ARTICLE

Maternal and newborn impact of epidural dexamethasone as an adjuvant for labor analgesia: a meta-analysis

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BACKGROUND: Dexamethasone, an anti-inflammatory drug, has an assumed analgesic effect when given epidurally, with less side effects[5,7]. Although numerous studies have evaluated dexamethasone, there is a paucity of studies assessing its intrapartum use[6]

OBJECTIVES*:* To determine the effectiveness of epidural dexamethasone when used as an adjuvant for labor analgesia.

MATERIALS AND METHODS: A meta-analysis guided by the Cochrane handbook was performed. Articles were searched through PubMed, MEDLINE, CENTRAL, Google Scholar and ClinicalTrials.gov using search strategies such as keywords and MeSH terms. Cochrane version 2 risk-of-bias tool for randomized trials (RoB 2) was used to assess for quality. Quantitative data were pooled and analyzed using Review Manager 5.4.1.

RESULTS: A total of five trials involving 309 women in labor were analyzed. The pooled mean difference showed prolonged duration of epidural analgesia on patients who received epidural dexamethasone; pooled risk ratio between the experimental and control group demonstrated no significant maternal adverse events such as nausea and vomiting, shivering, hypotension, and fever. Pooled risk ratio and mean difference also showed that epidural dexamethasone had no significant effect on the neonatal APGAR and neonatal umbilical pH.

CONCLUSION: : Present data demonstrated the potential role of dexamethasone as an adjuvant to epidural solution during labor analgesia on providing local anesthetic dose sparing effect through prolongation of the duration of epidural analgesia, with limited maternal and neonatal adverse events. These results should be interpreted with caution before adopting this technique in routine clinical practice.

KEYWORDS: *Dexamethasone; Epidural; Labor analgesia; Meta-analysis*

INTRODUCTION

Labor is seen as one of the most intense and painful events in a woman's life. Pain causes a neuroendocrine stress response with effects on multiple maternal and fetal organ systems. The cardiopulmonary physiologic responses to pain are usually well tolerated by healthy parturients with normal pregnancies but may be of more concern in parturients with cardiopulmonary disease and at-risk fetuses[1]. The provision of labor analgesia reduces the plasma concentration of epinephrine. By reducing the maternal secretion of catecholamines, epidural analgesia may shift a previously dysfunctional labor pattern to a normal one[2,3]. Local anesthetic (LA) agents such as bupivacaine, levobupivacaine and ropivacaine are routinely used for producing analgesia. Current drugs used are short acting relative to the duration of labor, thus, use of an adjuvant is desirable. The addition of an analgesic adjuvant to regional anesthetic techniques is widely practiced with the aim of not only improving both quality and duration of anesthesia and prolonging postoperative analgesia, but also limiting dose related LA side effects[4]. Several adjuvants such as opioids, alpha-adrenergic agonists, neostigmine, midazolam, ketamine have been examined along with LA, but none showed an ideal analgesic property[5]. The optimal mixture for epidural analgesia does not exist yet. Clinically safe epidural usage of drugs should be pursued to enhance quality of pain relief while not compromising the safety of both the mother and the fetus. If there is no added benefit of administering an adjuvant, this should be omitted, or use of another agent should be preferred. Some newer adjuvants such as clonidine and neostigmine have been used for labor analgesia but are associated with side effects like hypotension, bradycardia and sedation[6].

Dexamethasone, a well-known anti-inflammatory drug, has also been investigated for its analgesic efficacy as an adjunct. It is under the class of corticosteroids, known to inhibit phospholipase A2 and expression of cyclooxygenase2, reducing prostaglandin synthesis. It is also known to block nociceptive C-fiber transmission and suppress neurologic ectopic discharge which represses hyperalgesia associated with acute nociception. The rationale for using dexamethasone epidurally was an assumed analgesic effect that was at least like other adjuvants but with less side effects than the others[5,7]. Researchers have deemed epidural dexamethasone safe. Thomas et al. showed that epidural dexamethasone reduced postoperative pain and analgesic requirements in patients undergoing laparoscopic cholecystectomy. Khafagy et al. demonstrated efficacy of epidural dexamethasone on postoperative analgesia in patients undergoing

lower abdominal surgeries. Research regarding new epidural drugs and drug combination is ever increasing. Prior meta-analyses evaluating the analgesic properties of dexamethasone did not identify studies performed in labor analgesia[8]. Although numerous studies have evaluated dexamethasone, there is a paucity of studies assessing its intrapartum use[6].

We aimed to determine the effectiveness and safety of epidural dexamethasone when used as an adjuvant for labor analgesia. Specific objectives were to determine the maternal effect of epidural dexamethasone with regards to the duration of epidural analgesia, total LA consumed, visual analog scale (VAS), onset of sensory block and maternal adverse event; and to determine if there was a difference in the neonatal outcome with regards to the APGAR score and umbilical pH of the newborn.

METHODOLOGY

This meta-analysis was guided by the Cochrane Handbook[11,] and reporting was accomplished in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) Guidelines[12].

We performed a systematic literature search from various publicly accessible scientific journal databases such as PubMed, MEDLINE, Cochrane Central Registry of Controlled Trials, Google Scholar and database of unpublished trials in https:// clinicaltrials.gov was checked. Keywords and MeSH terms used in the literature search were "*dexamethasone*" [MeSH] or "*steroid*" or "*corticosteroid*" and "*epidural*" or "*epidural analgesia*" [MeSH] or "*epidural anesthesia*" [MeSH] or "*labor analgesia*" [MeSH] or "*obstetric analgesia*" [MeSH] OR "*obstetric anesthesia*" [MeSH].

No language or date restriction was applied. A manual search was done in the reference lists of the resulting list of publications for any relevant trials. Duplicate studies were removed, and screening of titles and abstracts were done. Studies were excluded using the inclusion and exclusion criteria and remaining studies were screened using their full text. Two review authors (primary investigator and co-investigator) independently screened the abstracts and titles of studies with reference to the specified eligibility criteria.

Prospective, randomized controlled trials comparing the effectiveness of epidural dexamethasone when used as an adjuvant to labor analgesia were included in this meta-analysis. Language restriction was not imposed. Prospective observational studies, retrospective analysis, trials conducted in pediatric populations, case reports, case series, animal studies, and studies not reporting on any of the predefined outcome

were excluded from the analysis. Studies that were included were parturients for labor analgesia, belonging to the American Society of Anesthesiologist (ASA) physical status II-III, 18 years of age or more, regardless of gravidity and cervical dilatation at the time of epidural insertion. Studies whose participants refused to undergo regional anesthesia, had deranged coagulation profile, with local infection, spine deformity, history of allergy to any medications to be used and with other contraindications to regional anesthesia were excluded from the study. Patients who were classified as ASA IV or more, with preexisting or gestational diabetes mellitus, already receiving steroids and with history of immunosuppression were also omitted.

The primary intervention was any dose of epidural dexamethasone used as an adjuvant to LA (such as bupivacaine, levobupivacaine, ropivacaine). The comparator was normal saline. Studies where dexamethasone was administered intrathecally were excluded.

The primary outcome was the duration of epidural analgesia and the total LA consumed for the whole course of labor. Secondary outcomes were other maternal and neonatal effects such as pain assessment, onset of sensory block, maternal adverse events and hemodynamics, neonate's APGAR, and umbilical pH.

