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Effects of Epidural Dexamethasone Versus Intravenous Dexamethasone in Patients Undergoing Hysterectomy

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ABSTRACT

BACKGROUND

Role of steroids as a component of multi-model analgesia is well established. The limiting factor is hyperglycemia,decreased wound healing with high intravenous doses, especially in obese and those with impaired glucose tolerence. We tried to achieve the beneficial effects with smaller epidural dose.

AIM

To compare the hyperglycemic response to dexamethasone used intravenously with a smaller dose used epidurally. Antiemetic and opiod sparing effects are also studied.

MATERIALS AND METHODS

50 patients in each group undergoing total abdominal hystrectomy were randomly allocated to group A receiving 8mg of dexamethasone intravenously and group B receiving 2mg of dexamethasone epidurally. Average postoperative analgesic requirement over 24 hours was found to be 160± 5ml in group A and 164 ±5ml in group B. Clinical investigation revealed that average increase in blood glucose concentrations 4 hours after gynecologic surgery from the baseline were 41 ± 7 mg/dL in group A patients receiving iv dexamethasone and 6 ± 7 mg/dl in group B patients receiving epidural dexamethasone.

RESULTS

Intravenous dexamethasone was found to rise blood sugar significantly while lower epidural dose was found to be equipotent in terms of analgesic sparing effects and reducing PONV.

KEYWORDS Epidural dexamethasone, intravenous dexamethasone, postoperative hyperglycemia

INTRODUCTION

Acute postoperative pain can delay functional recovery for patients undergoing surgical procedures. Multimodal analgesic approaches have been used as an important strategy to mitigate postoperative pain. Opioids are used for both intra and postoperative analgesia but are associated with unwanted side-effects like respiratory depression, nausea and vomiting, itching, increased duration of postoperative ileus, and others.These side effects can be reduced with a reduction in the amount of opioid drugs administered, but this requires the addition of co-analgesic drugs..Dexamethasone is a potent corticosteroid with analgesic, antiemetic & immunomodulating effects. Its antiinflammatory effect contributes to postoperative analgesia. Dexamethasone enhances clinical recovery in by modulating the inflammatory & neuroendocrine stress response induced by surgical stimulus. Preoperative dexamethasone 8 mg reduces nausea, fatigue and pain & enhances the quality of recovery. Recent studies shows that surgical patients who receive dexamethasone 8 mg developed significant increases in blood glucose in 6 to 12 hours postoperatively in normal subjects(1) balanced anaesthesia using propofol, fentanyl, remifentanil, cisatracurium, desflurane in oxygen/air(2) obese(2), in patients with impaired glucose tolerance(2), & type 2 diabetic(3).We, therefore, investigated the analgesic effect,anti emetic effect and postoperative physiological status (–measured as blood sugar, urea and serum creatinine values)of non diabetic patients who received 8 mg of intravenous dexamethasone versus patients who received 2 mg dexamethasone via epidural catheter in patients undergoing hysterectomy.

Methods

Study was conducted at SreeGokulam Medical College & Research Foundation, Trivandrum between 15th October 2014 and 10th April 2015. This randomized double-blind study was approved by the hospital Ethics Committee, American Society of Anesthesiologists (ASA) physical status grade 1& 2non diabetic females in the age groupof 40- 60 years scheduled for total abdominal hysterectomy were enrolled in this study. A written informed content was obtained from each patient. Exclusion criteria was: any contraindication to any study medications ;preoperative use of antiemetic drugs or steroids; preoperative diagnosis of severe renal impairement(serum creatinine >1.6 mg/dL) or liver disease (liver enzymes >2x normal values); Type I or II diabetes(HbA1c >6.5); or ASA physical status I I I and above . abnormal coagulation parameters & thrombocytopenia, systemic/local infections or any other contraindications to subarachnoid or epidural anesthesia were excluded from the research study

50 patients were allocated randomly (block randomization) to 2 groups, group A and group B. All patients were kept nil per oral for 8 hours and received Tab. Alprazolam 0.5mg and Tab. Pantoprazole 40mg on preoperative night and on the day of surgery.

Before initiation, peripheral vascular access was obtained with a 18-gauge (G) intravenous cannula in all patients. All patients received a Standard premedication of 1 mg midazolam. Patient's arterial blood pressures-systolic and diastolic and mean arterial blood pressure were recorded by non invasive methods. Heart rate and rhythm were be monitored by ECG and peripheral oxygen saturation by pulse oxymeter.

