



RESEARCH ARTICLE

NEONATAL OUTCOME OF CESAREAN SECTION IN PREGNANCY COMPLICATED WITH FOETAL DISTRESS: A COMPARISON BETWEEN HYDROCORTISONE PRE-TREATMENT AND PLACEBO

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ABSTRACT

Background of the study: Foetal distress is a serious complication of pregnancy which can lead to early neonatal morbidity and mortality. In the past, general anaesthesia was the choice of anaesthesia in the face of foetal distress but presently, spinal anaesthesia has been found to be a better choice. There is a major lack of a prospective study evaluating the effects of hydrocortisone pretreatment on neonatal outcomes in emergency cesarean section for foetal distress. Therefore, we evaluated the effects of hydrocortisone pretreatment on neonatal outcome in mothers with foetal distress scheduled for cesarean deliveries under spinal anaesthesia. **Aim and objective:** The study was conducted to compare neonatal outcomes in pregnant women complicated with foetal distress undergoing caesarean section under subarachnoid block with or without hydrocortisone pre-treatment. **Methods:** Sixty pregnant women with foetal distress scheduled for cesarean section under spinal anaesthesia were randomized into two groups and received either hydrocortisone or placebo pre-treatment using a non-probability purposive sampling technique. Thirty parturients in HP group had spinal anaesthesia and intravenous administration of 10 ml of 100 mg hydrocortisone solution, while 30 parturients in PP group had spinal anaesthesia and intravenous administration of 10 ml of normal saline. Maternal and neonatal outcomes were recorded. **Results:** The result of the study revealed that incidence of intraoperative hypotension in the mothers (16 vs 8) was significantly higher in the parturients in placebo group than in parturients in hydrocortisone group ($P=0.020$). The number of neonates with less than 7 Apgar Score in one minute was insignificantly higher in parturients who had placebo pretreatment (16 vs 13) than in parturients who had hydrocortisone pretreatment ($P=0.772$). However, the recovery 5 minute Apgar scores in neonates in parturients with hydrocortisone pretreatment (2 neonates with Apgar score < 7) was significantly better than that of the neonates in parturients with placebo pretreatment (9 neonates with Apgar score < 7), ($P=0.013$). **Conclusion:** The study concluded that a single bolus hydrocortisone before induction of spinal anaesthesia is effective in reducing incidence of poor neonatal outcome during cesarean section in pregnant women complicated with foetal distress.

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INTRODUCTION

In pregnancy complicated with foetal distress, spinal anaesthesia is becoming anaesthetic technique of choice (Afolayan *et al.*, 2014; Kinsella *et al.*, 2010). Emergency cesarean section in pregnancy complicated with foetal distress is challenging for the obstetric anaesthetists, because such cases are typically associated with life-threatening conditions for the foetus or the mother (Kinsella *et al.*, 2010 and Parer, 1990). Spinal anaesthesia was used for the patients in our study. The reason being that it has been documented that spinal anaesthesia is beneficial to both mothers and foetus (Afolayan *et al.*, 2014; Kinsella *et al.*, 2010 and Parer, 1990). It has been observed that the use of spinal anaesthesia, in pregnant women with foetal distress, has contributed to favourable maternal and neonatal outcomes (Afolayan *et al.*, 2014; Parer, 1990). Subarachnoid block is associated with high patients satisfaction, avoidance of aspiration pneumonitis, avoidance of awareness, patients' free discussion with caregivers,

reduced incidence of PONV, avoidance of placental transfer of multiple drugs and immediate return to oral intake and cost effectiveness (Afolayan, *et al.*, 2014). For women requiring emergency cesarean section, including the one for foetal distress, a 30-minute decision-to-delivery interval for cesarean section has become the standard target in clinical practice (Mackenzi, 2002 and Racine, Mackenzi and Cooke, 2002). The guidelines put forward by the Royal College of Obstetricians and Gynaecologists (RCOG) suggest that cesarean section should be carried out "with an urgency appropriate to the risk to the baby and the safety of the mother (Racine, 1989). Accumulating evidence demonstrates that there are lots of benefits of hydrocortisone treatment in the management of foetus with respiratory distress syndrome (Hallman, 2006; Parker *et al.*, 1993; Stutchfield *et al.*, 2005; Buning *et al.*, 2015; Davis *et al.*, 2011; Ashwood *et al.*, 2006). Prenatal exposure to glucocorticoids is one of the reasons for these beneficial effects (Ashwood *et al.*, 2006; Ballard *et al.*, 1980; Calixto, 2002).