All studies identified using the above search strategy were screened by two reviewers for relevance based on their titles and abstract that met the criteria. Studies which were deemed irrelevant were removed from the pool of studies. After the initial screening, the full texts of each identified article were retrieved for in-depth screening using the eligibility criteria. The decision to include or exclude were cross-checked by each reviewer. Duplicate studies were identified and screened for completeness. The two reviewers then compared their list of included studies and discrepancies were discussed until an agreement was made. Reasons for exclusion of the ineligible studies were identified and recorded. PRISMA flow diagram[12] was used to show the screening process of the study inclusion and exclusion.

Assessment for risk of bias was performed using the Review Manager program and version 2 of the Cochrane risk-of-bias tool for randomized trials tool (RoB 2.0). Each article included was appraised by the primary investigator and co-investigator based on 5 bias domains: randomization process, deviations from the intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. Within each domain, a series of signaling questions were answered with the aim to elicit information about features of the trial that were relevant to risk of bias. An algorithm based on answers to the signaling questions generated a proposed judgment about the risk of bias arising from each domain.

Judgment was either "Low" or "High" risk of bias or expressed as "Some concerns". Differences were resolved by reexamination of the original articles and through discussion.

A form to extract data was designed. For eligible studies, at least two review authors extracted the data using the agreed form. Discrepancies were resolved through discussion. The list of potential abstracts and citations of final studies included were saved and managed in a Microsoft Excel spreadsheet. Full text copies of studies included were saved in a Google drive accessible to the investigators. Risk of bias scorings and extracted data from the studies were managed using Review Manager software. The main data extracted from the included studies were:

Methods: study design, study setting, withdrawals, date of study

Participants: number, age, gender, inclusion criteria, exclusion criteria, other relevant characteristics

Interventions: intervention components, comparison, fidelity assessment

Outcomes: main and other outcomes specified and collected

The meta-analysis was performed using the Reviewer Manager Software, version 5.4.1[14]. All data were analyzed using a random-effects model due to clinical or methodological heterogeneity. The mean difference for the duration of analgesia, total LA consumed, VAS, onset of sensory block and neonatal umbilical pH between the groups were used. Relative risk for nausea and vomiting, shivering, hypotension, fever, APGAR were estimated. Forest plots of the outcomes of interest were generated to display effect estimates and confidence intervals for both individual studies and meta-analysis. The level of statistical significance was set at $p<0.05$ values with a 95% confidence interval. To assess heterogeneity between studies for the outcome, chi-square test was used as included in the forest plot of RevMan program, with $P<0.10$ indicating significant heterogeneity, and I^2 with suggested thresholds for low (24-49%), moderate (50-74%) and high (>75%) values. Heterogeneity was explored by performing a sensitivity analysis excluding outlier studies if they were methodologically different from other studies. Risk of publication bias was detected with the use of funnel plot.

RESULTS

The initial search through databases and other sources yielded 850 references. Most articles were excluded due to duplicate records, different study designs, population, interventions, and outcomes used. Eighteen full text articles were reviewed for eligibility. Out of the eighteen, thirteen full text articles were excluded due to different patient population and intervention used. A total of five studies were then included in the analysis.

No local study was found during the systematic search. An article not in English language was translated by the American Journal of Translation Research. A flowchart of study selection was summarized in Figure I below.

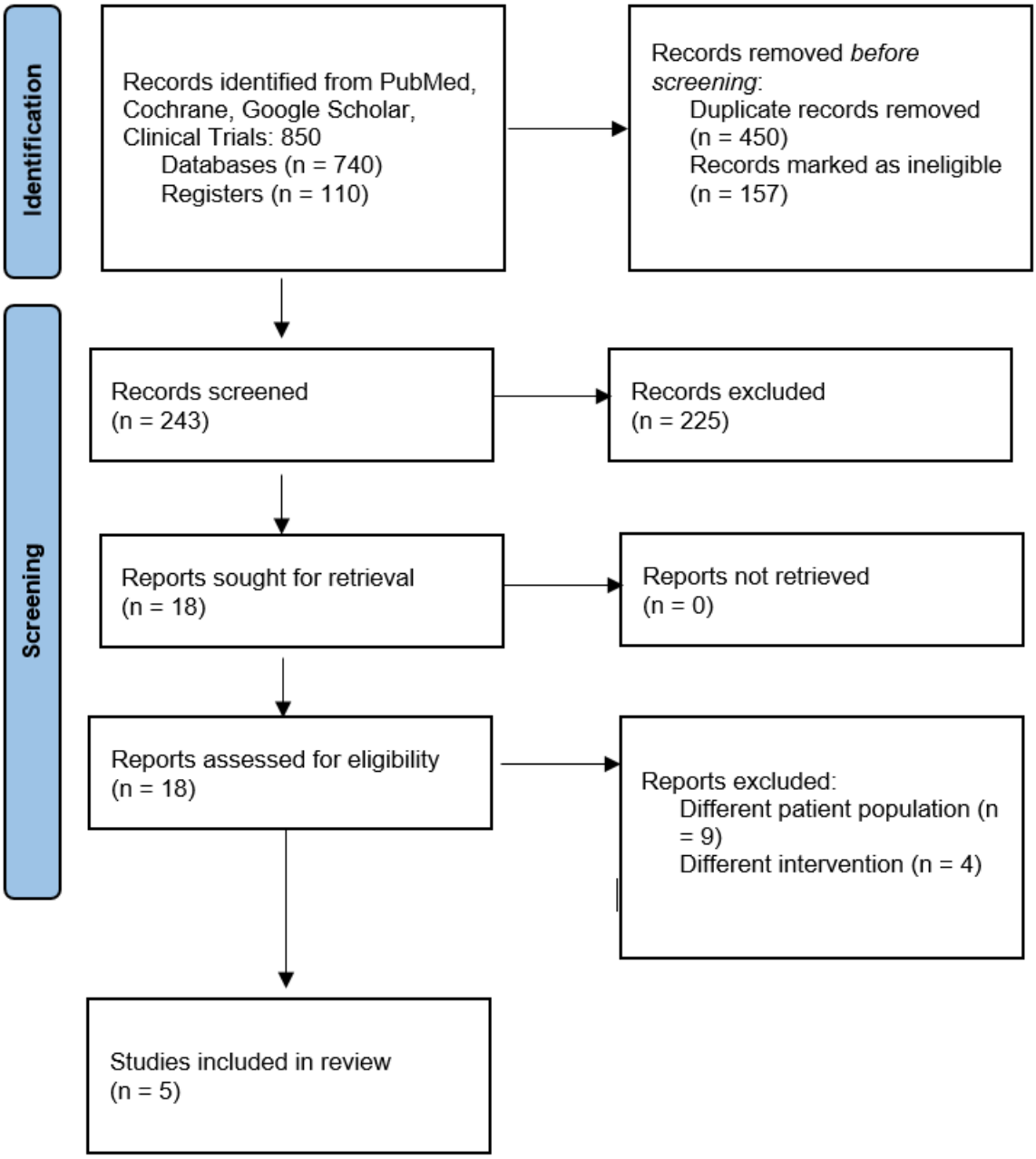


Figure 1: *PRISMA Flow Chart of Literature Search*[12]

Table 1: Characteristics of Included Studies[15]