All patients undergoing combined spinal epidural anesthesia patients were positioned in right lateral position and under strict asepsis , L2-3 space was identified.After giving local anesthesia with 2%lignocaine 2ml, an 18 guage tuohy's needle was introduced to epidural space, epidural space was confirmed by LOR technique using 3cc air, then epidural catheter was introduced and fixed @9-10cm,ensuring that catheter is 5cm inside and 1st dose was given with 3ml lignocaine 2% with adrenaline 1in 2lakh .LP was done using the midline approach with a 25 guage Quincke needle at the L3-4 intervertebral space. After checking the free cerebrospinal flow, 3ml of 0.5% hyperbaric bupivacaine was injected. A sensory dermatome of at least T6 was judged as an appropriate sensory block level.

Upon block placement,: group A patients received plus 8 mg of intravenous dexamethasone ,while group B received 2 mg dexamethasone via epidural catheter & epidural infusion was started 60min later with bupivacaine0.25% and fentanyl infusion2mcg/ml via epidural catheter Both groups were provided with 4 L/min of oxygen through simple face masks. All monitoring measurements were recorded every 2 minutes for the first 10 minutes after starting anesthesia, and then recorded every 5 minutes. Hypotension with mean blood pressure reduction >20% from baseline and was treated with fluid bolus or IV vasopressors(phenyl ephrine 50 µg IV.) Upon block placement, baseline characteristics, analgesic requirements as well as early intraoperative glucose concentrations was monitored. Postoperative care was standardized. All postoperative variables were obtained by PACU nursing staff who were blinded to the route of dexamethasone administration. A data collection sheet was provided in the Post anesthesia ICU unit to record recovery variables. Postoperative RBS was the primary outcome variables, which were measured using a glucose meter (Accu Chek Performa, CE-0088). Data were collected for research purposes. Treatment with insulin for increased RBS values on formal laboratory testing was at the discretion of the surgeons. Capillary blood samples from finger prick drawn from a warmed upper extremity was used to determine glucose concentrations. In both group A &B intraoperative and 4th hr postoperative glucose concentrations were recorded. Patients in both group A&B were monitered for the presence of nausea or vomiting every 15 minutes & need for rescue antiemetics (ondansetron 4 mg) assessed. Analgesic requirements were monitored by analyzing the total amount of epidural analgesia required, which was titrated according to patient's requirement. VAS scores were obtained by pain PACU nursing staff who were blinded to the route of dexamethasone administration. Any patient with VAS >5 received an additional bolus of 5ml epidural infusion. Preoperative as well as 48th hr postoperative blood urea& serum creatinine were also monitored

Data after collecting were entered into a Microsoft excel worksheet and was analyzed by SPSS statistical package trial version 20.0 Statistical hypothesis was tested using independent sample t test for quantitative variables, and Wilcoxon signed rank test for qualitative variables . P value < 0.05 was considered statistically significant

Results

There were no dropouts, and all patients completed the study. The two groups were comparable for demographic data and baseline variables. No statistical difference was observed between ASA status and baseline hemodynamic variables. Average duration of surgery was also not significantly different between groups.

A clinical observation indicated that in Group A – 9/25 patients developed hypotension and needed vasopressor and Group B – 10/25 patients developed hypotension and required vasopressor. Incidence of PONV was nil in both groups. Average postoperative analgesic requirement over 24 hours was found to be 160± 5ml in group A and 164 ±5ml in group B. Investigations revealed that average increase in GRBS values 4 hours after surgery from the baseline were 41 ± 7 mg/dL in group A patients (receiving 8mg iv dexamethasone) and 6 ± 7 mg/dl in group B patients (receiving epidural 2mg dexamethasone). Average postoperative increase in blood urea was found to be 0.18± 0.007in group A and 0.18 ±0.007 in group B and increase in serum creatinine in group A was 0.001± 0.0001 and in group B 0.001±0.00011.

P value for difference in incidence of post operative hyperglycemia was 0.001

All other variables studied - incidence of hypotension, analgesia requirement, serum creatinine & blood urea were proved statistically insignificant in this study.

