The Effect of Single-Dose Dexmedetomidine on Cough Response During Tracheal Extubation

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Introduction: Optimal strategy for smooth, cough less extubation is still not well established. We aimed to study the effect of single dose of dexmedetomidine (0.5ug/kg) given prior to extubation on cough response during extubation.

Methods: 220 patients undergoing laparoscopic cholecystectomy under general anaesthesia were included in the study. Group D (n=110) received IV dexmedetomidine 0.5ug/kg diluted in 100 ml saline and Group S (n=110) received 100ml saline 15 minutes before extubation. Primary outcome was incidence and severity of cough at the time of extubation. Secondary outcome was haemodynamic parameters and sedation. The severity of cough was graded on a four-point scale. Statistical analysis was performed using chi square test and independent t test.

Results: The incidence of coughing was significantly lower in Group D than Group S (49.1% vs. 70.9%, p = 0.002). Lower grades of cough was observed more in Group D than Group S (17.2% vs. 30.9% p = 0.018). The mean heart rate and blood pressure were lower in Group D. (p <0.001) Sedation score was similar in both groups. (p=0.07)

Conclusion: Use of single bolus dose of dexmedetomidine prior to extubation reduces the incidence and severity of cough grade. In addition, it also attenuated haemodynamic response to tracheal extubation without affecting recovery.

Key Words: Dexmedetomidine, extubation, cough.

Introduction

Coughless smooth extubation has been need of an hour during the current Covid-19 pandemic. The difficult airway society has given guidelines for successful extubation but there is no uniform consensus regarding criteria for smooth extubation. Smooth extubation requires lack of straining, coughing and laryngospasm [1]. There are plenty of strategies to alleviate stressful response to intubation but strategies to reduce extubation stress response are not adequately studied. Smooth tracheal extubation is defined as no gross purposeful muscular movement, such as coughing, within 1 min of tracheal tube removal [2].

Dexmedetomidine at various doses and with addition of opioids have shown to improve quality of extubation. We hypothesized that single dose of dexmedetomidine (0.5ug/kg) before extubation might reduce the incidence and severity of cough during extubation.

Methods

This prospective, double blind, randomized study was approved by hospital ethical committee MSRMC/EC/AP-65/10-2019. We enrolled 220 patients scheduled for laparoscopic cholecystectomy under general anaesthesia. ASA 1 or 2 patients aged between 18 to 60 years were included. ASA 3 or 4 patients, patients with upper or lower

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respiratory tract infection, COPD, anticipated difficult airway, were excluded from the study. Informed consent was taken from the participants.

Patients were randomly divided into two groups using computer generated random numbers. The allocation was concealed by sealed envelope technique. The anaesthetist not involved in the study prepared the drug. Group D received dexmedetomidine 0.5µg/kg diluted in 100ml saline and Group S received 100ml saline. The drug was administered intravenously to the patient 30 minutes before the expected extubation tim**e,** and the administration was completed over 15 minutes.

Intravenous access was established with 18G cannula. Inside operation theatre standard ASA monitors i**.e.,** ECG, NIBP and SPO2 were attached. Baseline haemodynamic parameters were noted. General anaesthesia was induced with IV propofol of 2 mg/kg and IV fentanyl of 2 mcg/kg. Adequate neuromuscular relaxation was obtained with initial loading dose of IV atracurium at 0.5mg/kg and thereafter repeated at 0.1mg/kg as required. Standard sized cuffed endotracheal tubes of size 7-7.5 in females and 8-8.5 in males were used. Topical lignocaine was not used. Anaesthesia was maintained with Oxygen + Air + Isoflurane 1.0 -1.5MAC to ensure adequate anaesthetic depth during surgery. Intravenous paracetamol 1gm was given for analgesia. IV fentanyl 0.5ug/kg was repeated as per anaesthesiologist's discretion.

Towards the end of skin closure suturing isoflurane was titrated to lower doses. The airway was suctioned once to clear secretions and no further suctioning was done and isoflurane was discontinued. The patient was ventilated with 100% oxygen. A 'No touch extubation technique' was used.[3] When spontaneous breathing efforts were observed, neuromuscular block was reversed. Once return of adequate spontaneous ventilation was confirmed patient was extubated. Patients were monitored for 15 minutes and then shifted to post-anaesthesia care unit (PACU).