Study ID, Author, Year, Location	Study Title	Population	Method/ Design	Anesthetic Technique	Comparator, LA Used, Sample Size	Intervention, LA Used, Sample Size	Study Outcomes
A Wu et al. 2021 China (Department of Anesthesiology, Yichun People's Hospital)	Feasibility of epidural injection of ropivacaine and dexamethasone for labor analgesia in women with preeclampsia	Inclusion: met the diagnostic criteria for preeclampsia and presented with typical symptoms; conscious and cooperated with the study; clinical data of the subjects were complete; ASA I-III; subjects agreed and signed the informed consent; vaginal delivery Exclusion: concurrent psychiatric disorders; multiple births; in active labor; allergic to the investigational drugs; severe cardiopulmonary disorders; placenta abruptio or placenta previa; <28 weeks of gestation; intermediate cesarean delivery	Randomized controlled trial	CLEA	Epidural ropivacaine 0.125% 39	Epidural ropivacaine 0.125% with dexamethasone 2mg 41	Maternal adverse events such as nausea/vomiting, hypotension, fever, bradycardia, motor block; APGAR in 1 & 5min

Study ID, Author, Year, Location	Study Title	Population	Method / Design	Anesthetic Technique	Comparator, LA Used, Sample Size	Intervention, LA Used, Sample Size	Study Outcomes
B Wahdan et al. 2019 Egypt (Department of Anesthesiology, Surgical ICU and Pain Management, Cairo University)	Epidural levobupivacaine versus a combination of levobupivacaine and dexamethasone in patients receiving epidural analgesia	Inclusion: 18 - 35 years of age; for normal vaginal delivery; ASA class I-II; no contraindication to regional anesthesia; with informed consent Exclusion: patient refusal; with failed epidurals; fetal distress; conversion to CS	Prospective double-blind trial	CLEA	Epidural levobupivacaine 0.125% 30	Epidural levobupivacaine 0.125% with dexamethasone 4mg 30	Duration of analgesia; Total amount of LA used; Pain score before after the block; Onset of sensory block; Maternal adverse events such as nausea/ vomiting, shivering; Maternal satisfaction; Neonatal umbilical pH

Study ID, Author, Year, Location	Study Title	Population	Method / Design	Anesthetic Technique	Comparator, LA Used, Sample Size	Intervention, LA Used, Sample Size	Study Outcomes
C Dhal, et al. 2018 India (Department of Anaesthesia and Intensive Care, Government Medical College and Hospital)	Can Epidural Dexamethasone Reduce Patient-Controlled Epidural Consumption in Laboring Women? A Double-Blind, Randomized, Placebo- Controlled Trial	Inclusion: ASA I-II; > 18 years old; primigravida with single gestation and cephalic presentation; at >= 37 weeks of gestation; cervical dilation <= 5 cm; pain score >30; requesting epidural analgesia Exclusion: patient refusal; administration of oral or parenteral analgesics in last 4 h before the start of neuraxial block; gestational age <37 weeks; history of obstetric complication; fetus with non-reassuring non- stress test; congenital abnormality; allergy to study drugs; preexisting or gestational diabetes mellitus; receiving steroids; history of immunosuppression; with local infection; deranged coagulation profile	Prospective, double-blind, randomized, controlled trial	CSEA	Intrathecal bupivacaine hyperbaric 0.5%, 2.5mg Epidural levobupivacaine 0.1% 30	Intrathecal bupivacaine hyperbaric 0.5%, 2.5mg Epidural levobupivacaine 0.1% with dexamethasone 8mg 30	Hourly drug consumption; Pain score before and after the block; Onset of analgesia; Maternal adverse events such as nausea/vomiting, shivering, fever, motor block; Maternal satisfaction; APGAR in 1 and 5 min

Study ID, Author, Year, Location	Study Title	Population	Method / Design	Anesthetic Technique	Comparator, LA Used, Sample Size	Intervention, LA Used, Sample Size	Study Outcomes
D Ali, et al. 2018 Egypt (Department of Anesthesia, Faculty of Medicine, Cairo University)	Using dexamethasone as an adjuvant to levobupivacaine in epidural anesthesia to change the pain intensity and duration in painless labor	Inclusion: between 21 and 35 years of age; for normal vaginal delivery; with cervical dilatation 4 cm or more; ASA II Exclusion: patient refusal; history of allergy to any medications to be used; coagulopathy; ASA III or more; spine deformity; any contraindications to neuraxial blocks; failed epidural; fetal distress; shift to cesarean section	Prospective double-blinded controlled trial	CLEA	Epidural levobupivacaine 0.125% 26	Epidural levobupivacaine 0.125% with dexamethasone 8mg 23	Duration of analgesia; Total amount of LA used; Pain score before and after the block; Onset of sensory block; Maternal adverse events such as nausea/vomiting, shivering; BP; HR; Maternal satisfaction; APGAR in 5 min; Neonatal umbilical pH

Study ID, Author, Year, Location	Study Title	Population	Method / Design	Anesthetic Technique	Comparator, LA Used, Sample Size	Intervention, LA Used, Sample Size	Study Outcomes
E Wang, et al. 2010 China (Department of Anesthesiology, Jiaxing Maternity and Child Health Care Hospital)	Influence of epidural dexamethasone on maternal temperature and serum cytokine concentration after labor epidural analgesia	Inclusion: healthy nulliparas ; spontaneous labor; singleton cephalic presentation; term (more than 37 weeks of pregnancy); requested epidural analgesia Exclusion: baseline temperature of 37.5 °C or more; metabolic disease; pregnancy-related complication such as diabetes mellitus or preeclampsia; increased risk of cesarean delivery; contraindication to epidural analgesia	Randomized, controlled trial	CLEA	Epidural bupivacaine 0.125% 30	Epidural bupivacaine 0.125% with dexamethasone 5.8mg 30	Total amount of LA used; Pain assessment before the block; Intrapartum fever; APGAR in 1 and 5 min

Study Characteristics

This meta-analysis included 5 randomized controlled trials[15-19] to determine the effectiveness of epidural dexamethasone when used as an adjuvant for labor analgesia (Table 1). It encompassed data for 309 women, in which 154 of them were randomized to the treatment group who received dexamethasone to the epidural solution and the remaining 155 fell to the control group who received the usual epidural solution. The population of these trials range from 49 (Ali et al) to 80 (Wu et al) parturients for vaginal delivery. One study was done in 2021 (Wu et al), another in 2019 (Wahdan et al), two studies done in 2018 (Dhal et al and Ali, et al) and the last study in 2010 (Wang et al).

The anesthetic technique used for labor analgesia by four of the five studies (Wu et al, Wahdan et al, Ali et al and Wang et al) was epidural anesthesia, while one study (Dhal et al) made use of the CSEA. The LA used for the epidural solution by three of the five studies (Wahdan et al, Dhal et al and Ali et al) was levobupivacaine, while the study by Wu et al used ropivacaine and the study by Wang et al used bupivacaine. Out of the five studies, two studies (Dhal et al and Ali et al) used 8mg of dexamethasone, one study (Wu et al) used 2mg dexamethasone, another (Wahdan et al) with 4mg dexamethasone, while Wang et al used 5.8mg dexamethasone.