The role of hydrocortisone in shaping developmental outcomes has been documented (Hallman, 2006; Parker *et al.*, 1993; Stutchfield *et al.*, 2005; Buning *et al.*, 2015; NIH, 1995; Crowley, 1995). These can accelerate fetal lung maturation, they decrease morbidity, mortality, respiratory distress syndrome, and intraventricular haemorrhage among infants born preterm (Hallman, 2006; Buning *et al.*, 2015; Davis *et al.*, 2011). In view of the fact that there is a major lack of a prospective study evaluating the effects of hydrocortisone pretreatment on neonatal morbidity in emergency cesarean section for foetal distress, we conducted the present study to identify the neonatal benefits of hydrocortisone pretreatment among pregnant women with foetal distress scheduled for cesarean section in our hospital.

METHODS

This prospective study received Institutional Ethical Committee Research Review approval from Ekiti State University Teaching Hospital, Ado-Ekiti, Nigeria. Sixty parturients, complicated with foetal distress, ASA physical status 1 or 2 scheduled for emergency cesarean section under subarachnoid block were enrolled in the study. Exclusion criteria included age under 18 years, height <150cm, weight <65kg, bleeding disorders, chronic hypertension, pregnancy induced hypertension, preeclampsia, eclampsia, known cardiovascular diseases, gestational age less than 35 weeks, packed cell volume of less than 30%, or any contraindication to spinal anaesthesia. Informed consent was received directly from all patients who participated in the study. They were reliably informed that their procedure could be converted to general anaesthesia if there was any failed or difficult spinal anaesthesia. All patients received ranitidine 50mg and 10mg metoclopramide intravenously prior to surgery. For each of the patients, 16G intravenous cannula was put in place for the purpose of this study. Following the application of routine monitoring, non-invasive monitoring was commenced and documented including non-invasive blood pressure, oxygen saturation, pulse rate, systolic blood pressure, diastolic blood pressure. Each patient had a total fluid of 2 litres for both preload and coload. Induction of spinal anaesthesia was achieved with patients in sitting position. Using a Whitacre® type pencil needle of 25 or 27 and with clear CSF flow, the hyperbaric solution of bupivacaine was injected as slowly as possible, without air bubbles. Each patient had 2.5ml of 0.5% hyperbaric bupivacaine over 15s intrathecally in the L₃₋₄ or L₂₋₃ intervertebral space. In addition, patients in HP group received 10 ml of 100 mg hydrocortisone intravenously, while patients in PP group received 10 ml of normal saline intravenously.

The patients were immediately put in supine position with a 15° left lateral tilt using wedge under the right hip. Sensory block height was assessed using loss of sensation to gentle pin prick test. A sensory block height of T6 was the minimum desired level of block for the commencement of the cesarean section. Following the delivery of the baby, the mother was given 10 units of oxytocin intravenously, then she had infusion of 40 units of oxytocin in 500 mls normal saline to run for 4 hours. Maternal hypotension was defined as a decrease in systolic blood pressure to less than 80% of the baseline systolic blood pressure or systolic blood pressure less than 90 mmHg. Hypotension was managed with intravenous fluid as first line of management. Ephedrine in aliquots of 3 or 6mg, was administered whenever there were two consecutive readings of hypotension or hypotension was unresponsive to rapid fluid management. Total amount of rescue ephedrine and fluid administered were documented. Management of hypotension continued until systolic blood pressure recovered to the baseline reading. The primary objective of the study was to decrease the poor neonatal outcome following cesarean section in pregnant women from 11%, based on previous report, (16) while using spinal anaesthesia alone to 6.6% if intravenous hydrocortisone was used alongside with spinal anaesthesia. On the basis of this, a power analysis indicated that a minimum of 30 subjects per group would be sufficient enough to detect this 40% reduction in poor neonatal outcome with a study power of 80% and alpha =0.05. P < 0.05. Qualitative and quantitative data were analysed using SPSS version 26. Data were presented as frequency and percentages. Tests of

