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EFFECT OF A SINGLE PRE-OPERATIVE DOSE OF DEXMEDOTOMIDINE VERSUS FENTANYL ON ANESTHETIC REQUIREMENT AND PERI-OPERATIVE HEMODYNAMIC STRESS RESPONSE

Anesthesiology

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ABSTRACT

Laryngoscopy is a part of intubation which leads to stress response. Dexmedetomidine and fentanyl attenuate stress response during laryngoscopy ,provide hemodynamic stability and reduce anesthetic requirements. Prospective randomized controlled study was carried out in 99 patients of ASA grade I and II, age group of 18-60 years, scheduled for surgery under general anesthesia. Patients were randomly divided in two groups.50 patients of group I received a single preoperative dose of dexmedetomidine 1 µg/kg and 49 patients of group II received injection fentanyl 2µg/kg 10 minutes prior to intubation. Intraoperative pulse, blood pressure,spo2,BIS value were recorded before induction,during laryngoscopy and intraoperatively till extubation. Adverse effects like nausea, vomiting, bradycardia, hypotension were noted.We observed that Dexmedetomidine and Fentanyl reduce stress response during laryngoscopy.Dexmedetomidine reduces the usage of anesthetic requirements more as compared to fentanyl,hence provide smooth recovery without undue sedation.

KEYWORDS

Endotracheal Intubation, Stress Response, Dexmedetomidine, Fentanyl

INTRODUCTION:

The stimulation of sympathetic nervous system by laryngoscopy and intubation during induction of general anesthesia causes release of catecholamines which leads to increase in arterial blood pressure, tachycardia and arrhythmia causing hemodynamic instability. This response reaches its maximum level within 1 min and ends within 5-10 min after intubation.[13] The degree of the reflex response to laryngoscopy and intubation will depend upon the depth of anesthesia, patient's age, co-existing medical conditions like hypertension, diabetes or heart disease, etc[13]

The series of physiological changes (stress response) due to anesthesia and surgery in the form of endocrine or autonomic disturbances may increase the risk during perioperative period. Understanding of these physiological changes, knowledge of the precipitating factors and applying modulatory therapeutic methods in time have reduced peri-operative morbidity and mortality in past few years.[15] The research work for effective blockage of the pressor response using various techniques and pharmacological methods like; increasing depth of anesthesia, topical spray of local anaesthetic agent (lignocaine), intravenous drugs like (lignocaine, esmolol, Fentanyl, Clonidine), etc have been carried out.[23] Inhalation anesthesia is used but requires deep levels, which may delay recovery after short operation and can cause cardiovascular depression. Adrenergic blockers are effective but longer acting agents outlast the transient intubation response and may cause hypotension and bradycardia.[6]

Dexmedetomidine, adrenergic agonist with high selectivity for α_2 receptors provides sedation, anxiolysis, hypnosis, analgesia and sympatholysis.[1]

Fentanyl, a short acting, synthetic opioid preserves cardiac stability at therapeutic doses and effectively blocks the sympathetic stress response to surgical stimulus and provides further hemodynamic stability.(Donald martinet et al,1982).

The Bispectral Index (BIS) is a derived electroencephalographic parameter that has been extensively validated as a monitor for depth of anesthesia. BIS value in the range of 40–60 are recommended as an indicator of adequate depth of general anesthesia and may be used to guide titration of anesthetic agents, instead of routine clinical signs.[25]

The aim of this study is to compare the effects of Dexmedetomidine and Fentanyl given as a bolus dose prior to induction in blunting the hemodynamic stress response to laryngoscopy and endotracheal intubation and to provide peri-operative hemodynamic stability as well as to reduce intraoperative anesthetic requirement and provide smooth recovery profile with the usage of BIS monitoring.

AIM AND OBJECTIVE

1. To compare the effect of single pre-operative dose of Dexmede tomidine versus Fentanyl on hemodynamic response during laryngoscopy and intubation.
2. To compare a single pre-operative dose of Dexmedetomidine versus Fentanyl on anesthetic requirement.
3. To compare the cost effectiveness of both the drugs for maintenance of surgical plane of anesthesia and quantifiable measure of the sedative and hypnotic effect of anesthetic agents on CNS with the usage of Bispectral Index Monitoring.
4. To assess post-operative sedation score and pain score.