For the primary outcome, only two studies (Wahdan et al and Ali et al) analyzed the duration of epidural analgesia in minutes. Four studies determined the total LA used; however, the study by Dhal et al measured the drug consumption per hour, while the remaining three studies (Wahdan et al, Ali et al and Wang et al) measured the total drug consumed through the course of labor. The secondary outcome assessed other maternal and neonatal effects of epidural dexamethasone. Pain before and after the block and onset of sensory block was assessed by three studies (Wahdan et al, Dhal et al and Ali et al). These five studies reported different adverse events such as nausea and vomiting (Wu et al, Wahdan et al, Dhal et al, Ali et al), shivering (Wahdan et al, Dhal et al, Ali et al), hypotension (Wu et al, Dhal et al) and fever (Dhal et al, Wang et al). The incidence of bradycardia was noted by Wu et al while Ali et al measured this by beats per minute. Maternal satisfaction was assessed by incidence (Wahdan et al), through 1-100 scale (Dhal et al) and by 0-3 scale (Ali et al). APGAR was included in four studies (Wu et al, Dhal et al, Ali et al and Wang et al) while only two studies (Wahdan et al and Ali et al) measured the neonatal umbilical pH. Characteristics of included studies were tabulated in Table 2.

All studies had low risk for bias from the randomization process and measurement of the outcome. Four from the five studies

had low risk of bias due to deviations from intended intervention and in selection of reported result while only three studies had low risk of bias due to missing outcome data (Figure 2).

The risk of bias of the selected studies was judged based on Risk of bias tool (ROB 2)[20]. Three out of the five included studies in this paper had low risk of bias based on the five different domains as summarized in Figure 3 below.

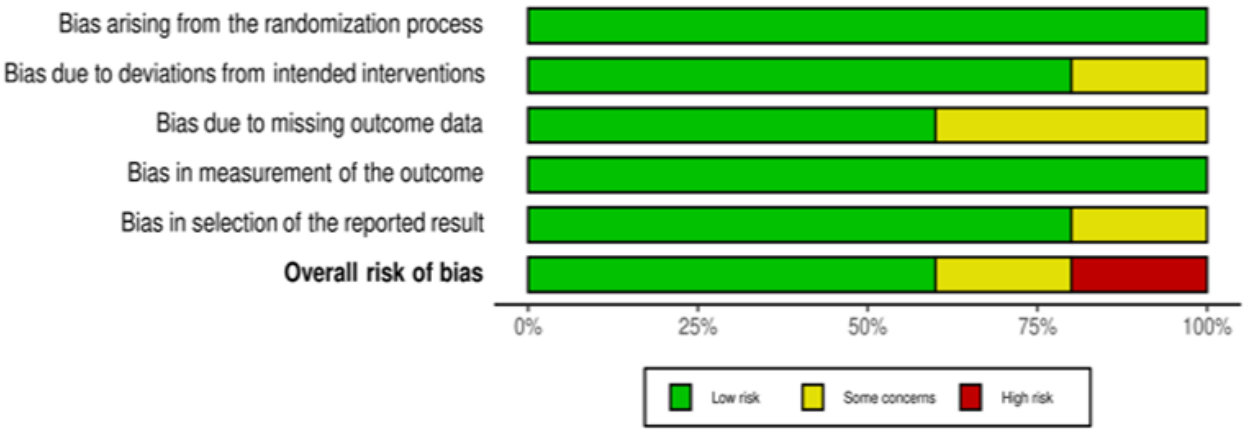


Figure 2: *Risk of bias graph of included studies*

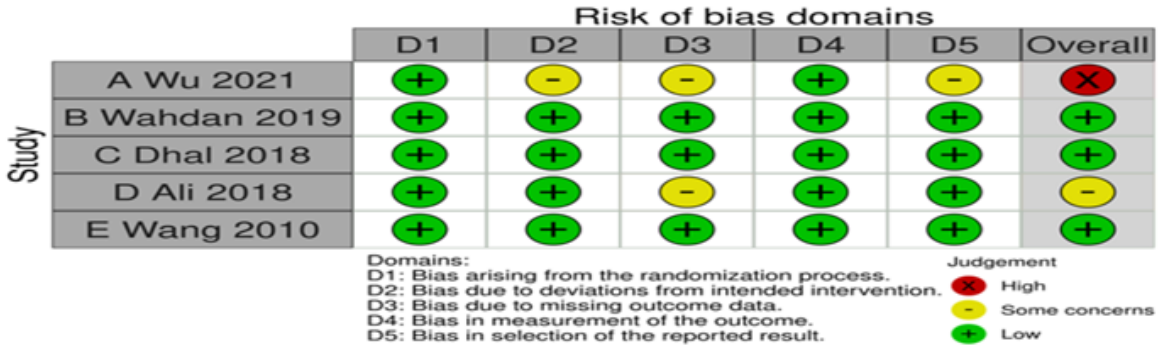


Figure 3: *Risk of bias summary of included studies*

Comparison of Outcomes

Mean duration of epidural analgesia (in minutes) for both the experimental and comparator group were primarily pooled in this study where the overall effect estimate was calculated as the mean difference with 95% confidence interval. . Pooled summary estimate was derived using the random effects model. Among the five included studies, only two reported the mean duration of epidural analgesia.

Figure 4 indicates that patients who had epidural dexamethasone as an adjuvant for labor analgesia had longer duration of analgesia by an average of 18.3 minutes compared to the group without dexamethasone. The level of heterogeneity using I^2 was 0% (low).

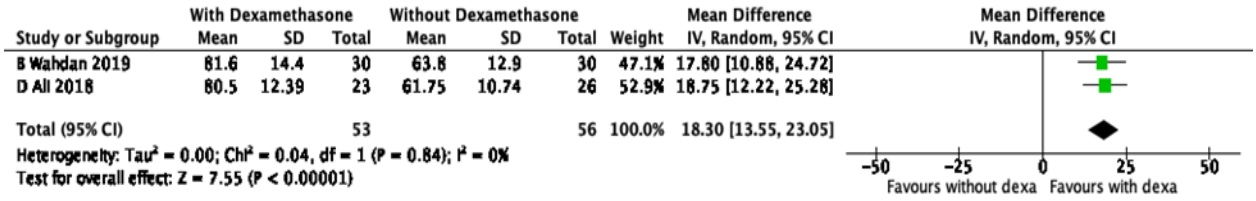


Figure 4: *Effect on the duration of epidural analgesia*

The total analgesic dose used for both experimental and comparator group were primarily pooled. The overall effect estimate was calculated as the mean difference with 95% confidence interval. Pooled summary estimate was derived using the random effects method. Three of the five included studies reported the total LA consumed through the course of labor (Figure 5). Overall, the pooled mean difference showed no significant difference between the two groups. The studies however, demonstrated high heterogeneity (I^2=87%).