An anaesthetist who was blind to the study drugs noted down observations of the study. At the time of extubation, the cough if present is graded according to a 4-point scale. The cough was graded as 0 = no cough, 1 = single cough, 2 = more than one episode of non-sustained cough, and 3 = sustained and repetitive cough with head lift.[4] The hemodynamic parameters i.e., heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, and oxygen saturation are recorded at 4 points of time during and after the surgery. T0- basal parameters before anaesthetic induction, T1- after completion of dexmedetomidin**e/** saline infusion, T2- immediately after extubation, T3- 5 minutes after extubation. In addition, occurrence of adverse events namely, oxygen desaturation (spo2<92%), breath holding spells (apnoea>15 seconds), laryngospasm was recorded if they occurred at this time.

In PACU, sedation was measured using the Ramsay sedation scale [5] 1 = the patient is anxious and restless or agitated, or both; 2 = the patient is cooperative, tranquil, and oriented; 3 = the patient responds to commands only; 4 = the patient exhibits a brisk response to a loud auditory stimuli or a light glabellar tap; 5 = the patient exhibits a sluggish response to a loud auditory stimulus or a light glabellar tap; and 6 = the patient exhibits no response.

The primary objective of the study was the incidence and severity of cough at extubation. The secondary objective was to study haemodynamic response and sedation.

Statistical Analysis

Lee et al. have found that the incidence of severe cough with a single bolus dose of dexmedetomidine prior to extubation was

reduced by 13%.[6] In the present study, with 80% power and 95% confidence level, and a minimum detectable difference between the groups of 13%, the study requires a minimum of 107 subjects in each group. In our study to compensate for dropout from the study, 110 subjects were recruited in each of the two groups.

Continuous data was presented as mean ± SD. Descriptive statistics of the incidence of cough (cough grade 1 and above) and its grades was presented as numbers or percentage. Nominal data was analysed by chi-square test/Fisher's exact test. Independent t-test was used to compare the hemodynamic parameters. Levene`s test for homogeneity of variance has been performed to assess the homogeneity of variance. Repeated measures of ANOVA was used to compare mean hemodynamic measures between the repeated measurements at different times (T0 – T3) of the intervention. P-values < 0.05 were considered statistically significant. All reported p values are two sided. Statistical Package for the Social Sciences (SPSS) ™ version 26, (International Business Machines Corp. (IBM)) software was used for analysis of the data.

Results

Total 235 patients were assessed for the study. Out of them, 220 patients who satisfied inclusion criteria were enrolled in the study and were allocated to either group D (n = 110) or group S (n = 110). A total of 220 patients completed the study and were subjected to analysis. (Figure 1)The demographic characteristic, duration of anaesthesia and IV fentanyl usage were comparable in both groups. (Table 1)

The incidence and severity of cough during extubation is shown in Table no 2. The incidence of cough was significantly lower in Group D than Group S (49.1% vs. 70.9%, p = 0.002). Overall severe cough grade was low in both groups (0.9% vs. 2.7%) Lower grades of cough were significantly observed in Group D compared to Group S (17.2% vs. 30.9% p = 0.018).

Ramsay sedation grade is shown in Figure 3. The median sedation grade was 2 [2-3] in Group D and 2 [1-2] in Group S but this was not a statistically significant (p = 0.070)

The haemodynamic parameters (HR, MAP) at four time point (T0, T1, T2, T3) is shown in Figure 4-A and 4-B. Hemodynamic parameters were comparable at baseline (T0). At times T1 and T2, mean heart rate and blood pressure were significantly lower in group D group. (p < 0.001) However, at time T3, heart rate was comparable between both the groups while the blood pressures in Group D continued to remain low. (p = 0.699, p < 0.001)

No episode of laryngospasm, desaturation, airway obstrucion or bradycardia / hypotension requiring intervention were noted in both the groups.

Discussion

In this prospective, randomized study we found that single bolus dose of dexmedetomidine (0.5ug/kg) before extubation significantly reduces incidence coughing. In addition to incidence, severity of cough was less with dexmedetomidine. Use of dexmedetomidine also suppressed the haemodynamic response to extubation without causing undue sedation.

