



RESEARCH ARTICLE

ADMINISTRATION OF DEXAMETHASONE FOR NAUSEA AND VOMIT PROPHYLAXIS POSTOPERATIVE IN PATIENTS WITH GESTATIONAL DIABETES

Jesús Ricardo Canseco Nieto*, Jaquelina Martínez Sotomayor-Melero, Juan Manuel Colunga.Matta, Belia Inés Garduño-Chávez and Norma Guadalupe Lopez Cabrera

Department of Anesthesiology, University Hospital "Dr. José Eleuterio González", Universidad Autonoma de Nuevo Leon (U.A.N.L.), Monterrey, Nuevo Leon, Mexico

ARTICLE INFO

Article History:

Received 20th October, 2020

Received in revised form

28th November, 2020

Accepted 14th December, 2020

Published online 30th January, 2021

Keywords:

Dexamethasone, Prophylaxis, Nausea, Vomiting, Gestational Diabetes.

ABSTRACT

Introduction: Postoperative nausea and vomiting of one of the most frequent adverse effects in the postoperative period, with an incidence of up to 70%. Dexamethasone administered alone or in combination with other antiemetics is effective as a prophylaxis for postoperative nausea and vomiting. **Material and Methods:** It is a prospective, observational, cross-sectional, descriptive study conducted in 48 female patients, sometimes an elective cesarean section with diagnosis of gestational diabetes that meet the selection criteria. **Results:** 48 women of 27.9 ± 6.0 years with a diagnosis of gestational diabetes who sometimes went to cesarean delivery were included. A case of nausea was reported at baseline measurement (2.1%), however, the incidence of nausea, vomiting and a second antiemetic requirement was 0%. Insulin administration was required in 4 patients, 1 (2.1%) at recovery, 2 (4.2%) at 4 hours and 1 (2.1%) at 24 hours. **Conclusions:** In our study we were able to completely prevent the incidence of nausea and vomiting by co-administering it with metoclorpramide. Both are drugs of low cost and with greater accessibility than 5HT-3 antagonists, so it can be a useful alternative in practice for the prevention of nausea and vomiting.

INTRODUCTION

Postoperative nausea and vomiting (PONV) is one of the most frequent adverse effects in the postoperative period, with an incidence of up to 70% (1). It is considered one of the most unpleasant experiences, it can also result in surgical complications and prolong the stay in the recovery unit, increasing costs (1). There are different risk factors for PONV, among which are: female gender, history of motion sickness or nausea and persistent vomiting, non-smoking status, history of gynecological or laparoscopic surgery and the use of opioids after Surgery. There are different drugs to prevent postoperative nausea and vomiting. The first choice drug must be the safest and the most economical. Dexamethasone is a glucocorticoid with almost no mineralocorticoid activity, which has a variety of uses in medicine, and its use may be useful in patients with acute exacerbations of multiple sclerosis, allergies, cerebral edema, inflammation and shock, as well as in conditions of hypersensitivity and neoplasms. In addition, it can be useful for the assessment of Cushing's syndrome (2). Dexamethasone administered alone or in combination with other antiemetic is effective as a prophylaxis for postoperative nausea and vomiting (1, 3).

Its mechanism of action is not known, but it is believed that it may be through prostaglandin antagonism or decreased intestinal serotonin. Its use in the perioperative environment derives from the observation of its effectiveness as prophylaxis for chemotherapy emesis. Its low cost and the lack of important adverse effects make it an attractive option for the management of postoperative nausea and vomiting. The study hypothesis was to show that the use of dexamethasone at dose for prophylaxis of nausea and postoperative vomiting is related to a blood glucose level does not put the patient with gestational diabetes at risk. The objective of this study was to record the level of blood glucose caused by dexamethasone and assess its effectiveness with the cost-benefit for the patient.

MATERIALS AND METHODS

It is a prospective, observational, cross-sectional, descriptive study. It was performed in the operating rooms of the University Hospital "Dr. José Eleuterio González" in female patients undergoing elective caesarean section with diagnosis of gestational diabetes that meet the selection criteria. The present study was submitted for evaluation before the ethics committee. After correct identification of the patient to be operated, during the pre-anesthetic assessment, the patient was discussed explaining in detail the anesthetic procedure to be performed (continuous epidural block) and the medication that was used, emphasis will be placed on the risks and benefits of the procedure.

