International Journal of Medical and Health Research
ISSN: 2454-9142
Received: 17-08-2019; Accepted: 21-09-2019
www.medicalsciencejournal.com
Volume 5; Issue 11; November 2019; Page No. 92-96

Clinical outcomes of effect of dexmedetomidine on hemodynamic responses during tracheal Extubation

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Abstract
Early recovery and extubation in the operating room is the preferred method when the pre-operative state of consciousness is relatively normal and surgery does not involve critical brain areas or extensive manipulation. In the complicated or unstable patient, the risks of early extubation may outweigh the benefits. Patients with increased intracranial pressure (ICP) are prone to severe cardiac and or cerebral complications following emergence from general anesthesia and during the recovery period. Hence the present study was planned to evaluate the effect of dexmedetomidine on hemodynamic responses during tracheal extubation.
The present study was planned in Department of Anesthesia, Nalanda Medical College and Hospital, Patna, Bihar. Total 30 Patients were enrolled in the present study. The 15 patients were enrolled in Group I as cases and 15 patients were enrolled as control patients in Group II. Group I patients received 0.5 µg/kg inj. dexmedetomidine in 100 ml normal saline slow IV infusion over 10 minutes and Group II patients received 100 ml normal saline IV infusion over a period of 10 minutes. Study drugs were given at the time of skin closure. Patients were kept nil orally for 6 hours before procedure. All patients were uniformly premeditated with inj. glycopyrrolate 0.2 mg IM 30 minutes before shifting to operation theatre.
The data generated from the present study concludes that use of dexmedetomidine before extubation attenuates the hemodynamic response to extubation. It enables smooth extubation of the trachea and provides adequate sedation postoperatively. Dexmedetomidine increases the incidence of bradycardia and hypotension, but does not cause side effects like respiratory depression, laryngospasm, bronchospasm, undue sedation and desaturation.

Keywords: Extubation, dexmedetomidine, haemodynamic response, ETC

Introduction
Tracheal intubation, usually simply referred to as intubation, is the placement of a flexible plastic tube into the trachea (windpipe) to maintain an open airway or to serve as a conduit through which to administer certain drugs. It is frequently performed in critically injured, ill, or anesthetized patients to facilitate ventilation of the lungs, including mechanical ventilation, and to prevent the possibility of asphyxiation or airway obstruction.
The most widely used route is orotracheal, in which an endotracheal tube is passed through the mouth and vocal apparatus into the trachea. In a nasotracheal procedure, an endotracheal tube is passed through the nose and vocal apparatus into the trachea. Other methods of intubation involve surgery and include the cricothyrotomy (used almost exclusively in emergency circumstances) and the tracheotomy, used primarily in situations where a prolonged need for airway support is anticipated.
Because it is an invasive and uncomfortable medical procedure, intubation is usually performed after administration of general anesthesia and a neuromuscular-blocking drug. It can however be performed in the awake patient with local or topical anesthesia or in an emergency without any anesthesia at all. Intubation is normally facilitated by using a conventional laryngoscope, flexible fiberoptic bronchoscope, or video laryngoscope to identify the vocal cords and pass the tube between them into the trachea instead of into the esophagus. Other devices and techniques may be used alternatively.
After the trachea has been intubated, a balloon cuff is typically inflated just above the far end of the tube to help secure it in place, to prevent leakage of respiratory gases, and to protect the tracheobronchial tree from receiving undesirable material such as stomach acid. The tube is then secured to the face or neck and connected to a T-piece, anesthesia breathing circuit, bag valve mask device, or a mechanical ventilator. Once there is no longer a need for ventilatory assistance and/or protection of the airway, the tracheal tube is removed; this is referred to as extubation of the trachea (or decannulation, in the case of a surgical airway such as a cricothyrotomy or a tracheotomy).
For centuries, tracheotomy was considered the only reliable method for intubation of the trachea. However, because only a minority of patients survived the operation, physicians undertook tracheotomy only as a last resort, on patients who were nearly dead. It was not until the late 19th century however that advances in understanding of anatomy and physiology, as well an appreciation of the germ theory of disease, had improved the outcome of this operation to the point that it could be considered an acceptable treatment option. Also at that time, advances in endoscopic instrumentation had improved to such a degree that direct laryngoscopy had become a viable means to secure the airway by the non-surgical orotracheal route. By the mid-

20th century, the tracheotomy as well as endoscopy and non-surgical tracheal intubation had evolved from rarely employed procedures to becoming essential components of the practices of anesthesiology, critical care medicine, emergency medicine, and laryngology.

