

Hyperglycemic Response of Non-diabetic Women Undergoing Abdominal Hysterectomy Who Have Received Prophylactic Dexamethasone to Alleviate Nausea and Vomiting

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ARTICLE INFO

Article history:

Received 02 August 2020

Revised 24 August 2020

Accepted 09 September 2020

Keywords:

Abdominal hysterectomy;

Dexamethasone;

Nausea and vomiting;

Blood sugar

ABSTRACT

Background: This study has been designed to assess the hyperglycemic response in non-diabetic patients in women undergoing abdominal hysterectomy; who have received a prophylactic dose of dexamethasone to alleviate post-operative nausea and vomiting (PONV).

Methods: This was a double blind randomized clinical trial involving seventy women who were candidates for abdominal hysterectomy. The women were randomly assigned into two groups. Group A received 8mgs (in 50 mls normal saline) of IV dexamethasone; post-anesthetic induction and pre-surgery. Group B received 50 mls of normal saline post-anesthetic induction and pre-surgery. Patients were asked whether they had any nausea and vomiting during recovery. The patients' blood sugar (BS) levels were assessed before surgery, during recovery and then 1, 6, 12, 18, and 24 hours after surgery.

Results: Thirty-three women in each group were monitored. Assessment of the results indicates that nausea and vomiting were not significantly different between the two groups. The age and BS before surgery of the patients were not significantly different. BS levels after surgery were significantly higher for the group receiving dexamethasone; with the exception of the levels during the first hour.

Conclusion: The BS of women undergoing abdominal hysterectomy is significantly higher for those receiving a single dose of dexamethasone, post-operatively, compared to patients receiving a placebo. The finding of this study does not support the role of dexamethasone in the prophylactic anti-emetic treatment in abdominal hysterectomy.

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Following surgery involving general anesthesia, patients can unfortunately suffer from post-operative nausea and vomiting (PONV) [1]. For those who do, it can result in a longer hospital stay and complications including an increased morbidity due to aspiration, incision site dehiscence, haematoma formation, electrolyte imbalance, dehydration and an inability to take oral medications [2-3].

PONV is suffered by 20-30% of patients; though this could be as high as 70-80% for high-risk cases [3,6]. After pain management, controlling PONV for patients is the most challenging issue for surgeons and anesthesiologists. It is a multi-factorial problem with a complex pathophysiology. The medical condition and history of the patient will affect PONV. It is more likely

The authors declare no conflicts of interest.

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to occur during prolonged surgeries and when general anesthesia is used [3-5].

Different medications such as butyrophenones, benzamides, histamine receptor antagonists and 5-HT₃ (5-hydroxy tryptamine-3) receptor antagonists are used to treat PONV [7]. In current anaesthesiology practice, dexamethasone and 5-hydroxy tryptamine-3 receptor antagonist are the most often used medications to treat PONV [8].

Dexamethasone is a long-acting glucocorticoid with a half-life of between 36 and 72 hrs. It is a low cost drug which is readily available and easy to administer [7]. The exact mechanism is unclear but it can affect serotonin (5-HT₃) receptors, which are present in the nucleus tractus solitarius, and by inhibiting prostaglandins synthesis [9-10].

There are complications with the use of prophylactic dexamethasone as an anti-emetic. These include hyperglycemia and wound infection [6]. Its use in diabetic and obese patients has been studied and it is relatively contraindicated in unstable diabetic patients [10]. This study looks at the benefits and risks of giving dexamethasone prophylaxis for PONV in non-diabetic patients.

Methods

This was a double-blind randomized clinical trial which was conducted in Yas Hospital, which is affiliated with Tehran University of Medical Sciences, between December 2019 and April 2020.

Inclusion criteria were non-diabetic women aged between 30 and 65 years who due to undergo an abdominal hysterectomy. Excluded were those with an allergy to corticosteroids, who had received an anti-emetic in the previous 24 hr. period prior to surgery, who had suffered from motion sickness, had OCP consumption or a history of smoking.

The study protocol was approved by the Ethics Committee of Tehran University of Medical Sciences (IR.TUMS.MEDICINE.REC.1398.658) and was registered in the Iranian Registry of Clinical Trials (IRCT20120624010102N3).

Seventy women were randomly assigned to the intervention or control group: All gave informed consent. A specialist nurse undertook the randomization using block randomisation. Each block contained four letters. Standard procedures and monitoring were undertaken and adhered to. To ensure the highest levels of patient safety, all patients included in the trial were injected with 4mg ondansetron 30 minutes before the end of surgery.