Review of literature:-

The noxious stimuli during induction of general anesthesia and surgery leads to increase in plasma catecholamine concentration due to increase in sympathetic adrenal activity. This increased concentration of catecholamine causes increase in blood pressure, heart rate and Oxygen consumption leading to hemodynamic instability.. Many research work for attenuation of stress response by different drugs and techniques have been studied in past and recent years, with varied outcome.

In 1992 B. Scheinin et al studied the effect of Dexmedetomidine on sympathoadrenal response to tracheal intubation along with its dose sparing effect on induction agent (Pentothal) and opioids (Fentanyl).One Group was given 0.6 µg/kg Dexmedetomidine 10 minutes before induction and other Group received normal saline before 3 minutes of induction.They concluded that Dexmedetomidine attenuates the cardiovascular and sympathoadrenal responses to laryngoscopy and intubation and decreases anaesthetics and opioid requirements during and after surgery. [2] In 1997, C. J. Lawrence et al, had carried out a double-blind, placebo-controlled study. They investigated the effect of a single pre-induction intravenous dose of Dexmedetomidine (2µg/kg) on anaesthetic requirements and peri-operative hemodynamic stability in 50 patients undergoing minor orthopaedic and general surgery.

Patients were anesthetised with Nitrous Oxide (2/3) /Oxygen (1/3)/Fentanyl and supplemented with Isoflurane if necessary. they stated that a bolus dose of Dexmedetomidine before induction can effectively blunt laryngoscopic stress response, reduce plasma catecholamine levels and also reduce peri-operative requirement of anaesthetic agents.[5]

METHOD:-

After approval by institutional ethical committee and taking written informed consent, 99 patients of either sex, between age Group of 18 – 60 years, ASA Grade I and Grade II, scheduled for surgery under general anesthesia were randomly selected and included in this study.

Thourough preoperative examination, basic laboratory investigations like complete haemogram, blood sugar, renal function test, ECG and CHEST X-RAY were carried out.

All patients were confirmed for nil by mouth status and were premedicated with injection Glycopyrrolate 5-10 µg/kg i.m. 30 minutes before induction of anesthesia.Pre-operative vitals and BISvalues were noted in the operation room before giving the study drug and considered as baseline.Patients were randomly divided into 2 Groups.Group1- Received Inj. Dexmedetomidine 1 µg/Kg 10 and Group 2- Received Inj. Fentanyl 2 µg/kg 10 minutes before induction.

In both the Groups general anesthesia was administered after preoxygenation for 3 minutes with Inj. Sodium Thiopentone (2.5%) 4-6 mg/kg to produce loss of eyelash reflex followed by Inj. Succinylcholine 1.5-2 mg/kg. Patients were ventilated with 100% O_2 and on achieving complete relaxation intubation was done with appropriate sized cuff portex endotracheal tube.Anesthesia was maintained in both the Groups with O_2 (66%), N_2O (33%), Isoflurane, Inj. Vecuronium 0.1 mg/kg as initial dose and 0.02 mg/kg as maintenance dose, and ventilation was continued with IPPV (intermittent positive pressure ventilation).

Pulse, blood pressure Spo_2 and BIS value were recorded before induction, during laryngoscopy, every 1 minute upto 5 minutes after intubation and then every 10 minutes till extubation.Volatile anesthetics were titrated to maintain BIS value between 40-60, ideal for surgical plane of anesthesia.Patients were reversed with injection Glycopyrrolate (0.008mg/kg) and injection Neostigmine (0.05mg/kg) intravenously at the end of the surgery. Duration of surgery, duration of anesthesia, total dosage of Vecuronium (mg) was recorded .Total dosage of Isoflurane (ml/hr) was measured by using EHRENWORTH AND EISENKRAFT formula. (3 x FGF x Volume%) Post-operative vitals, Ramsay sedation score and Visual Aaxnalouge Score for pain were recorded.Patients were observed for adverse effects like nausea, vomiting, bradycardia, hypotension.

