

The Effect of Dexamethasone on Nausea and Vomiting during Labor and Labor Pain in Parturients Undergoing Normal Vaginal Delivery

Nasrin Faridi Tazeh kand^{1*}, Ashraf Moeini^{2,3}, Hadith Rastad⁴, Bitā Eslami², Nahid Manouchehrian⁵, Mehdi Sanatkar⁶

Background: Clinical trials in surgical procedures have shown that dexamethasone reduced pain, nausea and vomiting postoperatively. The aim of this study was to compare the effect of dexamethasone on nausea and vomiting and labor pain in women who were candidates for normal vaginal delivery.

Methods: In a clinical trial, 60 pregnant women during labor were allocated to two groups receiving 8 mg dexamethasone intravenously (IV) slowly plus 50 mg pethidine intramuscularly (IM) (Group D), and 25 mg promethazine IV slowly plus 50 mg pethidine IM (Group P). The nausea and vomiting during labor and labor pain in our patients were recorded.

Results: Group D had significantly lower nausea and vomiting during labor rather than group P ($P = 0.03$ and 0.008 ; respectively). The level of satisfaction and pain relief was not statistically different between two groups.

Conclusion: It seems that dexamethasone is better than promethazine added to pethidine during labor in selected parturients.

Keywords: dexamethasone; nausea and vomiting; labor pain

The pain of childbirth is one of the most severe pains that a woman can experience during her lifetime. The pain of labor not only has physiological changes but also has emotional distress that affects the fetus [1]. The mother must be educated to take an active role in decision making in using methods for pain relief [2]. In order to reduce the demand for cesarean section, pain medication is very important. There are varieties of pharmacologic and nonpharmacologic options to manage the pain of labor. Pharmacologic options are classified as systemic or loco-regional [3]. Regional technique has been shown to be the most effective [4]. However, in some parturients it may not be chosen or may be technically impossible. Of available opioids, the most commonly used in our country is pethidine that is usually given intramuscularly in doses of 50-100 mg.

Systemic opioids, are associated with adverse effects on mother including sedation, respiratory depression, nausea and vomiting [5].

In our center the most commonly used agent in combination with an opioid is promethazine. Promethazine potentiates analgesia and decreases side effects of pethidine such as nausea and vomiting [5]. Effectiveness of dexamethasone on nausea and vomiting was demonstrated that was equal to or better than other antiemetic agents [6]. Several clinical trials in surgical procedures have shown that dexamethasone reduced pain, nausea and vomiting postoperatively following cholecystectomy or pediatric and gynecological surgery [7-10]. Therefore, the objective of our study was to compare the effect of dexamethasone plus pethidine with promethazine plus pethidine on nausea and vomiting during labor and labor pain in parturients undergoing normal vaginal delivery.

Methods

The study was approved by the clinical research ethics committee of Tehran University of Medical Sciences. Written informed consent was obtained from all participants. Inclusion criteria were singleton term pregnancies, cephalic presentation, aged 18 and 40 years, ASA class I, II, parturient without any maternal and fetal complications such as preeclampsia. Exclusion criteria were fetal distress, known uterine anomalies, the decision of immediate analgesia, request for epidural analgesia, any contraindication to pethidine or intramuscular injections, and a history of diabetes mellitus or drug abuse.

All women were in active labor (cervical dilation of 4-5 cm). Use of a 100-mm visual analogue scale (VAS) for the

From the ¹Department of Anesthesiology and Critical Care, Roointan-Arash Hospital, Tehran University of Medical Sciences, Tehran, Iran.

²Department of Gynecology and Obstetrics, Roointan-Arash Hospital, Tehran University of Medical Sciences, Tehran, Iran.

³Department of Endocrinology and Female Infertility, Royan Institute, ACECR, Tehran, Iran.

⁴Research Development Center, Roointan-Arash Hospital, Tehran university of medical sciences, Tehran, Iran.

⁵Department of Anesthesiology and Critical Care, Fatemeh Hospital, Hamedan University of Medical Sciences, Hamedan, Iran.

⁶Anesthesiology Department, Farabi Hospital, Tehran University of Medical Sciences, Tehran, Iran.

Received: 30 September 2015, Revised: 23 October 2015, Accepted: 6 November 2015

The authors declare no conflicts of interest.