Tracheal intubation can be associated with minor complications such as broken teeth or lacerations of the tissues of the upper airway. It can also be associated with potentially fatal complications such as pulmonary aspiration of stomach contents which can result in a severe and sometimes fatal chemical aspiration pneumonitis, or unrecognized intubation of the esophagus which can lead to potentially fatal anoxia. Because of this, the potential for difficulty or complications due to the presence of unusual airway anatomy or other uncontrolled variables is carefully evaluated before undertaking tracheal intubation. Alternative strategies for securing the airway must always be readily available.

Tracheal intubation is indicated in a variety of situations when illness or a medical procedure prevents a person from maintaining a clear airway, breathing, and oxygenating the blood. In these circumstances, oxygen supplementation using a simple face mask is inadequate. Perhaps the most common indication for tracheal intubation is for the placement of a conduit through which nitrous oxide or volatile anesthetics may be administered. General anesthetic agents, opioids, and neuromuscular-blocking drugs may diminish or even abolish the respiratory drive. Although it is not the only means to maintain a patent airway during general anesthesia, intubation of the trachea provides the most reliable means of oxygenation and ventilation [1] and the greatest degree of protection against regurgitation and pulmonary aspiration [2].

Damage to the brain (such as from a massive stroke, non-penetrating head injury, intoxication or poisoning) may result in a depressed level of consciousness. When this becomes severe to the point of stupor or coma (defined as a score on the Glasgow Coma Scale of less than 8) [3], dynamic collapse of the extrinsic muscles of the airway can obstruct the airway, impeding the free flow of air into the lungs. Furthermore, protective airway reflexes such as coughing and swallowing may be diminished or absent. Tracheal intubation is often required to restore patency (the relative absence of blockage) of the airway and protect the tracheobronchial tree from pulmonary aspiration of gastric contents [4].

Intubation may be necessary for a patient with decreased oxygen content and oxygen saturation of the blood caused when their breathing is inadequate (hypoventilation), suspended (apnea), or when the lungs are unable to sufficiently transfer gasses to the blood. Such patients, who may be awake and alert, are typically critically ill with a multisystem disease or multiple severe injuries [1]. Examples of such conditions include cervical spine injury, multiple rib fractures, severe pneumonia, acute respiratory distress syndrome (ARDS), or near-drowning. Specifically, intubation is considered if the arterial partial pressure of oxygen (PaO2) is less than 60 millimeters of mercury (mm Hg) while breathing an inspired O2 concentration (FIO2) of 50% or greater. In patients with elevated arterial carbon dioxide, an arterial partial pressure of CO2 (PaCO2) greater than 45 mm Hg in the setting of acidemia would prompt intubation, especially if a series of measurements demonstrate a worsening respiratory acidosis. Regardless of the laboratory values, these guidelines are always interpreted in the clinical context [5].

Actual or impending airway obstruction is a common indication for intubation of the trachea. Life-threatening airway obstruction may occur when a foreign body becomes lodged in the airway; this is especially common in infants and toddlers. Severe blunt or penetrating injury to the face or neck may be accompanied by swelling and an expanding hematoma, or injury to the larynx, trachea or bronchi. Airway obstruction is also common in people who have suffered smoke inhalation or burns within or near the airway or epiglottitis. Sustained generalized seizure activity and angioedema are other common causes of life-threatening airway obstruction which may require tracheal intubation to secure the airwa [6]. Diagnostic or therapeutic manipulation of the airway (such as bronchoscopy, laser therapy or stenting of the bronchi) may intermittently interfere with the ability to breathe; intubation may be necessary in such situations [7].