OBSERVATION AND RESULTS:

RESULTS:-99 patients were included in the study. Baseline characteristics of both the groups were not significantly different.

AGE &WEIGHT

PARTICULARS	GROUP 1 (MEAN±SD)	GROUP 2 (MEAN±SD)	P VALUE
AGE(YEARS)	33.18±9.8	36.84±11.38	P>0.05
WEIGHT(KG)	58.4 ±7.63	54.69 ± 8.8	P>0.05

TABLE 2 Sex Distribution Of The Patients

GROUP	MALE(%)	FEMALE(%)
GROUP 1	17(34%)	33(66%)
GROUP 2	16(33%)	33(67%)

TABLE 3 Duration of Surgery:-

DURATION OF SURGERY(MINUTES)	GROUP 1	GROUP 2	P VALUE
MEAN	109	101.63	P>0.05
SD	20.4	21.3	P>0.05

There was no significant difference in age,weight,sex and mean duration of surgery between two Groups. (P>0.05).

TABLE 4:-Mean Heart Rate

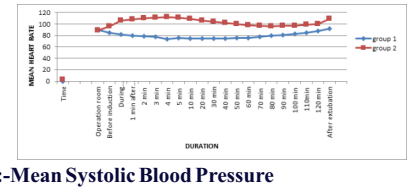


TABLE 5:-Mean Systolic Blood Pressure

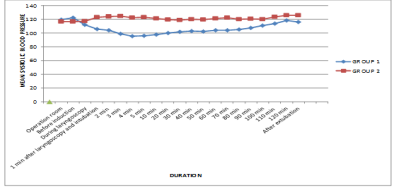
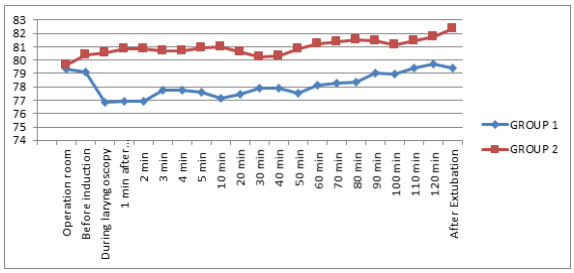


TABLE 6:- Mean Diastolic Blood Pressure:-



- Baseline mean heart rate, systolic blood pressure and diastolic blood pressure were comparable in both the groups. There was no statistical difference between them (P>0.05).
- The significant rise in the mean heart rate, systolic blood pressure and diastolic blood pressure were observed during laryngoscopy ,at every 1 minute upto 5 minutes after intubation and then every 10 minutes till extubation in Group 2 (Fentanyl) compared to Group 1(Dexmedetomidine),which was statistically significant(P<0.001).
- There was no difference observed between BIS value and spo2 in both the groups.

TABLE 7 Volume (ml/hr) of Isoflurane usage:-

GROUPS	MEAN±SD	P value
Group 1	7.41±1.34	P<0.001
Group 2	14.25±2.43	

Usage of isoflurane was very less in dexmedetomidine group as compared to fentanyl group with BIS monitor, hence it was possible to maintain adequate depth of anesthesia and reduce requirement of anesthetic agents. Thus using BIS monitor, during surgery and anesthesia, proves cost-effective.

In Fentanyl Group, 11 patients had mild to moderate pain (VAS score 1) in the immediate post-operative period, while in Dexmedetomidine Group none of the patient had pain post-operatively (P <0.05).

None of the patients was sedated after discontinuation of anesthesia

TABLE 8 Adverse Effects:-

Adverse effects	No. of patients	
	Group 1	Group 2
Nausea/ Vomiting	0	0
Shivering	0	0
Hypotension	0	0
Bradycardia	1	0

DISCUSSION:-

In modern anesthesia practice, knowledge regarding the series of physiological changes (stress response),that occur during and after laryngoscopy is essential. Stress response under anesthesia has been universally recognized phenomenon (J. Zargar et al,2002).Stress response is accompanied by an increased stimulation of sympathetic efferent tracks, resulting in adrenergic response.