*Corresponding author: Nasrin Faridi Tazeh-kand, Department of Anesthesiology, Roointan-Arash Hospital, Tehran University of Medical Sciences, Tehran, Iran. e-mail: nfaridi@sina.tums.ac.ir

Copyright © 2015 Tehran University of Medical Sciences

measurement of pain (0 mm = no pain, 100 mm = worst pain imaginable) was explained for parturients. The women were randomly allocated in two groups by sequentially numbered, sealed opaque envelopes prepared by an independent practitioner. The group D (n=30) received dexamethasone (DEXADIC, Caspian Tamin Pharmaceutical Co., Rasht, Iran) 8 mg IV slowly plus 50 mg pethidine (Pethidine-hameln, Germany) IM. The group P (n=30) received Promethazine (Promethazine 50 mg/2ml, Tehran Chemic, Iran) 25 mg IV slowly plus 50 mg Pethidine IM. Intrapartum management was according to our usual standardized labor ward protocol. Arterial pressure, heart rate, respiratory rate, pulse oximetry, observer sedation score (1= fully awake, 2 = drowsy, 3 = eye closed but unresponsiveness), fetal heart rate, and presence or absence of nausea and vomiting were recorded. Pain was assessed with continuous Visual Analogue Scale (VAS). Participants were asked to mark on the line the worst pain they had felt during their last contraction after it had finished. Baseline recordings were made and the measurements were taken every 30 min after starting analgesia. Surface ultrasound was utilized in order to continuously monitor fetal heart rate (FHR), and 1 and 5-min Apgar Scores were recorded.

The study was stopped if a woman requested regional analgesia. The overall effective analgesia was rated after delivery by the mother within 2 h of delivery on a five point verbal scale ranging from excellent to poor (Likert scale: 5 = Excellent, 4 = very good, 3 = good, 2 = fair, 1= poor). For sample size calculation, we estimated that in this trial, the incidence of vomiting will be reduced about 35 % based on the other studies. So in order to find the result, 30 samples in each group were needed.

Statistical analysis was performed with SPSS (ver. 13, Chicago, IL, USA). Numerical variables were presented as mean \pm standard deviation (SD), and categorical variables were presented as number and percentage. Repeated measurement ANOVA was conducted to evaluate the differences between four trials of time and two groups. A P value less than 0.05 was considered as statistically significant.

Results

The demographic and labor characteristics of the participants of both treatment groups were identified in (Table 1). Comparing characteristics including age, body mass index (BMI), parity, gestational age, Apgar score between treatment groups showed no statistically significant differences. The proportion of women received oxytocin in group P was higher than the group D but this difference was not statistically significant (P= 0.64). In terms of awareness during sedation, higher percent of patients in group D were fully awake (79.31% compared with 56.67%) although the difference between two proportions was not statistically significant (P= 0.14). In terms of complication, there were significant differences in the incidence of nausea and vomiting between two groups (P = 0.03 and 0.008; respectively). It means patients in group D suffering from

these complications were more than group P. The level of satisfaction was not statistically different between two groups (P= 0.18). As it was mentioned in (Table 2), the high level of satisfaction was higher in group D compared to another group. (Table 3) shows the descriptive statistics of VAS score in two groups with 5 trials. As it shows the baseline VAS score was significantly different between two groups (4.73 ± 2.01 vs 6.80 ± 2.23 , P -value <0.001). Therefore, in repeated measurement ANOVA, the baseline VAS was adjusted as a covariate. Test of within subject effect by Sphericity assumed showed evaluation of VAS score between four trials had significant differences (Mean square = 13.02, df = 3, F=13.13, P <0.0001). Although the value of Partial Eta squared showed the effect of trial was about 0.25 on this model. Test of between subject effect showed these two series of trials were not statistically different between two groups (Mean square = 4.33, df = 1, F =0.46, P- value = 0.50). The estimation of VAS score in group D and group P were respectively [(6.37; 95% CI: 5.57 - 7.18) vs (6.01; 95% CI: 5.35 - 6.66)].

Discussion

In the present study, the effects of dexamethasone and promethazine in combination with pethidine, on nausea and vomiting during labor and labor pain were compared. According to our finding, dexamethasone had a better antiemetic efficacy compared with promethazine. Allen et al., in a systematic review and meta-analysis reported that dexamethasone was an effective antiemetic for patients receiving neuraxial morphine for cesarean delivery and abdominal hysterectomy [10]. Several studies showed that dexamethasone decreased postoperative nausea and vomiting [11-17]. Also dexamethasone is the most widely used corticosteroid in the treatment of chemotherapy induced nausea and vomiting (CINV), and is effective as monotherapy and in combination with other agents. It is recommended in both the acute and delayed settings [18]. Studies suggested that the antiemetic effect of steroids may be partially due to their activity on the central nervous system or activation of glucocorticoid receptors in the nucleus of the solitary tract in the medulla or antagonism of 5HT3A receptors [19-21]. Dexamethasone with anti-inflammatory effect has been used for reducing pain and inflammation after surgery [22-28]. In a systematic review, the impact of preoperative dexamethasone on postoperative analgesia concluded that a single IV preoperative dose of dexamethasone has small but statistically significant analgesic benefits [29].