Dexmedetomidine, sold under the trade name Precedex among others, is an anxiety reducing, sedative, and pain medication. Dexmedetomidine is notable for its ability to provide sedation without risk of respiratory depression (unlike other commonly used drugs such as propofol and fentanyl) and can provide cooperative or semi-arousable sedation. Similar to clonidine, it is an agonist of α2-adrenergic receptors in certain parts of the brain [6].

Dexmedetomidine is most often used in the intensive care setting for light to moderate sedation. It is not recommended for long-term deep sedation. A feature of dexmedetomidine is that it has analgesic properties in addition to its role as a hypnotic, but is opioid sparing; thus, it is not associated with significant respiratory depression (unlike propofol). Many studies suggest dexmedetomidine for sedation in mechanically ventilated adults may reduce time to extubation and ICU stay. People on dexmedetomidine can be rousable and cooperative, a benefit in some procedures. Compared with other sedatives, some studies suggest dexmedetomidine may be associated with less delirium. However, this finding is not consistent across multiple studies. At the very least, when aggregating many study results together, use of dexmedetomidine appears to be associated with less neurocognitive dysfunction compared to other sedatives. Whether this observation has a beneficial psychological impact is unclear. From an economic perspective, dexmedetomidine is associated with lower ICU costs, largely due to a shorter time to extubation [8].

Dexmedetomidine is a highly selective α2-adrenergic agonist. Unlike opioids and other sedatives such as propofol, dexmedetomidine is able to achieve its effects without causing respiratory depression. Dexmedetomidine induces sedation by decreasing activity of noradrenergic neurons in the locus ceruleus in the brain stem, thereby increasing the activity of inhibitory gamma-aminobutyric acid (GABA) neurons in the ventrolateral preoptic nucleus. In contrast [clarification needed], other sedatives like propofol and benzodiazepines directly increase activity of gamma-aminobutyric acid neurons. Sedation by dexmedetomidine mirrors natural sleep. As such, dexmedetomidine provides less amnesia than benzodiazepines. Dexmedetomidine also has analgesic effects at the spinal cord level and other supraspinal sites [9]. Thus, unlike other hypnotic agents like propofol, dexmedetomidine can be used as an adjunct medication to

help decrease the opioid requirements of people in pain while still providing similar analgesia.

Early recovery and extubation in the operating room is the preferred method when the pre-operative state of consciousness is relatively normal and surgery does not involve critical brain areas or extensive manipulation. In the complicated or unstable patient, the risks of early extubation may outweigh the benefits [10]. Patients with increased intracranial pressure (ICP) are prone to severe cardiac and or cerebral complications following emergence from general anesthesia and during the recovery period. Hence the present study was planned to evaluate the effect of dexmedetomidine on hemodynamic responses during tracheal extubation.

Methodology

The present study was planned in Department of Anesthesia, Nalanda Medical College and Hospital, Patna, Bihar. Total 30 Patients were enrolled in the present study. The 15 patients were enrolled in Group I as cases and 15 patients were enrolled as control patients in Group II. Group I patients received 0.5 µg/kg inj. dexmedetomidine in 100 ml normal saline slow IV infusion over 10 minutes and Group II patients received 100 ml normal saline IV infusion over a period of 10 minutes. Study drugs were given at the time of skin closure. Patients were kept nil orally for 6 hours before procedure. All patients were uniformly premeditated with inj. glycopyrrolate 0.2 mg IM 30 minutes before shifting to operation theatre.

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study. The pre anesthetic assessments of all the selected patients were done with complete history and physical examination. Routine investigations like complete blood count, blood sugar, blood urea, serum creatinine, chest X-ray and ECG were done.

Following was the inclusion and exclusion criteria for the present study.

Inclusion Criteria: ASA grade I and II, age group 18 to 50 years of either sex admitted for craniotomies for nonvascular ICSOL under general anaesthesia.

