. The full name of the source person must be provided for personal communications e.g. '...(Prof. Michael Jones, personal communication)'.

From submission to acceptance

Submission and peer-review

To submit an article:

- Please ensure that you have prepared your manuscript in line with the *SAJCH* requirements.
- All submissions should be submitted via Editorial Manager
- The following are required for your submission to be complete:
- Anonymous manuscript (unless otherwise stated)
- Author Agreement form [forthcoming]
- Manuscript
- Any supplementary files: figures, datasets, patient consent form, permissions for published images, etc.
- Once the submission has been successfully processed on Editorial Manager, it will undergo a technical check by the Editorial Office before it will be assigned to an editor who will handle the review process. If the author guidelines have not been appropriately followed, the manuscript may be sent back to the author for correcting.

Peer Review Process

All manuscripts are reviewed initially by the Editor-in-Chief and only those that meet the scientific and editorial standards of the journal, and fit within the aims and scope of the journal, will be sent for external peer review. Each manuscript is reviewed by either one or two reviewers selected on the basis of their expertise in the field. A double-blind review process is followed at SAJCH.
Authors are expected to receive feedback from reviewers and an editorial decision within approximately 6 weeks of submission. The time period of the entire review process may vary however depending upon the quality of the manuscript submitted, reviewers' responses and the time taken by the authors to submit the revised manuscript.
Manuscripts from review may be accepted, rejected or returned to the author for revision or resubmission for review. Authors will be directed to submit revised manuscripts within two months of receiving the editor's decision, and are requested to submit a point by point response to the reviewers' comments. Manuscripts which authors are requested to revise and resubmit will be sent for a second round of peer review, often to the original set of reviewers. All final decisions on a manuscript are at the Editor's discretion.

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Production process

The following process should usually take between 4 - 6 weeks:

1. An accepted manuscript is passed to a Managing Editor to assign to a copyeditor (CE).
2. The CE copyedits in Word, working on house style, format, spelling/grammar/punctuation, sense and consistency, and preparation for typesetting.
3. If the CE has an author queries, he/she will contact the corresponding author and send them the copyedited Word doc, asking them to solve the queries by means of track changes or comment boxes.
4. The authors are typically asked to respond within 1-3 days. Any comments/changes must be clearly indicated e.g. by means of track changes. Do not work in the original manuscript - work in the copyedited file sent to you and make your changes clear.
5. The CE will finalise the article and then it will be typeset.
6. Once typeset, the CE will send a PDF of the file to the authors to complete their final check, while simultaneously sending to the 2nd-eye proofreader.
7. The authors are typically asked to complete their final check and sign-off within 1-2 days. No major additional changes can be accommodated at this point.
8. The CE implements the authors' and proofreader's mark-ups, finalises the file, and prepares it for the upcoming issue.

Changing contact details or authorship

Please notify the Editorial Department of any contact detail changes, including email, to facilitate communication.

Errata and retractions

Errata

Should you become aware of an error or inaccuracy in yours or someone else's contribution after it has been published, please inform us as soon as possible via an email to publishing@hmpg.co.za,including the following details:

- Journal, volume and issue in which published
- Article title and authors
- Description of error and details of where it appears in the published article
- Full detail of proposed correction and rationale

We will investigate the issue and provide feedback. If appropriate, we will correct the web version immediately, and will publish anerratum in the next issue. All investigations will be conducted in accordance with guidelines provided by the Committee on Publication Ethics (COPE).

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Retraction of an article is the prerogative of either the original authors or the editorial team of HMPG. Should you wish to withdraw your article before publication, we need a signed statement from all the authors.

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Send an email to publishing@hmpg.co.za, including the following details:

- Journal, volume and issue to which article was submitted/in which article was published
- Article title and authors
- Description of reason for withdrawal/retraction.

We will make a decision on a case-by-case basis upon review by the editorial committee in line with international best practices. Comprehensive feedback will be communicated with the authors with regard to the process. In case where there is any suspected fraud or professional misconduct, we will follow due process as recommended by the Committee on Publication Ethics (COPE), and in liaison with any relevant institutions.

When a retraction is published, it will be linked to the original article.

Indexing

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- DOAJ
- AIM
- AJOL
- Crossref
- Sabinet
- Scielo
- EBSCO
- EMBASE

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Submission Preparation Checklist

As part of the submission process, authors are required to check off their submission's compliance with all of the following items, and submissions may be returned to authors that do not adhere to these guidelines.

1. Named authors consent to publication and meet the requirements of authorship as set out by the journal.
2. The submission has not been previously published, nor is it before another journal for consideration.
3. The text complies with the stylistic and bibliographic requirements in **Author Guidelines**.
4. The manuscript is in Microsoft Word or RTF document format. The text is single-spaced, in 12-point Times New Roman font, and contains no unnecessary formatting.
5. Illustrations/figures are high resolution/quality (not compressed) and in an acceptable format (preferably TIFF or PNG). These must be submitted as 'supplementary files' (not in the manuscript).
6. For illustrations/figures or tables that have been published elsewhere, the author has obtained written consent to republication from the copyright holder.