In our study dexamethasone and promethazine had equal pain relief in labor as judged by VAS pain scores. Since promethazine in combination with pethidine can potentiate analgesia, so it can be an explanation of our finding. Also source and severity of pain are different in labor and postoperatively.

In conclusion, it seems that dexamethasone is better than promethazine added to pethidine during labor in selected parturients.

Table 1- Patients' and labor characteristics in both groups

Variables	Group D	Group P	P
Age (yrs)	25.54 ± 5.07	24.90 ± 4.82	0.63
BMI (kg/m ²)	27.76 ± 3.65	28.17 ± 2.81	0.64
Gestational age (wks)	39.46 ± 1.17	39.10 ± 1.37	0.28
Parity			
1	17(58.62)	24(80)	
2	11(37.93)	5(16.67)	0.18
3	1(3.45)	1(3.33)	
Minimum O ₂ saturation	95.63 ± 1.50	95.53 ± 1.31	0.78
Oxytocin use	22(78.57)	25(83.33)	0.64
Sedation status			
Fully awake	23(79.31)	17(56.67)	
Drowsy	6(20.69)	12(40)	0.14
Eye closed but response to voice	0(0.00)	1(3.33)	
Complication			
Nausea	10(34.48)	19(63.33)	0.03
Vomiting	5(17.24)	15(50)	0.008
Infant' Apgar score			
1 min	8.93 ± 0.26	8.83 ± 0.53	0.37
5 min	10 ± 0.00	10 ± 0.00	1

Table 2- Overall effective analgesia within 2 hours of delivery

Satisfaction	Group D	Group P	P- value
Excellent	9(31.03)	7(23.33)	
Very good	11(37.93)	7(23.33)	
good	8(27.59)	12(40)	0.18
Fair	1(3.45)	4(13.33)	

Table 3- Evaluation of VAS score in Two groups by repeated measurement ANOVA

VAS score	Group D	Group P
Baseline	4.73 ± 2.01	6.80 ± 2.23
30	4.53 ± 1.74	5.92 ± 2.22
60	5.29 ± 1.90	6.48 ± 2.01
90	5.94 ± 1.71	6.60 ± 2.36
120	6.94 ± 2.14	6.92 ± 2.40
Estimation score in 30-120	6.37 (5.57-7.18)	6.01 (5.35-6.66)

References

1. Lowe NK. The nature of labor pain. *Am J Obstet Gynecol.* 2002; 186(5 Suppl Nature):S16-24.
2. Brownridge P. The nature and consequences of childbirth pain. *Eur J Obstet Gynecol Reprod Biol* 1995; 59 Suppl: S9-15.
3. Goetzl LM; ACOG Committee on Practice Bulletins-Obstetrics. ACOG Practice Bulletin. Clinical Management Guidelines for Obstetrician-Gynecologists Number 36, July 2002. Obstetric analgesia and anesthesia. *Obstet Gynecol.* 2002; 100(1):177-91.
4. Jones L, Othman M, Dowswell T, Alfirevic Z, Gates S, Newburn M, et al. Pain management for women in labour: an overview of systematic reviews. *Cochrane Database Syst Rev.* 2012; 3:CD009234.
5. Ullman R, Smith LA, Burns E, Mori R, Dowswell T. Parenteral opioids for maternal pain relief in labour. *Cochrane Database Syst Rev.* 2010; (9):CD007396.
6. Ondansetron versus metoclopramide, both combined with dexamethasone, in the prevention of cisplatin-induced delayed emesis. The Italian Group for Antiemetic Research. *J Clin Oncol.* 1997; 15(1):124-30.
7. Akkaya A, Yildiz I, Tekelioglu UY, Demirhan A, Bayir H, Ozlu T, et al. Dexamethasone added to levobupivacaine in ultrasound-guided transversus abdominis plain block increased the duration of postoperative analgesia after caesarean section: a randomized, double blind, controlled trial. *Eur Rev Med Pharmacol Sci.* 2014;

