

## ORIGINAL ARTICLE

## EFFECT OF DEXAMETHASONE VERSUS PLACEBO FOR IMPROVED RECOVERY IN PATIENTS UNDERGOING ANAESTHETIC INTERVENTIONS FOR GENERAL SURGICAL PROCEDURES

Sara Haider Malik, Nighat Begum, Allah Ditta Ashfaq\*, Huma Saleem\*, Muhammad Tariq Shah, Muhammad Hanif, Tariq Abbasi

Department of Anaesthesia, Ayub Teaching Hospital, Abbottabad, \*Anaesthesia and Pain Medicine, Shaukat Khanum Memorial Hospital, Lahore-Pakistan

**Background:** Endotracheal intubation is one of the basic prerequisites of general anaesthesia. Recovery of patients is delayed due to the development of post-operative nausea, vomiting, sore throat and shivering. This study was conducted to determine role of dexamethasone for improved recovery of patients. **Methods:** This randomized controlled trial was performed in the Department of Anaesthesia, Ayub Teaching Hospital, Abbottabad from June to November 2018. One hundred and twenty-two consenting patients of both genders, aged between 18–60 years, American Society of Anaesthesiologists (ASA) I and II, scheduled for general surgeries of 60–180 minutes duration under general anaesthesia were included. Patients with long duration surgeries, anticipated difficult airways, nasogastric tube in situ, upper respiratory tract infections, on steroid therapy and critically ill and emergency surgeries were excluded. They were randomly allocated into two groups by lottery method as dexamethasone (group A, n=61) or Placebo (group B, n=61). Post-operative nausea, vomiting, sore throat was observed at 2, 12 and 24 hours, shivering was observed at 2 hours only and patient satisfaction at 24 hours post-operatively. **Results:** Group A patients had statistically proven better outcomes at 2, 12 and 24 hours for post-operative sore throat, nausea and vomiting, shivering was controlled in 24.5% *p*-value (0.006). Patient satisfaction was found in 83.6% of group A patients. **Conclusion:** Thus, dexamethasone is effective drug for prevention of postoperative nausea, vomiting, sore throat and shivering in general surgical procedures thus improving patient satisfaction and their early discharge.

**Keywords:** Dexamethasone; Sore throat; Nausea; Vomiting; Shivering; Patient satisfaction

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### INTRODUCTION

Endotracheal intubation is one of the basic prerequisites of general anaesthesia. The procedure causes mucosal irritation of the airway depending upon the size of the tube, attempts of intubation, gender, expertise of the operator, cuff pressure, duration of intubation, suction and tube manipulation. Factors which may contribute to causing inflammation are oral flora, vomitus and gastric contents from reflux and high mallampati score. Most of the times these patients need to have a prolonged stay at the hospital as they may require treatment of their new post-operative symptoms.<sup>1</sup> The quality of recovery is significantly decreased due to the development of symptoms which occur post-operatively. Irritation of the upper airway causes local inflammation in the mucosa thus causing difficulty in speaking and swallowing. It ranges from nausea, vomiting, hoarseness of voice, sore throat to dysphagia. Even though these seems to be minor entities, the recovery of the patient is delayed and there is a decreased sense of well-being. Patients' morbidity is increased and their general sense of

well-being in post-operative stay and even after discharge is mostly chaotic. The rate of post-operative symptoms due to intubation is very high. In literature, it ranges between 6–90 percent.<sup>2</sup> The anti-inflammatory effects of Corticosteroids are well established. It has been tried in many studies for Post-Operative Sore throat (POST) syndrome. Different studies suggest the positive role of dexamethasone in relieving post-operative pain, sore throat, vomiting, nausea, hoarseness of voice, dysphagia, shivering and in improving patient's physical comfort and psychological well-being. It is administered intravenous pre-operatively and most of the results show that it is most efficient in the first 6 hours, with the effect decreasing with the duration of stay. The dose of dexamethasone used is not significant enough to cause any adverse effects like hyperglycaemia or infections. The effect of dexamethasone is blunted at 24 hours post-operatively.<sup>3</sup> The use of corticosteroids in the reduction of airway morbidity is irrespective of the type of surgery performed. The minimum dose that exerts significant effect on lowering airway

morbidity, quality of recovery and decreased analgesia requirement is 1 mg/kg.<sup>3,4</sup>