7. Where possible, references are accompanied by a digital object identifier (DOI) and PubMed ID (PMID)/PubMed Central ID (PMCID).
8. An abstract has been included where applicable.
9. The research was approved by a Research Ethics Committee (if applicable)
10. Any conflict of interest (or competing interests) is indicated by the author(s).

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Appendix IV: Reviewers comments

Reviewer #1

1. In the abstract:
i. The abbreviations RA and CTG are not defined.
ii. The final sentence appears incorrect: "This study provides novel baseline data in the setting, ..." What is "the setting"? Perhaps substitute "in a tertiary setting" or "in our setting".

2. Introduction: The introduction is fairly lengthy, and much of the content belongs in the discussion. I would aim to tighten up this section if possible and keep the introduction succinct.

3. The term "Preterm caesarean section delivery" is used in the manuscript: this could be shortened to "preterm caesarean deliveries", but is not essential.

4. Punctuation in places needs revision - please specifically check the semi-colons throughout the manuscript. For example: Page 3 line 11: "operative delivery such as;" Consider a colon instead of a semi-colon. In the data collection and analysis section: "Neonatal baseline characteristics included; birth weight, gestational age and gender. Maternal characteristics included; antenatal care, treatment with antenatal steroids, treatment with magnesium sulphate, maternal hypertension, gestational proteinuric hypertension and multiple gestation." Both the semicolons appear inappropriate.

5. In Methods, study setting: Groote Schuur Hospital is abbreviated to GSH - but the first use of this term is in the introduction. Define at first use.

6. Your conclusions discuss the appropriate allocation of staff, yet we are not told what staff has been involved in this study. I think the level of staffing could affect outcomes. Do we have information on the anaesthetic level of staffing (poor handling of hypotension or anaesthetic depth could affect Apgars)? Neonatal resuscitation levels are also relevant: a poor resuscitation might affect 5 minutes Apgars, and good resuscitation may account for your results showing no long-term differences in the

outcomes of the neonates. If the specific data are not available, at least comment on the expected norms in your setting.

7. Population: The initial inclusion criteria was 28-35 weeks, but there is also a weight cut-off of <1500g. This means that in fact your target group is very low-birth weight premature infants - this affects the generalisability of these results to that group and this should be noted.

8. In the data collection and analysis section, the authors note that the theatre register was used for the indication and anaesthesia type. How reliable is this registry? Are conversions from spinal to general anaesthesia noted? Interrogation of the anaesthetic records may also have found a number of factors that could affect Apgars: such as hypotension, maternal hypoxia, conversion to GA, etc…

9. There is inconsistent use of data as a singular or plural term throughout the manuscript. In the abstract, both forms are used ("There are inconsistent published data…", "Data was collected") This continues through the document: in general, the plural form is preferred - please check each use of the word.

10. The terms spinal anaesthesia and regional anaesthesia are used interchangeably in the manuscript: the former is actually a specific type of the latter. Were epidurals or combined spinal-epidurals used in any of the patients? While this is probably unlikely to be relevant, the emergence of concerns around epidurals in labour with links to maternal fever and neonatal outcomes make it a point worth mentioning. If only spinals were included, this could be stated to clarify this point.

11. Please check the spelling of the word "foetal" for the SAJCH. While both 'foetal' and 'fetal' are acceptable, the scientific community has tended to favour 'fetal'. I would advise complying with SAJCH standards in this regard.

12. The results section contains a fair amount of redundancy - many of the points made can be seen in the table. This can probably be shortened to the most significant findings.

13. Figures: In Figure 1: The box plot appears to be incomplete - where is the second whisker of the general anaesthetic plot? Please check this figure completely - for instance the median apgar at one minute in the GA group is written as 3 in the table, but appears closer to 4 in the GA box plot.

14. Tables: Abbreviations need to be defined in each table as if the table was on its own. Several have not defined again (Table 2: CTG, SA, GPH; Table 3 IQR, CTG, GA, SA, IVH, PVL)

15. The discussion is generally well-written and I believe the appropriate conclusions have been made. The opening paragraph could be improved: currently it just reads as an extension of the results section. I also think the last sentence of the 'strengths' section of the discussion could be tightened - it is currently a long and unwieldy sentence.

16. Please check the spelling of the word Apgars (Discussion, 4th paragraph (line 60) - it is currently 'Agar' (which is a gelatinous substance obtained from certain red seaweeds and used in biological culture media and as a thickener in foods).

Reviewer #2:

1. Patients with missing data were excluded

2. Cognizance was not taken of factors such as time from uterine incision to delivery

3. The large group of "CTG abnormalities" may not have been a homogeneous group

4. A big assumption was made that because the Apgars were lower in the GA group, then it must have been a sedative effect of the drugs. Factors such as maternal hypotension, bleeding, etc were not considered.