Exclusion Criteria: Patients with cardiopulmonary diseases, hepatic dysfunction, renal dysfunction, psychiatric illness, pregnant and lactating patients and any patient who required postoperative ventilation.

Results and Discussion

Extubation can be associated with several complications like coughing and respiratory complications (laryngospasm, airway obstruction, desaturation) and hemodynamic changes [11]. Numerous strategies have been used to prevent hemodynamic responses caused by emergence from anesthesia including extubation under deep anesthesia, administration of local anesthetics, vasodilators and short-acting opioids [12]. Administering vasodilators such as sodium nitroprusside, nitroglycerin, and hydralazine could be associated with complications like reflexive tachycardia and increase in the plasma renin activity [13].

Extubation can be associated with several complications like coughing and respiratory and hemodynamic alterations. These changes are usually transient and well tolerated by most patients, but may be deleterious in certain subgroups of patients. Dexmedetomidine has been successfully used to attenuate the hemodynamic responses to tracheal intubation. Basing on its characteristics of sedation, hemodynamic stability, and lack of respiratory depression, along with its relatively short half-life and analgesic effects, the present study was conducted to evaluate the effect of dexmedetomidine in a dose of 0.75 mcg/kg on hemodynamic responses during extubation, the quality of extubation, the level of postoperative sedation and the prevalence of complications.

Table 1: Demographic profile

Group	Group I	Group II
Group of	Cases	Control
No. of Cases	15	15
Variables	Mean ± SD	Mean ± SD
Age (years)	28 - 39	26 – 41
Sex		
Male	9	10
Female	6	5
Weight (Kg)	58 - 70	55 – 68
Duration of anaesthesia (minute)	182 ± 15	178 ± 14

Table 2: Comparison of changes in mean heart rate

Group	Group I	Group II
Group of	Cases	Control
No. of Cases	15	15
Time in minutes	Mean ± SD	Mean ± SD
At Drug Administration	84 ± 6	81 ± 5
After 3 mins of Drug Administration	74 ± 6	82 ± 7
After 5 mins of Drug Administration	75 ± 10	84 ± 9
At the time of extubation	89 ± 13	103 ± 12
After 3 mins of extubation	85 ± 11	98 ± 13
After 5 mins of extubation	82 ± 9	97 ± 11
After 10 mins of extubation	81 ± 8	95 ± 9
After 15 mins of extubation	77 ± 6	89 ± 8

Table 3: Comparison of changes in mean systolic blood pressure

Group	Group I	Group II
Group of	Cases	Control
No. of Cases	15	15
Time in minutes	Mean ± SD	Mean ± SD
At Drug Administration	119 ± 5	125 ± 6
After 3 mins of Drug Administration	113 ± 6	126 ± 7
After 5 mins of Drug Administration	116 ± 10	127 ± 9
At the time of extubation	123 ± 8	146 ± 9
After 3 mins of extubation	119 ± 7	139 ± 8
After 5 mins of extubation	115 ± 9	133 ± 11
After 10 mins of extubation	112 ± 9	129 ± 13
After 15 mins of extubation	109 ± 12	127 ± 13

Table 4: Comparison of changes in mean diastolic blood pressure

Group	Group I	Group II
Group of	Cases	Control
No. of Cases	15	15
Time in minutes	Mean ± SD	Mean ± SD
At Drug Administration	79 ± 7	77 ± 8
After 3 mins of Drug Administration	73 ± 6	78 ± 6
After 5 mins of Drug Administration	74 ± 6	77 ± 7
At the time of extubation	82 ± 7	96 ± 8
After 3 mins of extubation	77 ± 10	91 ± 7
After 5 mins of extubation	74 ± 6	90 ± 7
After 10 mins of extubation	73 ± 6	86 ± 7
After 15 mins of extubation	69 ± 8	83 ± 7