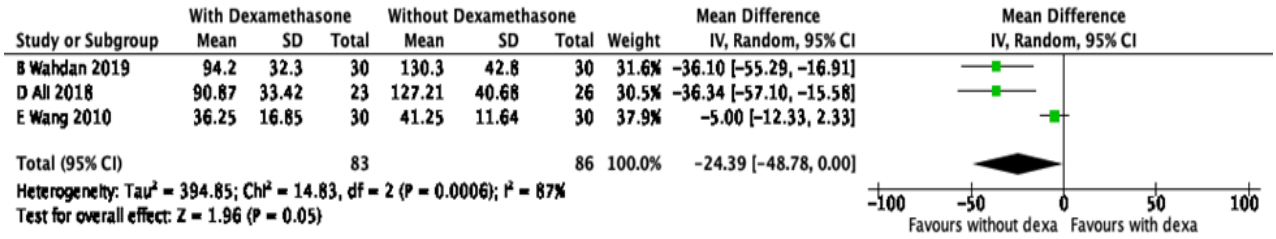
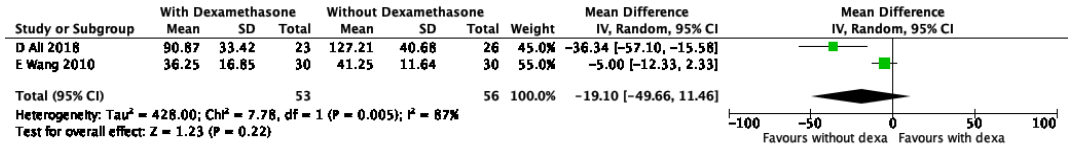


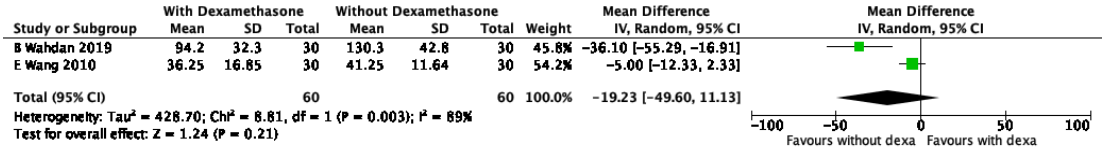
Figure 5: *Effect on the total LA consumed*

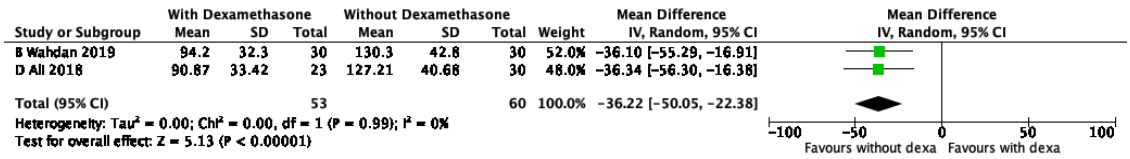
A sensitivity analysis omitting one study at a time was done to assess the robustness of the results as shown in Table 2. The three studies used different doses of dexamethasone 4mg (Wahdan et al), 8mg (Ali et al) and 5.8mg (Wang et al). Wang's trial also used Bupivacaine as its LA in the epidural solution while the other two studies used Levobupivacaine. Studies by Wahdan et al and Ali et al when removed, did not eliminate the large heterogeneity. When the study by Wang et al was removed, the heterogeneity on the total LA used between the two groups was eliminated (MD= -36.22mg; 95%CI=-50.05, -22.38; p-value=<0.00001; I^2=0%).

Table 2: Sensitivity analysis on the total LA consumed

Study removed	I^2	Pooled effect estimate
Wahdan 2019	87%	-19.10 (-49.66, 11.46); p=0.22
Ali 2018	89%	-19.23 (-49.60, 11.13); p=0.21
Wang 2019	0%	-36.22 (-50.05, -22.38); p<0.00001







Mean VAS before and after the block were primarily pooled in the study. The overall effect estimates were calculated as the mean difference with 95% confidence interval. Pooled summary estimates were derived using the random effects method. Three studies reported the pain scale before and 15 minutes after the performance of labor analgesia. The pooled mean differences in the parturients' VAS before (MD=0.19; 95%CI=-0.16, 0.54; p-value=0.28) and after (MD=0.00; 95% CI=-0.18, 0.19; p-value=0.97) the block showed no significant differences between the two groups. The studies showed low heterogeneity (I^2=37%; I^2=0%). (Figure 6 and 7)

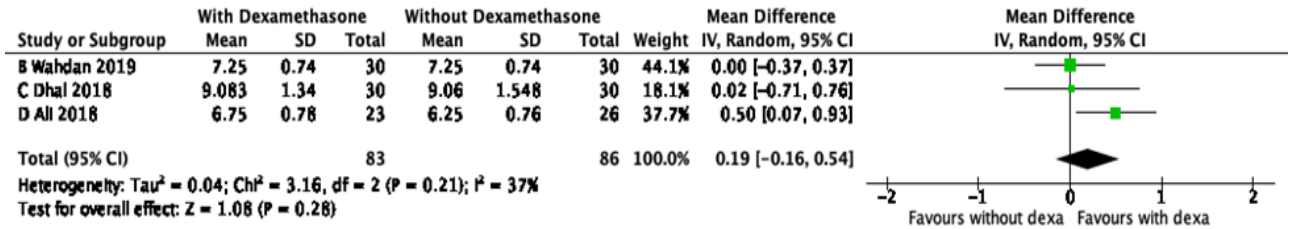


Figure 6: *Effect on the VAS before the block*

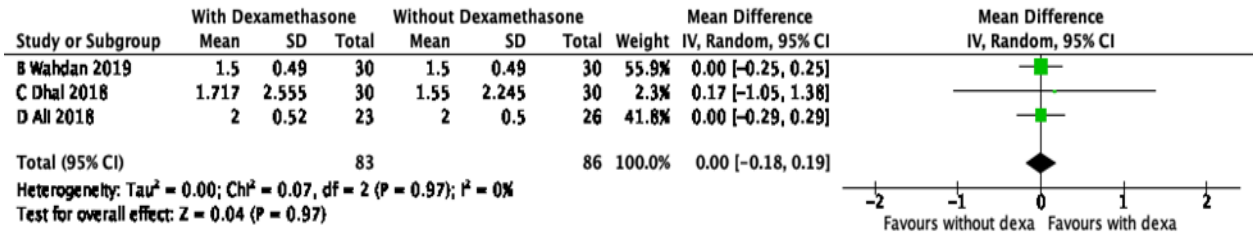


Figure 7: *Effect on the VAS after the block*

Mean onset of sensory block for both the experimental and control group were pooled. The overall effect estimate was calculated as the mean difference with 95% confidence interval. Pooled summary estimate was derived using the random effects method. Three studies reported the mean time for onset of sensory block among patients who received dexamethasone in the epidural solution and those who did not. As shown in Figure 8, the overall pooled mean difference between the two groups showed a statistical difference in the result (MD=1.81min; 95%CI=0.77, 2.85; p-value=0.0006). The level of heterogeneity using I^2 was 0% (low).