*Corresponding author: Jesús Ricardo Canseco Nieto, Department of Anesthesiology, University Hospital "Dr. José Eleuterio González", Universidad Autonoma de Nuevo Leon (U.A.N.L.), Monterrey, Nuevo Leon, Mexico.

The inclusion criteria that were integrated in this study were: Female patients between 18-50 years of age, patients ASA I, ASA II, ASA III, patients who signed the informed consent of anesthesia, patients diagnosed with gestational diabetes, patients who underwent caesarean section. The exclusion criteria taken into account were: ASA > IV patients, minor patients, emergency caesarean sections, refusal of informed consent, patients allergic to drugs. The elimination criteria integrated in this study were: incomplete clinical record, refusal to participate, patients who needed another medication to treat PONV.

The description of the design of this study consisted of starting a preoperative evaluation and then verifying that the patients had an 8-hour fast and that they had an intravenous route, after that they were admitted to the operating room where the patient was monitored and performed Non-invasive blood pressure, heart rate and pulse oximetry. The procedure that was performed for the purpose of the investigation is the capillary glucometry taking and recording the figure. Pre-anesthetic medication was administered: cephalothin 1gr, ranitidine 50mg, metoclopramide 10mg, dexamethasone 8mg in a 500 ml Hartmann, during the surgical procedure the liquid plans were Hartmann solution, then new glucometry was performed in recovery and every 4 hours until 24 hours. The liquid plan for oxytocin was prepared at Hartmann. Finally, the presence of PONV in the recovery area was assessed and recorded in the data record sheet.

In the descriptive statistics, the qualitative variables were presented using frequencies and percentages, while for the quantitative variables, mean and standard and median deviation and corresponding range were used. The normality of the distribution of the data was evaluated with the Kolmogorov-Smirnov test and depending on the result it was decided to use parametric tests or their non-parametric equivalent. In the analysis of qualitative variables, the Chi-square test or Fisher's exact test was used in the case of independent groups. For quantitative variables, they were evaluated with T student from independent samples for parametric distribution and Mann Whitney U test for non-parametric distribution. A value of $p < 0.05$ was taken as statistically significant. SPSS version 24 was used to perform the statistical analysis.

RESULTS

48 enrolled patients were approved to participate in dexamethasone treatment as prophylaxis of nausea and postoperative vomiting in pregnant patients with gestational diabetes. This study included patients with an average age of 27.9 ± 6.0 years and diagnosis of gestational diabetes who underwent caesarean section. Table 1 presents the sociodemographic and clinical data of the patients. The patients had a history of 3 (1-4) deeds and 12 (25%) were in their first pregnancy. The diagnosis of gestational diabetes was made in the second trimester in 16 (33.3%) patients, and in the third in the rest (66.7%). Caesarean section was performed at 38.4 ± 1.8 weeks gestation, and upon administration of dexamethasone, they had 10 (8-12) hours of fasting. During the procedure, a median of 1200 (1000-1500) ml was administered. Regarding the glucometers that were performed, we found a significant difference in the measurement of glucose at recovery (100.3 ± 9 mg / dL) and at 4 hours (96.4 ± 19.5 mg / dL) with respect to baseline measurement ($86.0 \pm$

12.9 mg / dL) ($P = 0.002$, table 1), however we found no differences in the rest of the measurements, and a plateau is established after 8 hours similar to the baseline measurements ($P > 0.05$, figure 1). A case of nausea was reported at baseline measurement (2.1%), however, the incidence of nausea, vomiting and a second antiemetic requirement was 0%. Insulin administration was required in 4 patients, 1 (2.1%) at recovery, 2 (4.2%) at 4 hours and 1 (2.1%) at 24 hours (Table 2).

Table 1. Sociodemographic and clinical data of the patients

| Variable | . |
|------------------------------|--------------------|
| Age (years)* | 27.9 ± 6.0 |
| Number of pregnancies** | 3 (1-4) |
| Diagnostic quarter n (%) | |
| Second | 16 (33.3%) |
| Third | 32 (66.7%) |
| Gestation weeks* | 38.4 ± 1.8 |
| Fasting hours** | 10 (8-12) |
| Transoperative fluids (ml)** | 1200 (1000-1500) |
| Product gender n (%) | |
| Male | 26 (54.2%) |
| Female | 22 (45.8%) |
| Product weight (g)** | 3229.8 ± 516.4 |

* Data reported in mean \pm standard deviation.