One of the most commonly used tools for evaluation of quality of recovery in post-operative patients is the QoR-40 questionnaire. It is a forty items questionnaire and has sub-scores for five categories of recovery, i.e., pain, physical independence, comfort, emotions and patient support. It is used extensively but its clinical utility is not definite.<sup>4</sup>

One of the common side effects of anaesthesia is post-operative nausea and vomiting (PONV). The use of inhaled anaesthetics, opioid analgesics and nitrous oxide increase the incidence of PONV. High risk of PONV can be measured through Apfel score which gives one point to each of: female gender, post-operative use of opioids, non-smoking status and previous history of PONV or motion sickness, each of which increases the risk of PONV by about 20 percent.<sup>5</sup> Along with pre-operative intravenous dexamethasone, post-operative tapering doses have also been tried in some studies. Most of the studies are limited to the duration of 24 hours post-operative as the acute inflammatory process peaks at 24 hours.<sup>6</sup> Different drugs other than dexamethasone have been tried for treating postoperative adverse outcomes of intubation. They include ketamine gargles, azulene sulphate and steroid gels.<sup>7</sup> Anaesthesia and surgery predisposes to shivering as well. Different mechanisms have been described to be responsible for this symptom. The exposure of a patient to cold environment, release of intraoperative cytokines and pain triggering the thermoregulatory centres are possible aetiologies. As the heat moves from body core to the surface and is lost via skin inducing shivering to the patient. It may lead to increased hypothermia and complications of hypothermia like decreased haemostasis, increased oxygen requirement and possible increase in myocardial infarctions in patients with history of ischemic heart disease. This response can be blunted through many ways like pre-warming patients and fluids, keeping a warm environmental temperature and also through the use of dexamethasone. Dexamethasone, by decreasing the response to inflammatory cytokines and by decreasing the pain of patient secondary to surgical stimulus, lowers the incidence of shivering. Many studies in which data was recorded using standardized questionnaires like QoR-40, demonstrate the effectiveness of Dexamethasone in this regard with statistical significance.<sup>8,9</sup>

The aim of the study is to compare dexamethasone with placebo for control of post-operative symptoms of general anaesthesia including nausea, vomiting, sore throat and shivering, as dexamethasone has now given a second show of

importance regarding additional new found roles in symptoms particularly PONV and shivering.

## MATERIAL AND METHODS

This prospective, double blinded, randomized placebo-controlled trial was conducted over a period of six months from July to December 2018. After obtaining the Institutional Ethics Committee's approval, 112 consenting patients of either gender, aged between 18–60 years, of American Society of Anaesthesiologists (ASA) physical status I and II, scheduled for elective general surgeries with an estimated duration of 60–180 minutes undergoing general anaesthesia requiring endotracheal intubation, were enrolled in this study. Patients who had unanticipated or long duration surgeries (more than three hours), with anticipated difficult airways, already having nasogastric tube, with upper respiratory tract infections, on steroid therapy and critically ill patients requiring emergency surgeries were excluded. The sample size was calculated based on similar studies<sup>9</sup> with an alpha level equal to 5% and the study power equal 90% and confidence interval 95% about 61 samples in each group and the total 122 samples using WHO sample size calculations. They were randomly allocated into two groups to receive either dexamethasone (group A, n=61) or normal saline (group B, n=61) with help of lottery method. All patients received midazolam 0.05 mg/kg (IV), 15 minutes before the start of the operation. On arrival to the operating room, the patients in the group A received dexamethasone in a dose of 8 mg IV while patients in the group B received 2 ml of normal saline IV just before induction of anaesthesia. Anaesthesia was induced with nalbuphine 0.1 mg/kg IV, propofol 2mg/kg IV after pre-oxygenation for 3 minutes. After muscle relaxation with atracurium 0.5 mg/kg IV, trachea was intubated by an experienced anaesthesiologist using disposable endotracheal tubes (7.0–8.5 mm ID for male patients and 6.0–7.5 mm ID for female patients). Macintosh blade size 3 or 4 was used for laryngoscopy. Anaesthesia was maintained with 50% oxygen and 50% isoflurane. At the end of operation, the oropharynx was cautiously toileted with a 14Fr disposable soft suction catheter and trachea extubated after standard reversal of muscle relaxation with neostigmine and glycopyrrolate.