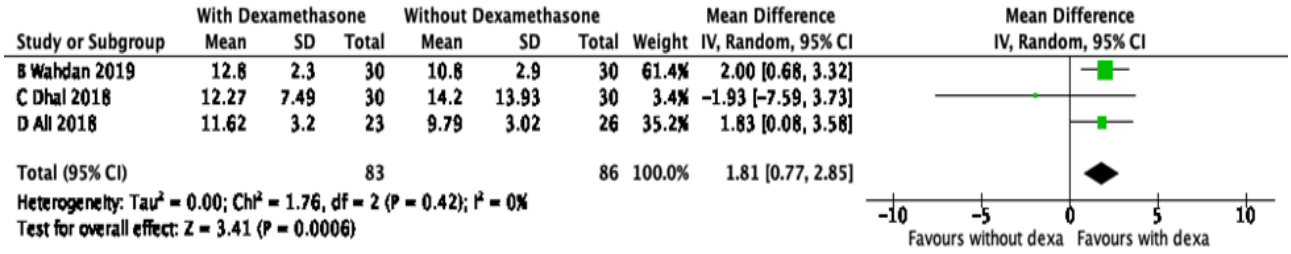


Figure 8: *Effect on the onset of sensory block*

Figures 9-12 show the risk of adverse events for both groups. The relative risk for the incidence of the observed complications and the random effects method were used to estimate the 95% confidence interval. A meta-analysis of clinical events such as nausea and vomiting (RR=1.15; 95%CI=0.68, 1.94; p-value=0.61; I^2=0%), shivering (RR=0.83; 95%CI=0.38, 1.81; p-value=0.65; I^2=19%), hypotension (RR=1.22; 95%CI=0.53, 2.85; p-value=0.64; I^2=0%) and fever (RR=1.16; 95%CI=0.02, 1.04; p-value=0.06; I^2=14%) showed no significant differences between the group who received dexamethasone and those who did not in their epidural solution. The studies demonstrated low heterogeneity.

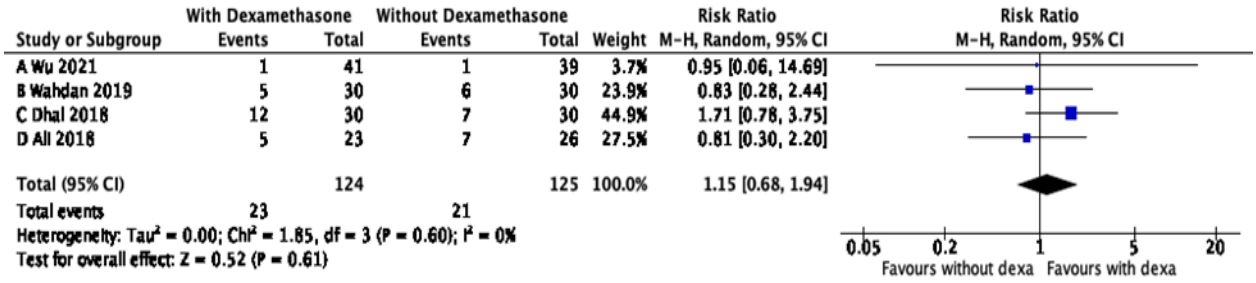


Figure 9: *Effect on the incidence of nausea and vomiting*

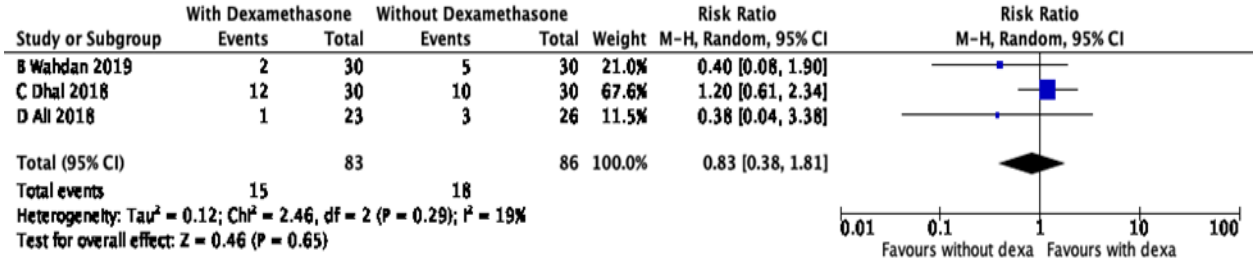


Figure 10: *Effect on the incidence of shivering*

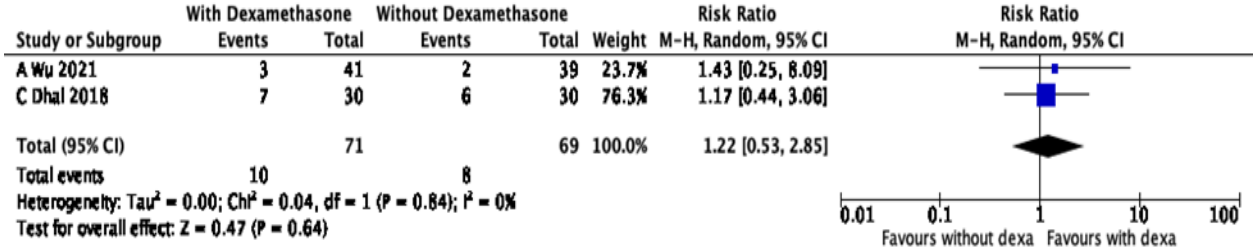


Figure 11: *Effect on the incidence of hypotension*

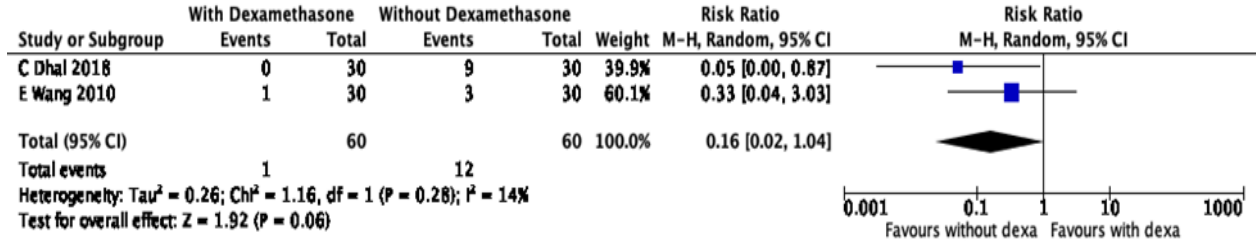


Figure 12: *Effect on the incidence of intrapartum fever*

Three studies reported the APGAR in 1 minute while four studies reported the APGAR in 5 minutes as their outcome. Relative risk for the incidence of APGAR score ≥7 in 1 and 5 minutes and random effects method were used to estimate the pooled effect with 95% confidence interval. Pooled risk ratio presented in Figures 13-14 showed no significant differences between the two groups in terms of APGAR score ≥7 in 1 and 5 minutes.