statistical significance were carried out using appropriate statistical tests. Chi Square or Fisher exact test was used to compare differences between proportions. The statistical tests were carried out at significance (P-value) of less than 0.05

RESULTS

Non-probability purposive sampling technique was used to recruit 60 parturients with foetal distress to the study; 30 in hydrocortisone group (HP group) and 30 in placebo group (PP group). None of the patients had her spinal anaesthesia converted to general anaesthesia. Demographic and obstetric variables were comparable among the study participants as shown in Table 1.

Table 1. Demographic data of the parturients complicated with foetal distress

Maternal Characteristics	HP (n=30)	PP (n=30)	P-value
Age (years)			
<30	7	3	
30-39	19	22	
≥40	4	5	0.310
Parity			
Nulliparous	12	15	
Multiparous	16	14	
Grand multiparous	2	1	0.581
Education			
Primary	11	8	
Secondary	15	19	
Tertiary	4	3	0.485
Booking status			
Booked	3	1	
Unbooked	27	29	0.391
Occupation			
Housewife	5	7	
Petty traders	14	15	
Students	2	3	
Civil servants	9	5	0.663
Gestational age			
35-37	27	24	
38-40	2	4	
≥40	1	0	0.200

Table 2. Preoperative and intraoperative clinical parameters

Parameter	HP	PP	Pvalue
Decision-anaesthesia	15(10-16)	14(9-16)	0.927
Decision-delivery	17(15-22)	17(14-21)	0.973
Decision-end of surgery	61(55-78)	60(53-86)	0.835
Duration of induction of Anaesth	9(7-10)	7(6-10)	0.510
Block height	T4(T4-T5)	T3(T3-T4)	0.611
Fetal heart rate			
Greater than 160/min	19	14	
Less than 120/min	11	16	0.229
Difficult spinal	0	1	0.892
Maternal Bradycardia	0	1	0.892
Maternal Hypotension	8	16	0.022
Total ephedrine used	24	32	0.007
Total blood loss	450±28	400±39	0.792
Total fluid intake	2555±421	2940±427	0.844

With exception of incidence of hypotension, preoperative and intraoperative clinical outcomes were comparable among the study population as documented in Table 2. The incidence of intraoperative hypotension in the mothers (16 vs 8) was significantly higher in the parturients in placebo group than in parturients in hydrocortisone group (P=0.020). As shown in Table 3, the number of neonates with less than 7 Apgar Score in one minute was insignificantly higher in parturients who had placebo pretreatment (16) than in parturients who had hydrocortisone pretreatment (13) (P=0.772). However, the recovery 5 minute Apgar scores in neonates in parturients with hydrocortisone pretreatment (2 neonates with Apgar score less than 7)

was significantly better than that of the neonates in parturients with placebo pretreatment (9 neonates with Apgar score less than 7)), ($P=0.013$). Twenty nine neonates of parturients who had hydrocortisone pretreatment before cesarean section were transferred into Postnatal ward alongside with the mothers. Whereas, twenty seven neonates of parturients who had placebo pretreatment before cesarean section were transferred into the Postnatal ward alongside with the mothers. The difference was not statistically significant. The other neonates were transferred to neonatal care unit of the hospital. There was no incidence of neonatal post operative ventilation or stillbirth.