** Data reported in median (interquartile range).

Table 2. Glucose values in each measurement

| Variable | Glucosa |
|----------|--------------------|
| Basal | 86.0 ± 12.9 |
| Recovery | $100.3 \pm 25.9^*$ |
| 4h | $96.4 \pm 19.5^*$ |
| 8h | 92.8 ± 17.0 |
| 12h | 90.7 ± 14.1 |
| 24h | 91.0 ± 15.1 |

* $P = 0.002$ with respect to baseline measurement

DISCUSSION

In our study we found that the incidence of postoperative nausea and vomiting in women with gestational diabetes was nil. Regarding glucose levels by glucometers, there was a statistically significant increase of baseline 86.0 ± 12.9 mg / dL at 100.3 ± 9.0 mg / dL at recovery ($P = 0.002$) and 96.4 ± 19.5 mg / dL at 4 hours ($P = 0.002$). In addition, the insulin infusion requirement was presented in 4 (8.4%) patients, of which 3 (75%) were presented in the first 4 hours after surgery. The use of dexamethasone is effective for the prevention of nausea and vomiting associated with chemotherapy (4, 5). It has also been reported that it is effective for the prevention of postoperative nausea and vomiting in operative patients due to thyroidectomy, tonsillectomy, hysterectomy and cholecystectomy (6-10).

In addition, it has been found that it can prevent the presence of nausea and vomiting associated with epidural morphine in patients who are operated by abdominal hysterectomy (9) and in patients receiving epidural morphine after cesarean delivery (11). The mechanism by which dexamethasone exerts its antiemetic effect is unknown, however it is believed that they can act through its anti-inflammatory effect, through direct action in the nucleus of the solitary tract, through interaction with the serotonin and tachykinin receptor proteins NK1 and NK2, alpha-adrenaline, among others; through the maintenance of normal physiological function throughout the body; regulating the hypothalamic-pituitary-adrenal chief; and reducing pain and concomitant use of opioids, which prevents nausea and vomiting secondary to opioids (12).

Table 3. Incidence of important outcomes to evaluate in the intervention

| Variable | Basal | Recovery | 4h | 8h | 12h | 24h |
|------------------|----------|----------|----------|--------|--------|----------|
| Nausea | 1 (2.1%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| Vomiting | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| Other antiemetic | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| Insulin | 0 (0%) | 1 (2.1%) | 2 (4.2%) | 0 (0%) | 0 (0%) | 1 (2.1%) |

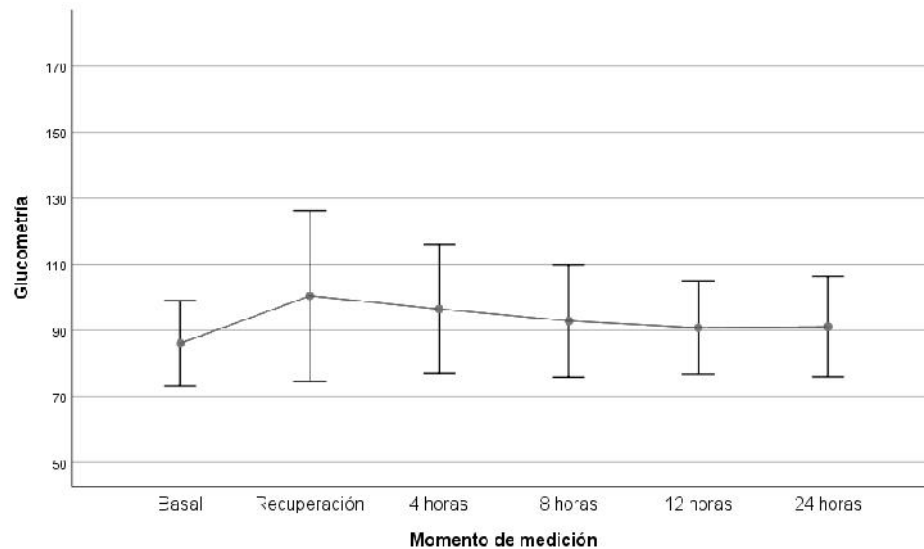


Figure 1. Monitoring of glucometers in patients before and after dexamethasone intervention

In addition, glucocorticoid receptors have been found in the nucleus of rafe and the area of the latter (13), which together with the nucleus of the solitary tract, are known to have significant neuronal activity in the regulation of nausea and vomiting (14, 15). The guidelines of the Society for Outpatient Anesthesia 2014 recommend the use of 4-5 mg of dexamethasone for induction of anesthesia due to its antiemetic properties (16), and although it has been seen that there is no significant difference between giving 4- 5 mg versus 8-10 mg (17), it has been reported that they can be used to save opioid use and improve pain scores (18), which may be related to a decreased risk of nausea and vomiting.