Outcome assessment for the incidence of sore throat, post-operative nausea and vomiting (PONV scale) was carried out by a junior doctor not involved in the study, at 2, 12 and 24 hours, shivering to be observe in PACU within 2 hours post-extubation and patient satisfaction was inquired as YES or NO at 24 hours post-

operatively. Data was represented as numerical (continuous and discrete) and categorical (nominal and ordinal) data. The data was analysed using SPSS for windows (version 21). Independent sample *t*-test was used for analysing numerical data and Chi-square test was utilized for analysing categorical data.

## RESULTS

One hundred and twenty-two patients were allocated into two groups of 61 each. As regards, mean age of patients, sex ratio within the groups, body mass index (BMI), attempts of intubation, duration of surgery and satisfaction scores there was no statistically significant difference among all the groups (*p*-value >0.05) [Table-1]. At 2 hour, 12 hours and 24 hours after extubation of the trachea, the incidence of sore throat and PONV

was quite reduced in the dexamethasone group as compared to the control group [Table-2] and [Table-3]. Incidence of shivering was observed in the first 2 hours when the patient was in immediate recovery phase in PACU. The results were found out to be significant on analysis [Table-4]. Also, none of the patients in either group experienced coughing, hoarseness, dysphonia, dysphagia or other side effects related to tracheal intubation.

All patients who were given dexamethasone 83.6% were satisfied 24 hours post operatively as compared to patients who were given placebo 26.2% of the patients. [Table-5]. \*Categorical data, analysed by Chi-square test. The rest are numerical data, analysed by Independent sample *t*-test.

**Table-1: Patient characteristics**

Patient Characteristics	Group A	Group B	<i>p</i> -value
Age	44.17 years (SD±13.236)	37.1 years (SD±10.0)	
Gender (male:female)	21 (47.7%): 40 (52.6%)	24 (52.3%): 37 (47.4%)	0.60
BMI	23.0±1.7	22.8±2.0	0.16
Intubation Attempts	1.4	1.5	0.96
Duration of Surgery	113.4±19.0	112.8±19.3	0.16

**Table-2: Incidence of Sore Throat**

Sore throat	Group A	Group B	<i>p</i> -value
At 2 hours	5 (8.19%)	13 (21.3%)	0.03
At 12 hours	6 (9.8%)	15 (24.6%)	0.02
At 24 hours	2 (3.27%)	8 (13.1%)	0.13

Numerical data, analysed by Independent sample *t*-test.

**Table-3: Incidence of Post-Operative Nausea Vomiting (PONV)**

PONV	Group A	Group B	<i>p</i> -value
At 2 hours	11 (18.0%)	21 (34.4%)	0.03
At 12 hours	7 (11.4%)	13 (21.3%)	0.02
At 24 hours	1 (1.63%)	7 (11.4%)	0.12

**Table-4 Incidence of Shivering**

Shivering	Group A	Group B	<i>p</i> -value
During first 2 hours	15 (24.5%)	29 (47.5%)	0.006

**Table-5 Patient Satisfaction**

Patient Satisfaction	Group A	Group B	<i>p</i> -value
At 24 hours	51 (83.6%)	16 (26.2%)	0.02

## DISCUSSION

Different interventions are implied to limit post-operative hospital stay, maintain physiological functions, reduce pain, enhance mobilization and facilitate early oral nutrition in the post-operative patients by reducing surgical stress. These protocols are collectively called Enhanced Recovery After Surgery (ERAS). These are evidence-based steps taken in the perioperative duration for the sake of increased patient satisfaction, quicker recovery and cost effectiveness. Thus, by decreasing the stay of the patients in the hospital, minimum resources are

utilized. This is an inter-disciplinary system which requires the mutual work in the anaesthesiology, surgical and nursing departments. It has been proven to be effective in general surgical, colorectal, bariatric, head and neck cancer surgeries.<sup>10</sup> Our results suggest the efficacy of dexamethasone in the reduction of hospital stay by decreasing the post-operative nausea, vomiting and analgesia requirement thereby proving the economic importance of adding dexamethasone to the routine preoperative drugs and taking it up as a part of the enhanced recovery after surgery.