Anesthetic guidelines and codes of practice were followed at all times. Anaesthetic induction was

undertaken using 0.05mg/kg midazolam, 2microgr/kg fentanyl, 2-2.5 mg/kg propofol, and 0.1 mg/kg cisatracurium. Patients were intubated with an endotracheal tube. Anaesthesia was maintained using a propofol infusion 0.1-0.2 mg/kg/ min and the continuous infusion of remifentanyl to both groups. The study group received 8 mgs of dexamethasone in 50 mls of normal saline via an intravenous injection. This was administered over 10 minutes after anesthetic induction and before surgery.

In the control group, 50 mls of normal saline was injected via intravenous injection over a 10 minute period after anesthetic induction and before surgery. At the end of surgery, 0.05 mg/kg neostigmine and 0.25 mg/kg of atropine were injected to reverse the neuromuscular blockade. Patients were asked about whether they were suffering from nausea and vomiting during recovery. This was recorded using a 4 point scoring system; where Score 0: No nausea or vomiting, Score 1: Nausea only, Score 2: Retching or vomiting, Score 3: Vomiting more than once. If the patient had both nausea and vomiting at the same time, the highest score was recorded.

Oral ibuprofen (400 mgs) was administered every 6 hours to treat postoperative pain. If patients could not tolerate oral medication or ibuprofen, ketorolac 15 mgs was injected intravenously every 8 hours. Following patient's choice, if the women requested an additional opioid to control their pain, 3mgs of intravenous morphine sulfate was injected. BS was assessed prior to surgery, during recovery and then 1, 6, 12, 18, and 24 hrs. post-surgery.

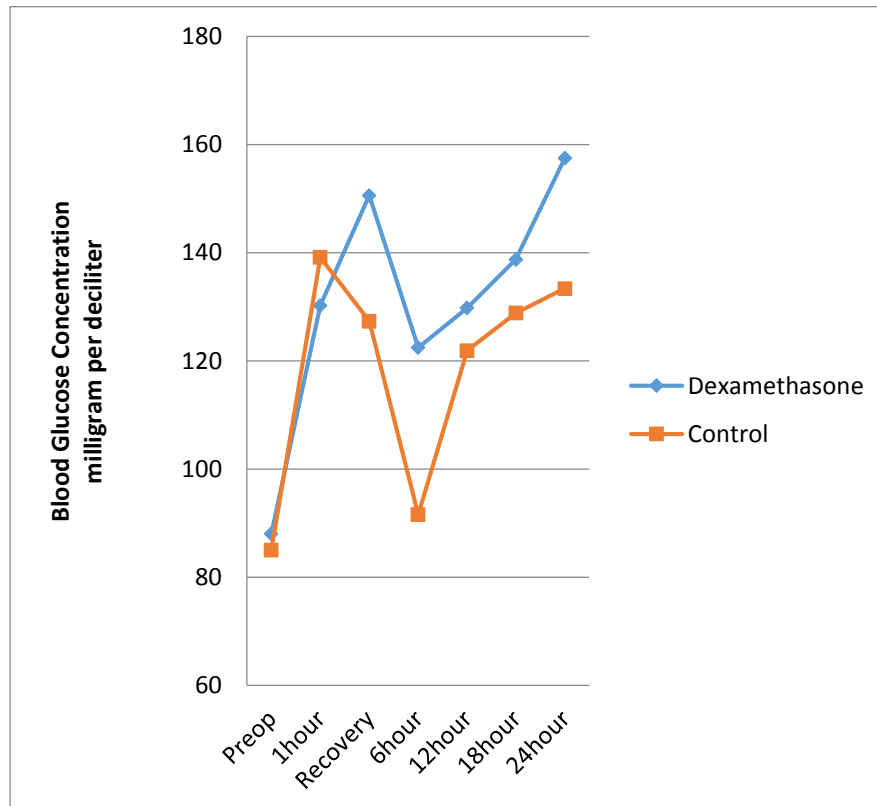
Data analysis was undertaken using SPSS software version 22 (SPSS Inc., Chicago, IL, USA). The information was presented as a Mean \pm SD with trends and categorical variables identified. Independent sample t-test and Fisher exact tests were used for comparison between quantitative and qualitative variables. A p-value of less than 0.05 was considered significant.

Results

Seventy women who were identified as patients requiring abdominal hysterectomy and who were non-diabetic were randomly assigned to an intervention or control group. Two patients from each group withdrew before the end of the study. The age of and BS before surgery of the women were not significantly different (Table 1). The BS levels post-surgery were significantly higher in the intervention group ($P < 0.01$); with the exception of first hour (Table 1) (Figure 1). There was no significant difference in how much nausea and vomiting the women in both groups experienced (Table 1).