The disadvantage that has been described about the use of dexamethasone is the increase in plasma glucose in diabetic and non-diabetic patients receiving dexamethasone on induction (3, 19, 20). One of the fears of hyperglycemia is a negative outcome in severe cases associated with increased risk of surgical wound infections and poor wound healing, as well as increased morbidity and mortality associated with cardiac and neurological surgeries (13-21). A study was conducted to evaluate the effect of doses of 4 and 8-10 mg of dexamethasone on postoperative glycemia in diabetic patients, and found a significant increase in blood glucose of 9 mg / dL when using 8-10 mg dose compared with 4 mg in the post-anesthesia care unit, and 25 mg / dL in the first 24 hours (24).

In our study, when using a single dose of 8 mg at induction, we found an increase of 14.3 mg / dL and 10.4 mg / dL of glucose during recovery and at 4 hours, respectively, with respect to baseline levels, and subsequently a plateau similar to baseline levels was established after 4 hours. Despite the reported increases, its clinical significance is questioned, given that we only found that 3 patients had levels > 130 mg / dL during their recovery, and 2 patients at 4 hours. Dexamethasone is a well tolerated glucocorticoid. Despite the existing risk of hyperglycemia and the precautions to be taken when using dexamethasone as prophylaxis for nausea and postoperative

vomiting, no significantly different degrees of hyperglycemia have been found between diabetic and non-diabetic patients, so it can be inferred that the hyperglycemic response is not exaggerated in diabetic patients (19,25,26). The use of 4 mg as a prophylaxis for postoperative nausea and vomiting has been suggested, however, in our study using 8 mg we found no significant long-term differences with respect to baseline levels. The use of dexamethasone could be a safe medication in those patients who have had adequate prior glycemic control, however, studies are needed to confirm this. There are other adverse effects that should be considered is insomnia, acne, gastrointestinal symptoms, increased appetite, and even the existence of nausea and vomiting has been reported after use (27).

Conclusion

In our study we were able to completely prevent the incidence of nausea and vomiting by co-administering it with methochlorpramide. Both are low-cost medications with greater accessibility than 5HT-3 antagonists, so it can be a useful alternative in practice for the prevention of nausea and vomiting.

REFERENCES

- Hernán RM, Mauricio EI, Verónica FM. Controlled trial of dexamethasone compared with droperidol and ondansetron for the treatment of postoperative nausea and vomiting. *Rev Med Chile* 2006; 697-702.
- Johnson DB, Kelley B. Dexamethasone. NCBI 2019. <https://www.ncbi.nlm.nih.gov/books/NBK482130/>.
- Nazar CE, Lacassie HJ, Lopez RA, Munoz HR. Dexamethasone for postoperative nausea and vomiting prophylaxis: effect on glycaemia in obese patients with impaired glucose tolerance. *European Journal of Anaesthesiology* 2009; 26:318-321.