5. What is the average 5 minute apgar in babies delivered by NVD?

6. Conclusions can only be drawn once the definitive prospective study is performed.

7. Typos are present, as are "data was" instead of "data were".

Appendix V: Response to authors

Reviewer #1

1.

I. We have changed RA to SA and defined it. CTG has now been defined.

II. Thank you. Should be “in our setting”. It has been corrected.

We have shortened the introduction – it now describes as succinctly as possible why prematurity and the study of Apgar scores after caesarean delivery is important and it briefly summarises the existing knowledge to provide a rationale for our study in our context.

3. We have shortened the term as recommended

4. This has been checked and the punctuation changed – most of the semi colons have been removed.

5. GSH has been defined at first use.

6. We have added the expected norms in the methods section under “study setting’

7. This has been noted as a limitation in the discussion.

8. The method of anaesthesia was the “final method” – two of the GA’s were performed after failed spinal. The register does not mention intraoperative complications but maternal hypotension is generally more frequent in spinal anaesthesia and this group had better Apgar scores, so it is unlikely to have played a role. We have added this consideration to the limitations.

9. We have checked this and made corrections to ensure the correct use of the word, “data” as a plural.

10. Only spinals were included in our study. We have clarified that in the methods. All reference to RA is to studies where both SA and RA were included – we have clarified that in the text at the first mention of RA.

11. We have standardised to the spelling as "fetal" but will defer to SAJCH editorial standards if they differ.

12. We have shortened the text in the results section so that it only summarises the most significant findings.

13. The box plot is not incomplete. The plot correctly shows that minimum value for the range and the value of the 25th centile are the same – 25% of the Apgar score were the same as the minimum value recorded. We have added an explanation in the results section.

The median Apgar is 3.5 – it was rounded down to 3 as it is not possible to have an Apgar score of 3.5, but after taking further statistical advice, we have changed it 3.5; half the scores were 3 or less and half were 4 or more.

The STATA table below supports the statements above.

```
. tabstat ap1, by(spinal) stats(n med p25 p75 min max)

Summary for variables: ap1
     by categories of: spinal
```

spinal	N	p50	p25	p75	min	max
No	18	3.5	1	5	1	7
Yes	121	6	5	8	1	10
Total	139	6	4	8	1	10

14. Abbreviations have been added to each table as recommended.

15. We have shortened the last sentence of the strength's section as recommended.

Our opening paragraph of the discussion is a statement of the principle findings. The SAJCH author guidelines indicate that the discussion should consider primary outcomes first and the SAMJ author guidelines suggest that the discussion begin with a statement of the principle findings.

16. We have changed the word to “Apgar scores”.

Reviewer #2:

1. This is mentioned as a limitation in the discussion

2. We have revised the discussion to include the following paragraph, “The labour ward register did not have data on uterine incision to delivery time so we are not able to comment on a potential effect that may have had on neonatal outcomes. However, a prospective two-year cohort study of 812 in-labour caesarean deliveries of nonanomalous term neonates did not find an association between incision to delivery time and hypoxia-associated morbidities. [18] A secondary analysis of a prospective cohort of 793 caesarean deliveries, including both term and preterm neonates, compared outcomes of neonates who had an incision to delivery interval of ≥ 2 minutes to those with shorter intervals – gestational age was the only variable independently associated with neonatal morbidity. [19] “

3. The “CTG abnormalities group” may not be entirely homogenous but the criteria for inclusion in this group were defined and babies with acute fetal emergencies were excluded. We have added this as a potential limitation in the discussion

4. We have acknowledged this issue in the paragraph on limitations. However, the fact that the were no differences in antenatal care, antenatal steroids, maternal hypertension and maternal GPH between the groups and the fact that babies were primarily delivered for fetal indications rather than maternal

indications, suggest that maternal morbidity is unlikely to have played a significant role.

5. Population-based cohort studies have determined that 95.2% of preterm neonates have a 5-minute Apgar score of ≥ 7, and 98.8% of neonates have a 5-minute Apgar score of ≥ 7 after normal vertex delivery. We have indicated and referenced this in the discussion.

6. We agree that firm conclusions to reliably inform further practice can only be drawn once the definitive prospective study is performed – we have amended our conclusion to state that, "prospective, matched, case-control studies are needed to provide more robust results."
7. We have run spell check again and reviewed and corrected several typos including the correct use of the word, "data" as a plural.

Appendix V: Data List

Date of birth
Anaesthetic method
Indication for caesarean section
CTG findings
Neonatal characteristics
- Birth weight
- Gestational age (weeks)
- Sex

Maternal characteristics
- Antenatal care
- Antenatal steroids
- Antenatal $MgSO_4$
- Maternal Hypertension
- Maternal GPH

Short term outcomes in pathological CTG group
- One-minute Apgar
- Five-minute Apgar
- Oxygen during resuscitation
- ETT delivery room
- Adrenalin delivery room
- CPR delivery room
- Surfactant any time
- Oxygen on D28
- Pneumothorax
- NEC
- Severe IVH
- cPVL
- Deaths