Discussion

Dexamethasone is a potent corticosteroid with analgesic, antiemetic antiinflammatory& immunomodulating effects. Its strong antiinflammatory effect contributes to postoperative analgesia as tissue injury plays a significant role in the pathophysiology of surgical pain. Combinations of analgesics with different mechanisms of action may reduce or even prevent postoperative pain and prevent emergence of anomoulous pain syndrome. The mechanism of action of epidural steroid may be related to its anti-inflammatory action. Patients who received pre-operative dexamethasone wasfound to have a reduction in pain and fatigue scores and lower C-reactive protein levels. Given the anti-inflammatory actions of dexamethasone, they are thus expected to be able to intervene in the cascades that lead to those anomalous pain states. This action is through 3 mechanisms- transrepression of pro inflammatory gene cascade, transactivation of anti inflammatory gene cascade,and non genomic effects(4). Epidural dexamethasone alleviates maternal temperature elevation after epidural analgesia. This effect has been attributed to the decrease in IL-6 levels(5). Epidural bupivacaine-dexamethasone admixture had almost the same analgesic potency as bupivacaine-fentanyl with opioid-sparing and antiemetic effects (16). Dose selection of dexamethasone was based on multiple studies which stated Epidural Dexamethasone 4 mg seems to be as effective as higher doses, and the optimal dose may indeed be lower than 4 mg, leading to further long-term safety and tolerability of this treatment (17)(18) The efficacy of dexamethasone 4 mg IV is comparable to droperidol 1.25 mg IV & ondansetron 4 mg IV for PONV prophylaxis,(6)one third of patients who undergo surgery will have postoperative nausea and vomiting. Although many trials have been conducted, the relative benefits of prophylactic antiemetic interventions given alone or in combination remain unknown.\n\nMETHODS: We enrolled 5199 patients at high risk for postoperative nausea and vomiting in a randomized, controlled trial of factorial design that was powered to evaluate interactions among as many as three antiemetic interventions. Of these patients, 4123 were randomly assigned to 1 of 64 possible combinations of six prophylactic interventions: 4 mg of ondansetron or no ondansetron; 4 mg of dexamethasone or no dexamethasone; 1.25 mg of droperidol or no droperidol; propofol or a volatile anesthetic; nitrogen or nitrous oxide; and remifentanil or fentanyl. The remaining patients were randomly assigned with respect to the first four interventions. The primary outcome was nausea and vomiting within 24 hours after surgery, which was evaluated blindly.\n\nRESULTS: Ondansetron, dexamethasone, and droperidol each reduced the risk of postoperative nausea and vomiting by about 26 percent. Propofol reduced the risk by 19 percent, and nitrogen by 12 percent; the risk reduction with both of these agents (i.e., total intravenous anesthesia(7). In addition to reducing PONV, pain and fatigue; preoperative dexamethasone enhances the quality of recovery.(8)vomiting, fatigue, and pain scores were recorded at the time of discharge from the postanesthesia care unit and ambulatory surgical unit. Hospital length of stay was also assessed.\n\nRESULTS: Global QoR-40 scores on postoperative day 1 were higher in the dexamethasone group (median [range], 178 [130-195] Clinical studies have proved that the administration of a single low-dose dexamethasone intraoperatively resulted in reduced pain scores and therefore reduced analgesic requirements,attenuated fatigue scores and overall improved