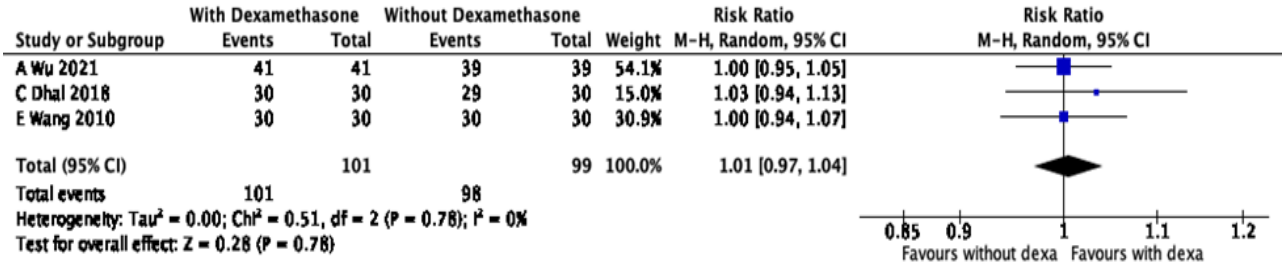


Figure 13: *APGAR score ≥7 in 1 minute*

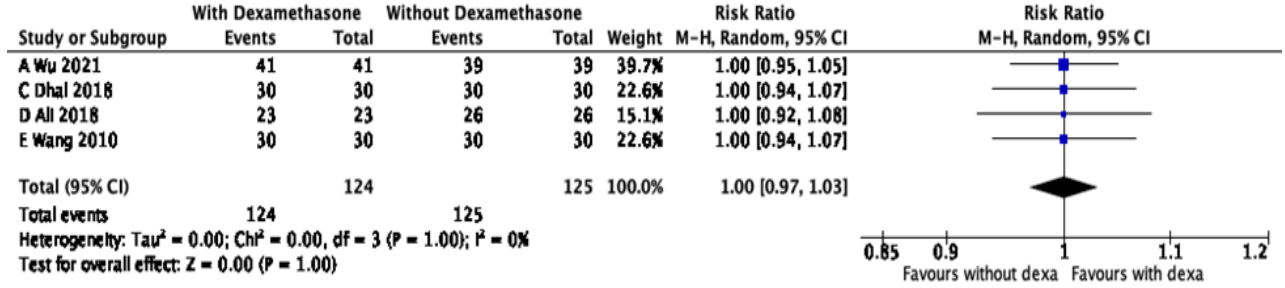


Figure 14: *APGAR score ≥7 in 5 minutes*

Only two studies reported the effect on the neonatal umbilical pH between the group with dexamethasone and the group without. The overall effect estimate was calculated as the mean difference with 95% confidence interval. Pooled summary estimates were derived using the random effects method. The pooled mean difference between the two groups was comparable as shown in Figure 15 (MD=-0.00; 95%CI=-0.04, 0.04; p-value=0.94). However, it showed moderate heterogeneity (I^2=68%). Ali's trial showed some concern on the overall risk of bias. The two studies also used different doses of dexamethasone, 4mg (Wahdan et al) and 8mg (Ali et al). Since this outcome only included two studies, sensitivity analysis omitting one study at a time to eliminate heterogeneity cannot be done.

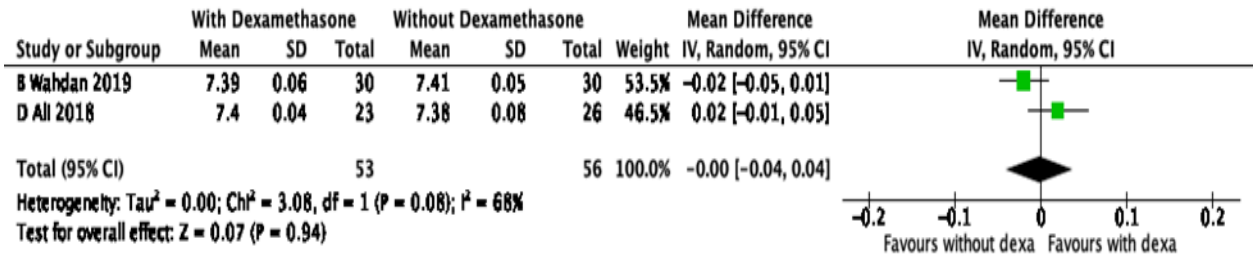


Figure 15: *Effect on the neonatal umbilical pH*

Funnel plot to address any publication bias was not done as there were <10 studies for each outcome.

DISCUSSION

In this study, we evaluated the effect of epidural dexamethasone on the maternal and newborn parameters during labor analgesia. Meta-analysis showed that parturients who were given epidural dexamethasone as an adjuvant for labor analgesia can have prolonged duration of analgesia by an average of 18.30 minutes (MD=18.30min; 95%CI=13.55, 23.05; p-value<0.00001; I^2 =0%). A longer duration of epidural analgesia limits additional administration of LA, limiting the possible dose related LA side effects. This reinforces the finding by Naghipour et al[21] on a randomized controlled trial that the duration of analgesia [with dexa (N=35) 372±58.1min vs without dexa (N=35) 234.6±24.3min; p-value=0.001] was significantly longer if dexamethasone was added to the epidural solution on patients undergoing abdominal or thoracic surgery.

In an RCT of dexamethasone via intrathecal route on parturients receiving combined spina-epidural analgesia, epidural consumption of LA [with dexa (N=40) 102.9±34.8mg vs without dexa (N=40) 120.1±41.9mg; p-value=0.049] was significantly lower in the group with intrathecal dexamethasone compared to the control group[22]. On the other hand, an RCT on dexamethasone via intravenous route demonstrated that the average hourly epidural drug consumption [with dexa (N=40) 10.34±1.79ml/h vs. without dexa (N=40) 11.34±1.83ml/h; p-value=0.015] was significantly lower in the dexamethasone group compared to the placebo group on patients undergoing labor analgesia[6]. In this meta-analysis, the pooled data on the effect on the total LA consumed through the course of labor initially showed that there was no difference between the group with epidural dexamethasone and the group without (MD=-24.39; 95%CI=-48.78, 0.00; p-value=0.05;

I^2=87%). When sensitivity analysis was conducted, significant heterogeneity was eliminated after excluding the study by Wang et al. This may be attributable to the use of a different LA. The resultant finding then revealed a statistical difference in the result (MD=-36.22mg; 95%CI=-50.05, -22.38; p-value=<0.00001; I^2=0%). The presence of heterogeneity involving this outcome reduced the robustness of the result and caution in dealing with the result is warranted.

A meta-analysis by Jebaraj et al[8] showed that epidural dexamethasone after abdominal surgery significantly decreased postoperative morphine consumption (MD=−7.89mg; 95%CI=−11.66, −3.71; p-value=0.0001) and number of patients requiring postoperative rescue analgesic boluses (RR=0.51; 95%CI=0.41, 0.63; p-value=0.00001). However, our present study on the analysis on pain assessment before (MD=0.19; 95%CI=-0.16, 0.54; p-value=0.28; I^2=37%) and after (MD=0.00; 95%CI=-0.18, 0.19; p-value=0.97; I^2=0%) labor analgesia showed no significant difference whether dexamethasone was administered in the epidural solution.

Pooled result on the effect on the onset of sensory block demonstrated that there is a statistical significance in the result of the two groups (MD=1.81min; 95%CI=0.77, 2.85; p-value=0.0006; I^2=0%). The group with epidural dexamethasone had a slightly longer onset by 1.81min. However, a difference of 1.81min is too short to have a significance in clinical practice on patients undergoing labor analgesia. Contradicting result was seen in a comparative study between intravenous and local dexamethasone as adjuvant to bupivacaine in perianal block demonstrating a rapid onset of blockade with administration of dexamethasone through either route compared to the group without dexamethasone at all [local dexa (N=18) 3.8$\pm$0.7min vs IV dexa (N=19) 3.8$\pm$0.9min vs without dexa (N=19) 5.5 +1.2min; p-value=<0.01][23].