- 18(5):717-22.
8. Fulcher PH Jr, Granese M, Chun Y, Welch CA, Seybold DJ, Randall G, et al. Intraoperative utilization of dexamethasone/bupivacaine/gentamicin solution in laparoscopic assisted vaginal hysterectomy and pain management. *W V Med J*. 2014; 110(1):10-5.
 9. Ryu JH, Chang JE, Kim HR, Hwang JW, Oh AY, Do SH. Ramosetron vs. ramosetron plus dexamethasone for the prevention of postoperative nausea and vomiting (PONV) after laparoscopic cholecystectomy: prospective, randomized, and double-blind study. *Int J Surg*. 2013; 11(2):183-7.
 10. Allen TK, Jones CA, Habib AS. Dexamethasone for the prophylaxis of postoperative nausea and vomiting associated with neuraxial morphine administration: a systematic review and meta-analysis. *Anesth Analg*. 2012; 114(4):813-22.
 11. Gan TJ, Meyer T, Apfel CC, Chung F, Davis PJ, Eubanks S, et al. Consensus guidelines for managing postoperative nausea and vomiting. *Anesth Analg*. 2003; 97(1):62-71.
 12. Wang JJ, Ho ST, Uen YH, Lin MT, Chen KT, Huang JC, et al. Small-dose dexamethasone reduces nausea and vomiting after laparoscopic cholecystectomy: a comparison of tropisetron with saline. *Anesth Analg*. 2002; 95(1):229-32.
 13. Fuji Y, Nakayama M. Dexamethasone for reduction of nausea and vomiting and analgesic use after gynecological laparoscopic surgery. *Int J Gynaecol Obstet*. 2008; 100(1):27-30.
 14. Thomas R, Jones N. Dexamethasone reduces nausea and vomiting after laparoscopy. *Br J Anaesth*. 2000; 85(2):328-9.
 15. Henzi I, Bernard W, Tramer MR. Dexamethasone for the Prevention of Postoperative Nausea and Vomiting: A Quantitative Systematic Review. *Anesth Analg*. 2000; 90(1):186-94.
 16. Golembiewski JI, Chernin E, Chopra T. Prevention and treatment of postoperative nausea and vomiting. *Am J Health Syst Pharm*. 2005; 62(12):1247-60.
 17. Liu K, Hsu CC, Chia YY. The Effective Dose of Dexamethasone for Antiemesis after Major Gynecological Surgery. *Anesth Analg*. 1999; 89(5):1316-8.
 18. Basch E, Prestrud AA, Hesketh PJ, Kris MG, Feyer PC, Somerfield MR, et al. Antiemetics: American Society of Clinical Oncology clinical practice guideline update. *J Clin Oncol*. 2011; 29(31):4189-98.
 19. Tanihata S, Oda S, Nakai S, Uchiyama T. Antiemetic effect of dexamethasone on cisplatin-induced early and delayed emesis in the pigeon. *Eur J Pharmacol*. 2004; 484(2-3):311-21.
 20. Ho CM, Ho ST, Wang JJ, Tsai SK, Chai CY. Dexamethasone has a central antiemetic mechanism in decerebrated cats. *Anesth Analg*. 2004; 99(3):734-9.
 21. Suzuki T, Sugimoto M, Koyama H, Mashimo T, Uchida I. Inhibitory effects of glucocorticoids on human-cloned 5-hydroxytryptamine_{3A} receptor expressed in *Xenopus* oocytes. *Anesthesiology*. 2004; 101(3):660-5.
 22. Asgari Z, Mozafar-Jalali S, Faridi-Tazehkand N, Sabet S. Intraperitoneal Dexamethasone as a new method for relieving postoperative pain after gynecologic laparoscopy. *Int J Fertil Steril*. 2012; 6(1):59-64.
 23. Holte K, Kehlet H. Perioperative single-dose glucocorticoid administration: pathophysiologic effects and clinical implications. *J Am Coll Surg*. 2002; 195(5):694-712.
 24. Salerno A, Hermann R. Efficacy and safety of steroid use for postoperative pain relief. Update and review of the medical literature. *J Bone Joint Surg Am*. 2006; 88(6):1361-72.
 25. Bisgaard T, Klarskov B, Kehket H, Rosenberg J. Preoperative dexamethasone improves surgical outcome after laparoscopic cholecystectomy: a randomized, double-blind placebo-controlled trial. *Ann Surg*. 2003; 238(5):651-60.
 26. Karst M1, Kegel T, Lukas A, Lüdemann W, Hussein S, Piepenbrock S. Effect of celecoxib and dexamethasone on postoperative pain after lumbar disc surgery. *Neurosurgery*. 2003; 53(2):331-6.
 27. Aminmansour B, Khalili HA, Ahmadi J, Nourian M. Effect of high-dose intravenous dexamethasone on postlumbar discectomy pain. *Spine (Phila Pa 1976)*. 2006; 31(21):2415-7.
 28. Kim MS, Coté CJ, Cristoloveanu C, Roth AG, Vornov P, Jennings MA, et al. There is no dose-escalation response to dexamethasone (0.0625-1.0 mg/kg) in pediatric tonsillectomy or adenotonsillectomy patients for preventing vomiting, reducing pain, shortening time to first liquid intake, or the incidence of voice change. *Anesth Analg*. 2007; 104(5):1052-8.
 29. Waldron NH, Jones CA, Gan TJ, Allen TK, Habib AS. Impact of perioperative dexamethasone on postoperative analgesia and side-effects: systematic review and meta-analysis. *Br J Anaesth*. 2013; 110(2):191-200.