Dexmedetomidine activates receptors in the medullary vasomotor center, reducing norepinephrine turnover and decreasing central sympathetic outflow, resulting in alterations in sympathetic function and decreased HR and BP. In the present study, the hemodynamic parameters in the study group were significantly on higher side during extubation when compared to the control group. Dexmedetomidine 0.5 mcg/kg administered 5 minutes before the end of surgery has been shown to stabilize hemodynamics, allow easy extubation, provide a more comfortable recovery and allow early neurological examination following intracranial operations [14]. Dexmedetomidine 0.5 mcg/kg, given 5 minutes before extubation has been found to be more effective than fentanyl 1 mcg/kg in attenuating airway reflex responses to tracheal extubation and maintaining hemodynamic stability without prolonging recovery [15]. In patients undergoing vascular surgery, dexmedetomidine (plasma concentrations in the range of 0.18 to 0.35 ng/ml) attenuated the increase in HR and plasma norepinephrine concentrations during emergence from anesthesia and did not attenuate postoperative increases in HR or BP after emergence from anesthesia or affect intraoperative anesthetic or postoperative analgesic requirements [16]. An infusion of dexmedetomidine started 20 minutes before anesthesia and continued until the start of skin closure in patients undergoing supratentorial brain tumor surgery was found to blunt tachycardic response to intubation and the hypertensive response to extubation [17].

The sedative properties of dexmedetomidine are well documented. 5, 6 The hypnotic and sedative action of dexmedetomidine is thought to be mediated primarily by post synaptic α2 adrenergic receptors. These effects differ depending on receptor location; in the locus caeruleus. Decreased noradrenergic output from the locus coeruleus allows for increased firing of inhibitory neurons including the alfa‑amino butyric acid system resulting in anxiolysis and sedation [18].

Dexmedetomidine offers a unique pharmacological profile with sedation, sympatholysis, analgesia, cardiovascular stability and with great advantage to avoid respiratory depression. In particular, dexmedetomidine can provide a dose-dependent cooperative sedation that allows ready interaction with the patient. All these above-said aspects of its pharmacological profile render it suitable as an anesthetic adjuvant and also as intensive care unit sedation.

Scheinin *et al*., [19] studied the effect of dexmedetomidine on tracheal intubation, required dose of induction agent and preoperative analgesic requirements. They concluded that the required dose of thiopentone was significantly lower in the dexmedetomidine group and the drug attenuated the hemodynamic responses to intubation. The concentration of noradrenaline in mixed venous plasma was lesser in the dexmedetomidine group.

Dexmedetomidine increases the hemodynamic stability by altering the stress-induced sympathoadrenal responses to intubation during surgery and during emergence from anesthesia [20]. Jaakola *et al*., [9] in their study concluded that dexmedetomidine attenuates the increase in heart rate and blood pressure during intubation. The dose used for this study was 0.6 mcg/kg, which is almost similar to the dose used by us.

Lawrence *et al*., [21] found that a single dose of 2 mcg/kg of dexmedetomidine before induction of anesthesia attenuated the hemodynamic response to intubation as well as that to extubation. Bradycardia was observed at the 1 st and 5 th min after administration. This might have been due to bolus administration. The dose of dexmedetomidine in our study was 0.5 mcg/kg as an infusion over 10 min. Hemodynamic response was better in the dexmedetomidine group and bradycardia was not observed during our study.

Studies suggest that perioperative use of dexmedetomidine may result in a decreased risk of adverse cardiac events, including myocardial ischemia [22]. Alfa-adrenoreceptors stimulation can beneficially modulate coronary blood flow during myocardial ischemia by preventing transmural redistribution of blood flow away from the ischemic endocardium, by specific epicardial vasoconstrictive effects, leading to improvement in endocardial perfusion (the reverse steal effect) and by decreasing heart rate. This property along with hemodynamic stability and attenuation of intubation response makes dexmedetomidine an ideal anesthetic adjuvant, particularly for patients undergoing coronary bypass grafting.

Conclusion

The data generated from the present study concludes that use of dexmedetomidine before extubation attenuates the hemodynamic response to extubation. It enables smooth extubation of the trachea and provides adequate sedation postoperatively. Dexmedetomidine increases the incidence of bradycardia and hypotension, but does not cause side effects like respiratory depression, laryngospasm, bronchospasm, undue sedation and desaturation.

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