Incidence of coughing after extubation varies from 12-90% [6-9]. The incidence of severe cough has been as high as 30%. In our study, dexmedetomidine reduced the incidence of coughing by 20%. Overall incidence of severe cough (Grade 3) was less and similar in both groups (0.9% vs. 2.7%). Lower grades of cough were observed with dexmedetomidine. Dexmedetomidine achieved smooth, coughless extubation in 50% patients. (Grade 0)

All previous studies have different incidence of coughing. These varying results might be due to different extubation protocols, different opioid-anaesthetic combinations and various surgical factors. There is no uniform guideline to reduce the occurrence of coughing. Few studies have demonstrated efficacy of single dose of dexmedetomidine in preventing cough response. Lee et al compared addition of dexmedetomidine (0.5ug/kg) to remifentanyl – sevoflurane based anesthesia with low dose remifentanyl infusion (targeting a Ce of 1ng/ml) alone in thyroid surgeries.[6] They found addition of dexmedetomidine significantly reduces cough response (64% vs. 91%), produces better haemodynamic stability without compromising recovery from anaesthesia. Similar study done by Kim et al. compared high dose remifentanyl infusion (targeting a Ce of2ng/ml) with combination of dexmedetomidine (0.5ug/kg) with low dose remifentanyl infusion (targeting a Ce of 1ng/ml) in thyroid surgeries. [10] They found incidence of coughing was similar in both groups. (70% vs. 81%) But they found dexmedetomidine–remifentanyl combination provides stable haemodynamics and reduces PONV. These studies have used combination of dexmedetomidine with various doses of remifentanyl maintenance infusion until extubation. Remifentanyl is an ultra-short acting opioid which has advantage of smooth recovery in addition to blunting cough response.[11] Hence it makes unclear about the contribution of each adjuvant in suppressing the cough response.

Dexmedetomidine has been used in the dose ranging 0.5ug – 1ug/kg . Bindu B et al. found 0.75ug/kg dose optimal for smooth extubation in terms of haemodynamic parameters.[12] Aksu R et al found 0.5ug/kg dose of dexmedetomidine to be superior than fentanyl 1ug/kg for suppressing cough response. [13] A meta-analysis performed by Salim B on various pharmacological interventions done for smooth extubation and found that dexmedetomidine at dose of 0.4 to 0.5 mcg/kg was associated with smooth extubation with minimal coughing.[14] Other pharmacological interventions such as local anesthetics, opioids and calcium channel blockers did not attenuate cough response. Higher doses (>0.5ug/kg) may results in bradycardia, hypotension and sedation. Dexmedetomidine also suppressed haemodynamic response to extubation. Dexmedetomidine is a sympatholytic drug which is known to suppress hypertensive and tachycardia response to extubation.[15] In our study we found that group D had overall lower heart rate and blood pressure at various time points of extubation.

Coughing during recovery from anaesthesia can be a troublesome problem. Endotracheal tube-induced irritant or stretch stimuli forms the basis for cough production. Coughing can have deleterious effect on haemodynamic parameters, respiratory mechanics and spread of fomites. Various approaches have been studied to prevent this cough response. Recently dexmedetomidine a highly selectiveα2-adrenoreceptor agonist has generated interest as an alternative technique for smooth extubation. Dexmedetomidine is proven to attenuate stress response for laryngoscopy and intubation but its role during extubation for preventing cough response is still not thoroughly studied. Dexmedetomidine itself doesn't have antitussive property but effect on cough is probably due to its sedative or analgesic effect.[16]

The most common technique practised for smooth extubation is extubation under deep anaesthesia. Various agents used for deep extubation are, propofol, opioids, inhalational agents, lignocaine or combinations of these agents. But to maintain balance between smooth and successful extubation could be tricky.

We have used dexmedetomidine as a sole anaesthesia agent for smooth extubation. It has opioid sparing action without delaying recovery. This is a simple and handy technique just to be initiated before extubation. It doesn't require bulky infusion pumps, intraoperative continuous infusion and additional plasma concentration monitoring. We found this technique to be very safe, simple and effective to avoid stressful extubation.

Limitations of the study are that we did not include difficult airway, oral and nasal surgeries. Extubation in these patients are more likely associated with severe coughing, straining and agitation. Further studies are required to assess the role of dexmedetomidine in such high-risk populations. Secondly, the anaesthesiologist assessing the cough grade could have guessed group allocation based on haemodynamic changes during emergence.

Conclusion

A single bolus dose of dexmedetomidine (0.5ug/kg) given prior to extubation significantly reduces the incidence and severity of cough response. In addition, it provides stable haemodynamic conditions without affecting the recovery profile.

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