Table 1- Laboratory findings and nausea/ vomiting between two groups

| | Intervention group N=33 | Control group N=33 | P value |
|---------------------------|----------------------------|-----------------------|---------|
| Age (mean \pm sd)(year) | 49.2 \pm 6.7 | 50 \pm 5.7 | 0.5 |
| BS before surgery | 88 \pm 9.6 | 85 \pm 9.4 | 0.2 |
| BS 1 h after surgery | 130.2 \pm 23.4 | 139.1 \pm 16.1 | 0.07 |
| BS at recovery | 150.5 \pm 19.6 | 127.3 \pm 9.1 | 0.001 |
| BS 6 h after surgery | 122.4 \pm 15.5 | 91.5 \pm 15.2 | 0.001 |
| BS 12 h after surgery | 129.7 \pm 20 | 21.8 \pm 14.1 | 0.03 |
| BS 18 h after surgery | 138.7 \pm 18.6 | 128.8 \pm 17.3 | 0.02 |
| BS 24 h after surgery | 157.4 \pm 19.3 | 133.3 \pm 12.5 | 0.001 |
| Nausea after surgery | 7(21.2%) | 3(9.1%) | 0.1 |
| Vomiting after surgery | 4(12.1%) | 3(9.1%) | 0.6 |

Figure 1- Blood glucose changes between two groups.

Discussion

This study showed that a single dose of dexamethasone before an abdominal hysterectomy may increase blood sugar significantly post-surgery. This could cause a significant risk to health for women who were diabetic. It

was shown that prophylactic dexamethasone did not reduce PONV experienced by patients. Dexamethasone has been used pre-operatively to control pain and nausea and vomiting as it is cost effective and readily available. Many studies have shown that a single dose of dexamethasone may cause short-lasting hyperglycemia, [10-12]. This study concurs.

Nazar et al showed that the administration of 8 mgs of dexamethasone at the start of laparoscopic surgery, in patients with impaired glucose tolerance, caused a significant increase in post-operative blood sugar [10]. Herbst et al. demonstrated that, despite the benefits of the dexamethasone in decreasing the length of hospital stay in diabetic and non-diabetic patients, it is associated with the risk of hyperglycemia in both patient groups [11].

Eberhart et al. found that frequent doses of dexamethasone, administered as a prophylactic for nausea and vomiting, could cause short-term hyperglycemia. The study highlighted that further examination into the potential benefit and risk of corticosteroids could be useful [12]. Ahmad et al. assessed 100 patients who underwent thyroidectomy and received a single dose of dexamethasone. They found that the mean pain score was significantly lower in patients who received dexamethasone. The study aligned with this study in concluding that there was no relationship between nausea and vomiting and dexamethasone administration [13].

Murphy et al. undertook a double-blind clinical trial on 122 patients who were undergoing laparoscopic cholecystectomy as an outpatient. The study found that administration of 8 mgs of dexamethasone resulted in an early discharge, lower rates of nausea, fatigue, and pain. It did not significantly effect of vomiting [14]. Thangaswamy et al. randomly assigned 55 women who were candidates for laparoscopic hysterectomy into three groups. The groups were given either saline, 4 mgs dexamethasone or 8 mgs dexamethasone. The study found that pain and PONV was significantly lower in patients who received 8 mgs of dexamethasone [15]. This is in contrast to the results of our study, where we have shown that dexamethasone has no effect on the level of PONV.

Sekhavat et al. assessed one hundred women who were candidates for abdominal hysterectomy. The women were randomly assigned to groups receiving either saline or both 8 mgs of dexamethasone and saline. The results demonstrated a lower rate of PONV [16]. Tzeng et al. administered 5 mgs of dexamethasone pre-operatively and reported a lower rate of nausea and vomiting in the group receiving dexamethasone than the metoclopramide group [17].

Umpierrez et al. showed in-hospital hyperglycemia as an important indicator of poor prognosis and mortality in patients with or without a background of diabetes [18]. By considering the risk-benefit ratio, regular monitoring of BS may be recommended after any dexamethasone administration. In high risk patients, such as diabetic patients or those with impaired glucose tolerance, the administration of dexamethasone should be performed with caution [4].

Conclusion

In women undergoing abdominal hysterectomy who received a single dose of dexamethasone, post-operative blood sugar increased significantly compared with women who had received a placebo. This finding does not support dexamethasone as a prophylactic anti-emetic during abdominal hysterectomy.

Acknowledgments

We would like to thank all the women who voluntarily consented to participate in this study. Any surgery is a traumatic experience and we applaud their strength and compassion in agreeing to be part of this study; which does not improve their care but the experience of other patients of the future. As always, we appreciate the co-operation and professionalism of all the clinical and support service staff, particularly the nurses involved in direct patient care of the women involved in this study, at Yas Hospital.

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