In this study, pooled results study on the maternal adverse events such as nausea and vomiting (RR=1.15; 95%CI=0.68, 1.94; p-value=0.61; I^2=0%), shivering (RR=0.83; 95%CI=0.38, 1.81; p-value=0.65; I^2=19%), hypotension (RR=1.22; 95%CI=0.53, 2.85; p-value=0.64; I^2=0%) and fever (RR=1.16; 95%CI=0.02, 1.04; p-value=0.06; I^2=14%) demonstrated that the group with epidural dexamethasone was not statistically significant to the group with only plain epidural solution. Adverse effects with a single dose of dexamethasone are probably extremely rare and minor in nature, and previous studies have demonstrated that short term (<24 hours) use of dexamethasone was safe[21]. Side effects could be related conventionally to the neuraxial anesthesia and labor itself and not to the added medication[2,24,25].Neuraxial anesthesia-induced sympathetic block can cause unopposed vagal stimulation of the gastrointestinal system leading to increased secretions, relaxation of the sphincters and constriction of the bowels.

This reason, together with the delayed gastric emptying of laboring women, may predispose patients to nausea and vomiting[2]. Patients at increased risk to this may be given prophylactic anti-emetics. Regional anesthesia also inhibits central thermoregulatory control, preventing vasoconstriction and shivering to the blocked segments. Shivering arises in the unblocked segments to try and maintain the body temperature[24]. To prevent this, active warming through warm infusions, warm air and coverings are essential. Sympathetic blockade induced by neuraxial anesthesia may also lead to peripheral vasodilation[2]. The hypotension associated with this can be avoided through prevention of extensive block and the administration of additional intravenous crystalloid and vasopressors. Trials have noted a gradual rise in core temperature over several hours in laboring women receiving epidural analgesia that was not observed in women receiving no analgesia, which is incompletely understood[26]. When maternal fever occurs, efforts should be made to lower the maternal temperature and identify and treat the presumed maternal infection. Use of labor analgesia prevents the activation of the neuroendocrine stress response, affecting both the mother's and the fetus' organ systems. With the application of safe anesthesia practice to limit the adverse events of neuraxial analgesia, complications may be preventable and are rare, outweighing the risks involved[25].

This review also noted bradycardia as another complication but due to the inconsistency on how this outcome was reported, meta-analysis could not be performed. Wu et al compared the two groups by incidence [no. (%)] {with dexa (N=41) [2 (4.88%)]; without dexa (N=39) [2(5.13%)]} while Ali et al expressed the data as mean measurement in beats per minute in a graph but without numerical values.

Three studies assessed the maternal satisfaction between the two groups. Wahdan et al presented the data as incidence [no. (%)] of satisfied patients {with dexa (N=30) [24 (80%)]; without dexa (N=30) [25(83.3%)]; p-value=0.2}. Dhal et al assessed this by a scale of 0-100 [with dexa (N=30) 95.43$\pm$12.04; without dexa (N=30) 93$\pm$10.80; p-value=0.166]. The third study by Ali et al assessed the maternal satisfaction in a scale of 0-3 but no data was shown. Due to non-uniformity of how these data were presented, meta-analysis could not be performed.

The neonatal APGAR score and umbilical pH are determining factors of mortality and general well-being of the newborn. In this regard, it is important to consider the type of medications administered to the parturient which also has a minimal effect to the fetus. The result of the analysis between the two groups indicated that epidural dexamethasone as an adjuvant had no significant effect on the neonatal APGAR score [(1 minute: RR=1.01; 95%CI=0.97,

1.04; p-value=0.78; I^2=0%), (5 minutes: RR=1.00; 95%CI=0.97, 1.03; p-value=0.64; I^2=0%)] and on the neonatal umbilical pH (MD=-0.00; 95%CI=-0.04, 0.04; p-value=0.94). However, only two studies were included on assessing the effect on the neonatal umbilical cord blood gases which showed moderate heterogeneity (I^2=68%). The following factors may have contributed to the heterogeneity of this outcome: 1) some concern on the overall risk of bias in Ali's trial and 2) use of different doses of dexamethasone, 4mg (Wahdan et al) and 8mg (Ali et al). Similar to the neonatal outcome of this meta-analysis, a study that tested dexamethasone through the intrathecal route found that there was no significant difference between the group with dexamethasone in the intrathecal solution and the control group concerning the APGAR score {with dexa (N=40) [8(6-9)]; without dexa (N=40) [8(6-9)]; p-value=0.377} and the umbilical blood pH {with dexa (N=40) [7.39(±0.08)]; without dexa (N=40) [7.41(±5.0.05)]; p-value=0.232} [27].

Conclusion and Recommendation

The results of this meta-analysis showed that the use of dexamethasone as an adjuvant to epidural solution during labor analgesia appears to be effective in prolonging the duration of epidural analgesia, limiting the total LA consumed, with limited maternal and neonatal adverse events. However, due to the presence of heterogeneity, these results should be interpreted with caution and additional studies are needed before adopting this technique in routine clinical practice.

This meta-analysis was not free from limitations. There were only 5 studies included in this analysis and the number of included trials on each outcome were limited. Hence, a single study has a large influence in the ultimate outcome, which may lead to biases. Heterogeneity was found in some of the outcomes. Heterogeneity may be due to difference in the dose of epidural dexamethasone, type of LA used and concerns on the risk of bias. Some of the outcomes have inconsistencies on how the data were presented, affecting the number of included trials on each outcome.

Because of the limitations mentioned on this study, application of these findings in the management of parturients in labor should be treated with caution. Future studies with rigorous design and larger sample size are needed to further identify the role of epidural dexamethasone as an adjuvant to labor analgesia. Better literature search through inclusion of quality studies and adherence on the methods used and uniformity on the reported outcome are critical to minimize bias and achieve findings that can be safely applied in clinical practice.

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ARTICLE

Caregiver satisfaction with the use of telemedicine in the neurodevelopmental evaluation of children at the Philippine Children's Medical Center

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OBJECTIVES*:* This study aims to assess caregiver satisfaction with the use of telemedicine in the evaluation of children referred for neurodevelopmental evaluation at the Philippine Children's Medical Center (PCMC) Neurodevelopmental Pediatrics Clinic.

MATERIALS AND METHODS: : A survey was conducted on caregivers of pediatric patients aged 3 months to 18 years and 11 months old for neurodevelopmental evaluation. A questionnaire to determine the demographic and clinical data and Parent/Caregiver-Reported Satisfaction Form were administered via email, Facebook messenger or phone call.

RESULTS: Seventy-three caregivers completed the questionnaire. Most (95.9%) were mothers, 47.9% were college graduates with one parent working and 43% have an income of 10,000-20,000. Almost half (47.9%) of the children they care for were ages 3-months to 2-year 11 -months, predominantly males, with 35.6% diagnosed with autism spectrum disorder, and 69.9% were new patients. Caregivers were very highly satisfied with telemedicine in all domains (technical functioning, comfort and perceived privacy, access to care and overall satisfaction) as it obtained a mean of 4.51 and median of 5.00. There was no significant difference in the responses based on the age of the child and type of visit.

CONCLUSION: Caregivers showed very high level of satisfaction with the use of telemedicine in the neurodevelopmental evaluation of children at PCMC and holds a significant promise for its use both within the context of the pandemic and beyond.

RECOMMENDATIONS: Further studies on caregivers' satisfaction with the use of telemedicine over a sustained period and comparing telemedicine and in-person assessment are recommended.

KEYWORDS: *Neurodevelopmental Pediatrics, Telemedicine, Satisfaction, Neurodevelopmental Evaluation*