Table 3. Neonatal post operative clinical parameters

Parameter	HP	PP	P value
APGAR SCORE			
In 1 minute <7	13	16	0.772
In 5 minutes <7	2	9	0.013
Resuscitation	1	4	0.521
Post op transfer			
Neonatal care unit	1	3	
Post natal ward	29	27	0.782
Post op ventilation	0	0	1.000
Stillbirths	0	0	1.000

DISCUSSION

A decision to delivery rule of 30 minutes was observed for all our patients in this present study. Median time of decision to delivery among our study population was 17 minutes with range of 14 to 22 minutes. We were able to achieve this because only experienced senior anaesthetists were allowed to institute spinal anaesthesia in this category of cesarean section. In this situation, a decision to delivery of 30 minutes, as prescribed by American College of Obstetricians and Gynecologists, was strictly adhered to (Racine, 1989). In cases with pregnancy complicated with foetal distress, spinal anaesthesia is becoming anaesthetic technique of choice. Emergency caesarean section in pregnancy complicated with fetal distress is challenging for the obstetric anaesthetists because such cases are typically associated with life-threatening conditions for the foetus or the mother (Ashwood *et al.*, and Ballard *et al.*). Spinal anaesthesia was used for the patients in our study. The reason being that it has been documented that spinal anaesthesia is beneficial to both mothers and fetus (Afolayan *et al.*, 2014; Kinsella, 2010 and Parer *et al.*, 1990). For women requiring emergency cesarean section, including the one with foetal distress, a 30-minute decision-to-delivery interval for cesarean section has become the standard target in clinical practice, although The guidelines put forward by the Royal College of Obstetricians and Gynaecologists (RCOG) suggest that caesarean section should be carried out "with an urgency appropriate to the risk to the baby and the safety of the mother (Racine *et al.*, 1989).

In the face of the limited time by the care givers and increased risk in both maternal and foetal outcome, anaesthetists need to be coordinated, vigilant and experienced in their choice of anaesthetic technique for pregnancy complicated with foetal distress (Afolayan, 2014 and Parer *et al.*, 1990). It has been documented that the choice of anaesthetic technique is of paramount importance in the management of these group of patients (Afolayan *et al.*, 2014; Kinsella *et al.*, 2010 and Parer *et al.*, 1990). Insufficient time was the remote reason why spinal anaesthesia was not recommended for foetal distress in the past. But with the advent of Rapid Sequence Induction of Spinal Anaesthesia and 30-minute Decision to Delivery time, spinal anaesthesia can be used for cesarean deliveries in parturients with foetal distress. Senior anaesthetists are saddled with the administration of induction of spinal anaesthesia in foetal distress (Afolayan *et al.*, 2014; Kinsella *et al.*, 2010 and Parer *et al.*, 1990). For emergency cesarean section in pregnant women complicated with foetal distress, regional anaesthesia is being used in most of the private hospitals in Nigeria. It is the practice in few of these hospitals to give hydrocortisone pretreatment to the mothers whose pregnancies are

complicated with foetal distress. The purpose of the drug, according to them, is to improve post operative neonatal outcomes. Despite the fact that spinal anaesthesia is the preferred anaesthetic technique for the majority of cesarean sections performed in mothers with fetal distress coupled with hydrocortisone pretreatment in these few private hospitals in Nigeria, no data is available regarding the benefits of hydrocortisone pretreatment in the management of fetal distress. Parker *et al.* 7 observed that distressed infants had lower serum levels of dehydroepiandrosterone sulfate (3992 +/- 246 nmol/L, mean +/- SE) than control infants (4853 +/- 283 nmol/L); distressed infants also had higher levels of cortisol (412 +/- 17 nmol/L) than did control infants (299 +/- 16 nmol/L). The dehydroepiandrosterone sulfate/cortisol ratios in control infants (17.7 +/- 1.2) were almost twice those of distressed infants (10.8 +/- 0.9). These same relationships also were noted when the infant pairs were segregated according to whether delivered vaginally (21 pairs) or by cesarean section (40 pairs). The abnormalities in steroid levels in the distressed infants were independent of the presence or absence of acidemia. Intrapartum stress acutely alters fetal adrenal steroidogenesis, leading to increased production of cortisol and decreased secretion of dehydroepiandrosterone sulfate (Parker, 1993). Hydrocortisone at doses corresponding or exceeding the endogenous corticosteroid secretion during stress has been studied in randomized trials (Hallman, 2006; Davis *et al.*, 2011; Ballard, 1980; Crowley, 1995). The aim has been to stabilize very low blood pressure or decrease the risk of bronchopulmonary dysplasia.