4. Italian Group for Antiemetic Research. Dexamethasone, granisetron, or both for prevention of nausea and vomiting during chemotherapy for cancer. *New England Journal of Medicine* 1995; 332:1-5.
5. Italian Group for Antiemetic Research. Ondansetron versus metoclopramide, both combined with dexamethasone in the prevention of cisplatin-induced delayed emesis. *Journal of Clinical Oncology* 1997; 15:124-30.
6. Wang JJ, Ho ST, Liu YH, Ho CM, Liu K, Chia YY. Dexamethasone decreases epidural morphine-related nausea and vomiting. *Anesthesia & Analgesia* 1999; 89:117-120.
7. Splinter, RM, and DJ Roberts. "Prophylaxis for vomiting by children after tonsillectomy: dexamethasone versus perphenazine." *Anesthesia & Analgesia* 1997; 85:534-7.
8. Splinter WM, Robert DJ. Dexamethasone decreases vomiting by children after tonsillectomy. *Anesthesia & Analgesia* 1996; 83:913-916.
9. Wang JJ, Ho ST, Lee SC, Liu YC, Liu YH, Liao YC. The prophylactic effect of dexamethasone on postoperative nausea and vomiting in women undergoing thyroidectomy: a comparison of droperidol with saline. *Anesthesia & Analgesia* 1999; 89:200-203.
10. Fujii Y, Tanaka H, Toyooka H. The effects of dexamethasone on antiemetics in female patients undergoing gynecologic surgery. *Anesthesia & Analgesia* 1997; 85:913-917.
11. Tzeng JI, Wang JJ, Ho ST, Tang CS, Liu YC, Lee SC. Dexamethasone for prophylaxis of nausea and vomiting after epidural morphine for post-Caesarean section analgesia: comparison of droperidol and saline. *British Journal of Anaesthesia* 2000; 85:865-868.
12. Chu CC, Hsing CH, Shieh JC, Chien CC, Ho CM, Wang JJ. The cellular mechanisms of the antiemetic action of dexamethasone and related glucocorticoids against vomiting. *European Journal of Pharmacology* 2014; 722:48-54.
13. Marimoto M, Morita N, Ozawa H, Yokoyama K, Kawata M. Distribution of glucocorticoid receptor immunoreactivity and mRNA in the rat brain: an immunohistochemical and in situ hybridization study. *Neuroscience Research* 1996; 26:235-269.
14. Chaney MA. Side effects of intrathecal and epidural opioids. *Canadian Journal of Anaesthesia* 1995; 42:891-903.
15. Watcha MF, White PF. Postoperative nausea and vomiting. Its etiology, treatment and prevention. *Anesthesiology* 1992; 77:162-184.
16. Gan TJ, Diemunsch P, Habib AS, Kovac A, Kranke P, Meyer TA. Consensus guidelines for the management of postoperative nausea and vomiting. *Anaesthesia & Analgesia* 2014; 118:85-113.
17. De Oliveira GS, Castro-Alves LJ, Ahmad S, Kendall MC, McCarthy RJ. Dexamethasone to prevent postoperative nausea and vomiting: an updated meta-analysis of randomized controlled trials. *Anaesthesia & Analgesia* 2013; 116:58-74.
18. De Oliveira GS, Almeida MD, Benzon HT, McCarthy RJ. Perioperative single dose systemic dexamethasone for postoperative pain: a meta-analysis of randomized controlled trials. *Anesthesiology* 2011; 115:575-588.
19. Hans P, Vanthyne A, Dewandre PY, Brichant JF, Bonhomme V. Blood glucose concentration profile after 10 mg dexamethasone in non-diabetic and type 2 diabetic patients undergoing abdominal surgery. *British Journal of Anaesthesia* 2006; 97:164-170.
20. Abdelmannan D, Tahboub R, Genuth S, Ismail-Beigi F. Effect of dexamethasone on oral glucose tolerance in healthy adults. *Endocrinology Practice* 2016; 16:770-777.
21. Lipshutz AK, Gropper MA. Perioperative glycemic control: an evidence-based review. *Anesthesiology* 2009; 110:408-21.
22. Atkins JH, Smith DS. A review of perioperative glucose control in the neurosurgical population. *Journal of Diabetes Science and Technology* 2009; 3:1352-1364.
23. Smith DK, Bowen J, Bucher L, Hawkins T, Jurkowitz C, Reed J. A study of perioperative hyperglycemia in patients with diabetes having colon, spine, and joint surgery. *Journal of Perianesthesia Nursing* 2009; 24:362-369.
24. Low Y, White WD, Habib AS. Postoperative hyperglycemia after 4- vs 8-10-mg dexamethasone for postoperative nausea and vomiting prophylaxis in patients with type II diabetes mellitus: a retrospective database analysis. *Journal of Clinical Anesthesia* 2015; 589:589-594.
25. Murphy GS, Szokol JW, Avram MJ, Greenberg SB, Shear T, Vender JS. The effect of single low-dose dexamethasone on blood glucose concentrations in the perioperative period: a randomized, placebo-controlled investigation in gynecologic surgical patients. *Anesthesia & Analgesia* 2014; 118:1204-1212.
26. Nazar, Echevarría, Lacassie, Flores, Muñoz. Effects on blood glucose of prophylactic dexamethasone for postoperative nausea and vomiting in diabetics and non-diabetics. *Revista Médica de Chile* 2011; 755-61.
27. Matheson EC, et al. Glucocorticoids and selumetinib are highly synergistic in RAS pathway-mutated childhood acute lymphoblastic leukemia through upregulation of BIM. *Haematologica* 2019; 104(9):1804-1811.