quality of recovery after surgery**.** A similar study showed that, patients receiving dexamethasone required less opioid and the incidence of sore throat, PONV, &muscle pain had significantly reduced.(9)although their effects on quality of recovery are not well characterized. The purpose of this study was to evaluate the dose-dependent effects of dexamethasone on patient recovery using the Quality of Recovery 40 questionnaire (QoR-40 A meta-analysis based on the evaluation of analgesic effects of preoperative dexamethasonefound that dexamethasone >0.1 mg/kg was effective in reducing postoperative opioid consumption.(10)the analgesic effects of dexamethasone are not well defined. The authors performed a meta-analysis to evaluate the dose-dependent analgesic effects of perioperative dexamethasone.\n\nMETHODS: We followed the PRISMA statement guidelines. A wide search was performed to identify randomized controlled trials that evaluated the effects of a single dose systemic dexamethasone on postoperative pain and opioid consumption. Meta-analysis was performed using a random-effect model. Effects of dexamethasone dose were evaluated by pooling studies into three dosage groups: low (less than 0.1 mg/kg(11)EMBASE, CINAHL, and the Cochrane Register were searched for randomized, controlled studies that compared dexamethasone vs placebo or an antiemetic in adult patients undergoing general anaesthesia and reported pain outcomes.\n\nRESULTS: Forty-five studies involving 5796 patients receiving dexamethasone 1.25-20 mg were included. Patients receiving dexamethasone had lower pain scores at 2 h {mean difference (MD. A routine prophylactic dose of iv dexamethasone 8 mg in adults in all patients may be considered in light of these additional benefits of better quality of recovery and better pain relief. Even a single dose of dexamethasone 8 mg has proved to be effective in reducing analgesic requirements in postoperative period after thyroidectomy (13) pain, and voice alteration frequently occur after thyroidectomy. Because steroids effectively reduce nausea and inflammation, a preoperative administration of steroids could improve these thyroidectomy outcomes.\n\nMETHODS: Seventy-two patients (men = 20, women = 52 and dental surgery(12)randomized, double-blind, placebo-controlled study.\n\nSETTING: University hospital.\n\nPATIENTS: One hundred twenty ASA physical status I and II patients (45 men, 75 women; aged 17-48 years .In majority of these studies, perioperative dexamethasone (especially if single dose) does not seem to increase the risk of surgical wound infection.(14)EMBASE, Cochrane Library, hand searching, bibliographies, all languages, up to April 1999 (10)the analgesic effects of dexamethasone are not well defined. The authors performed a meta-analysis to evaluate the dose-dependent analgesic effects of perioperative dexamethasone.\n\nMETHODS: We followed the PRISMA statement guidelines. A wide search was performed to identify randomized controlled trials that evaluated the effects of a single dose systemic dexamethasone on postoperative pain and opioid consumption. Meta-analysis was performed using a random-effect model. Effects of dexamethasone dose were evaluated by pooling studies into three dosage groups: low (less than 0.1 mg/kg.Considering the risk-benefit ratio, single dose of dexamethasone 4 to 8 mg appears to be safe when used for PONV prophylaxis.(15) Recent studies shows that surgical patients who receive dexamethasone 8 mg developed significant increases in blood glucose in 6 to 12 hours postoperatively in normal subjects(1)balanced anaesthesia using propofol, fentanyl, remifentanil, cisatracurium, desflurane in oxygen/air(2) obese(2), in patients with impaired glucose tolerance(2), & type 2 diabetic(3)

Through our study we have proved that epidural low dose dexamethasone is an equally effective analgesic and antiemetic but with no incidence of postoperative hyperglycemia or any other alteration in immediate physiological status.

CONCLUSION

Intravenous dexamethasone was found to rise blood sugar significantly while lower epidural dose was found to be equipotent in terms of analgesic sparing effects and reducing PONV with no incidence of postoperative hyperglycemia. These results suggest that clinicians can use low dose epidural dexamethasone for postoperative analgesia and nausea and vomiting prophylaxis without any fear of perioperative hyperglycemia.

Statistical Analysis

Table 1- demographic data	Group A	Group B	P value
Age (years)	46±3.3	47±3.2	0.764
BMI(kg/m2)	23.09±2 .11	22±2 .62	0.989
Duration of surgery(min)	90.33±15.7	93.8±16.6	0.737
ASA1/2	27/3	26/4	0.89

Table 2	Category	N	Mean	Std. Deviation	Std. Error Mean
post op increase in GRBS	A	25	41.2000	7.18215	1.43643
	B	25	6.1600	7.32393	1.46479

Table 3	Category	N	Mean	Std. Deviation	Std. Error Mean
post op anaigesia	A	25	160.07	5.007	1.429
	B	25	164.03	5.017	1.608

Table 4. Intraoperative hypotension				
no yes		intraoperative hypotension		Total
A	Count	16	9	25
	% of Total	32.0%	18.0%	50.0%
B	Count	15	10	25
	% of Total	30.0%	20.0%	50.0%
Total	Count	31	19	50
% of Total	62.0%	38.0%	100.0%	

Table 5	Category	N	Mean	Std. Deviation	Std. Error Mean
post op increase in blood urea	A	25	0.180	0.007	0.029
	B	25	0.181	0.006	0.008

Table 6	Category	N	Mean	Std. Deviation	Std. Error Mean
post op increase in serum creatinine	A	25	0.001	0.00010	0.009
	B	25	0.001	0.00011	0.008

Statistical Analysis

Parameters	T value	P value	95% Confidence interval	
			Lower	Upper
Difference in glycemic status	17.080	0.001	30.915	39.164
Difference in analgesic requirements	0.605	0.357	1.212	-1.692
Difference in incidence of hypotension	0.562	0.736	-1.366	2.433
Difference in blood urea	-0.029	0.989	-4.727	4.594
Difference in serum creatinine	-0.361	0.764	-6.762	4.695

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