The efficacy of dexamethasone for this purpose has been shown in literature in many

different types of studies throughout the literature. A study done by Wang J *et al* found that the incidence of PONV in patients needing rescue antiemetic was significantly less from the control group.<sup>11</sup> Wang J *et al* demonstrated in another study that the best time to get fruitful results was to administer the drug immediately before anaesthesia was induced. They proved that in this way the effect of dexamethasone for PONV reduction was found for as long as 24 hours. They also demonstrated that the administration of dexamethasone at the time of anaesthesia reversal was not successful in providing these effects for the first two post-operative hours. As far as pain is considered, they did not find any significant difference in the opioid consumption.<sup>12</sup>

The meta-analysis done by Henzi I *et al* included 17 trials, with a total of 1946 study participant studied. The most common dose studied was 8 mg or 10 mg, even though the number of different regimens of dexamethasone studied was 16. Almost all findings supported the statement that use of dexamethasone led to decreased incidence of PONV.<sup>13</sup>

Another meta-analysis was put together by Karanicolas P *et al* who also combined 17 trials. High quality or supporting evidence was presented for dexamethasone reducing the incidence of nausea, vomiting, individually, and in comparison, to placebo. Our study shows that there was a decreased incidence of PONV, sore throat and shivering. In this analysis there was no significant difference between dizziness and headache between groups under study as well as no sore throat and shivering was appreciated. Thus, recommending the use of prophylactic dexamethasone in all preoperative patients especially those who are at higher risk for vomiting.<sup>14</sup>

Another symptom which is bothersome for patients is shivering. Our data shows that in the preoperative period of an elective surgery, dexamethasone provides significant relief from shivering. Entezariasl M *et al* studied these effects. Dexamethasone and pethidine were individually compared to a placebo group. In the placebo group, the incidence of shivering was 19 (47.5%), in pethidine group it was found significantly higher than the dexamethasone group ( $p$ -value=0.001). Thus, in accordance with our results, the effectiveness of dexamethasone was well established.<sup>15</sup> Yared *et al*, who found that dexamethasone group had lower incidence of shivering when compared to the placebo group ( $p$ -value=0.039). These were the patients in the intent to treat group.<sup>16</sup> We also found a profound decrease in the incidence of post-operative sore throat. The evidence supporting this result can be found in the study conducted by Bagchi D *et al* and

the meta-analysis of 7 clinical trials done by Sun L.<sup>17,18</sup>

Two extensive double blinded studies by De Oliveira G *et al* and Liu K *et al* shows apparent worth of adding dexamethasone as a preoperative medication in patients undergoing general anaesthesia for the prevention of postoperative symptoms thus enhancing the early recovery of patients.<sup>19,20</sup>

## CONCLUSION

Thus, dexamethasone is effective drug for prevention of postoperative nausea, vomiting, sore throat and shivering in general surgical procedures thus improving patient satisfaction and their early discharge.

## LIMITATION

Since we did not use fibre optic bronchoscope and could not measure the cuff pressure to assess the amount of tissue damage, which is a limitation to our study.

## AUTHORS' CONTRIBUTION

SHM: conception, design, acquisition, write up, interpretation of data. NB: Data collection, literature search. ADA: supervised the study and proof read the manuscript. HS: conception, write up, data analysis, proof reading. MTS: data collection, write up. MH, TA: data collection, literature search.

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**Address for Correspondence:**

**Dr. Sara Haider Malik**, Department of Anaesthesia, Ayub Medical College, Abbottabad-Pakistan

**Cell:** +92 333 505 6069

**Email:** sarahaidermalik@gmail.com