According to experimental studies, the beneficial haemodynamic effects are largely a result of an increase in myocardial smooth muscle contractility. Corticosteroid increase cardiovascular adrenergic receptors and enhance the microvascular endothelium barrier function. Hydrocortisone has a mineralocorticoid-mediated effect on cardiac muscle (Hallman, 2006; Stutchfield *et al.*, 2005; Buning *et al.*, 2015). The closest study to our study was the study carried out by (Stutchfield *et al.*, 2005) who confirmed previous reports that elective cesarean section before 40 weeks' gestation increased neonatal admissions to the special care unit for respiratory distress especially transient tachypnoea of the newborn. In the control group of the randomised controlled trial, 11.4% were admitted at 37 weeks, 6.2% at 38 weeks, and 1.5% at 39 weeks. If women were given two intramuscular injections of 12 mg of betamethasone in the 48 hours before delivery the rates of admission were 5.2% at 37 weeks, 2.8% at 38 weeks, and 0.6% at 39 weeks. Although none of the babies in the control group died, admission would have increased parental anxiety and the cost to the NHS and might have long term sequelae. They concluded that giving mothers betamethasone before elective casesarean section halved neonatal respiratory morbidity, and asked if it was possible to give steroids to all mothers before delivery? (Stutchfield, 2005). Similar to our study, prenatal administration of betamethasone within 48 hours before delivery reduced the incidence of poor neonatal outcome from 11.4% to 5.2%. This shows that administration of steroids to pregnant women immediately before delivery has beneficial effects on neonatal outcomes.

With exception of incidence of hypotension, preoperative and intraoperative clinical outcomes were comparable among our study population. The active ingredients in 100mg hydrocortisone powder include hydrocortisone (100mg) and sodium succinate (6.2mg). These can increase both systolic and diastolic blood pressure (Buning, 2015). The incidence of intraoperative hypotension in the mothers (16 vs 8) was significantly higher in the parturients in placebo group than in parturients in hydrocortisone group ($P=0.020$) as shown in Table 3. The number of neonates with less than 7 Apgar Score in one minute was insignificantly higher in parturients who had placebo pretreatment (16 vs 13) than in parturients who had hydrocortisone pretreatment ($P=0.772$). However, the recovery 5 minute Apgar scores in neonates in parturients with hydrocortisone pretreatment (2 neonates with Apgar score less than 7) was significantly better than that of the neonates in parturients with placebo pretreatment (9 neonates with Apgar score less than 7)), ($P=0.013$). Twenty nine neonates of parturients who had hydrocortisone pretreatment before cesarean section were transferred into Postnatal ward alongside with the

mothers. Whereas, twenty seven neonates of patients who had placebo pretreatment before cesarean section were transferred into the Postnatal ward to be with the mothers. The difference was not statistically significant. The other neonates were transferred to neonatal care unit of the hospital. There was no incidence of neonatal post operative ventilation or stillbirth among the neonates.

Limitation: Our study is limited by unavailability of researches in this area of study. There was no previous research on effects of hydrocortisone pretreatment on neonatal outcomes in emergency cesarean section for pregnant women with foetal distress. The study is still open for further comparative researches. And a much larger population may be needed to detect any level of significant correlation between intravenous administration of steroids and neonatal serum cortisol level.

CONCLUSION

A single bolus of hydrocortisone before induction of spinal anaesthesia in pregnant women with foetal distress is significantly effective in reducing intraoperative incidence of maternal hypotension and in reducing incidence of poor neonatal outcome in 5 minute Apgar score. However, in 1 minute Apgar score, its effect is insignificantly better than placebo.

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