The adrenergic response due to stress leads to release of catecholamines in the circulation, which can cause severe hypertension, tachycardia, cardiac arrhythmias, myocardial ischemia, left ventricular dysfunction and rupture of cerebral aneurysm in susceptible individuals.[1]

Direct laryngoscopy and intubation are noxious stimuli that can provoke stress response in the cardiovascular, respiratory and other physiological system The magnitude of the response is greater with increasing force and duration of laryngoscopy. The response reaches its maximum level within 1 min and ends in 5-10 min after intubation.[13]. So we should limit the time for laryngoscopy to prevent rise in blood pressure. These changes are well tolerated by healthy individual, but may prove fatal in patients with hypertension, coronary artery disease and cerebrovascular disease.(Anil D mlde et al,2007)

Recently, various methods have been tried for reducing laryngoscopic stress response.

The present study was undertaken to evaluate and compare the effects of Dexmedetomidine and Fentanyl on laryngoscopic stress response and hemodynamic stability during general anesthesia.

In 1997,C.J. Lawrence et al conducted double-blind placebo controlled study to investigate the effect of a single pre-induction intravenous dose of Dexmedetomidine 2 µg/kg on anesthetic requirement and peri-operative hemodynamic stability.

They observed that laryngoscopy and tracheal intubation resulted in 0 and 31 mm of Hg increase in the mean systolic blood pressure, 1 and 26 mm of Hg increase in the mean diastolic blood pressure and 13 and 29 beats/minutes increase in the mean heart rate in Dexmedetomidine and Placebo Groups, respectively. The two Groups were compared during first 51 minutes after tracheal intubation. Mean systolic blood pressure, mean diastolic blood pressure and mean heart rate were significantly lower in the Dexmedetomidine Group during this period as compared to placebo Group($P<0.001$). One minute after post-extubation the mean systolic blood pressure and heart rate were significantly lower in the Dexmedetomidine Group as compared to placebo Group.($P<0.001$).Over a three hour period in the post anesthesia care unit, the mean systolic blood pressure, mean diastolic blood pressure and mean heart rate were significantly lower in Dexmedetomidine Group.($P<0.001$)[5]

Dexmedetomidine has sedative and analgesic property via central actions in the locus coeruleus and in the dorsal horn of the spinal cord. The primary action of all α_2 adrenergic agonist is an inhibition of norepinephrine release causing an attenuation of central nervous system excitation. So it will cause dose dependant decrease in the heart rate and blood pressure and also has dose sparing capacity of anesthetic agent.[8]

Dexmedetomidine has also been used in normal adult as well as in patients having coronary heart disease and it provides hemodynamic stability perioperatively.

Narcotics may block afferent nerve impulses resulting from stimulation of pharynx and larynx during intubation. Atweh and kuhar (1977) had found high concentration of opiate receptors in the solitary nuclei of the 9th and 10th cranial nerves, associated with visceral afferent fibers of these nerves which originate in the pharynx and larynx.

Further, vagal motor nuclei involved in monosynaptic pharyngeal and laryngeal motor reflex, also have a high concentration of opiate receptors. These receptors provide a possible mechanism for the blunting of the response to laryngeal stimulation (Donald E martin et al, 1982).

Fentanyl, a short acting, synthetic opioid, preserves cardiac stability at therapeutic dosages. It also effectively blocks the sympathetic stress response to surgical stimulus and provides further hemodynamic stability.

Fentanyl produces analgesia, sedation and in large doses unconsciou sness and anesthesia by virtue of its agonist effect on opioid receptor located in thalamus, hypothalamus, reticular system and gamma neurons. It inhibits release of substance-P along with pain pathway and release dopamine and acetylcholine in central nervous system. High dose of opioids blunt the neuroendocrine stress response to surgery.[21,22]

It was inferred that, Dexmedetomidine an α_2 agonist agent, when used as a pre-induction drug, attenuates stress response to laryngoscopy and tracheal intubation, thus reduces heart rate and blood pressure perioperatively.

Fentanyl, an opioid agonist agent, though increases the heart rate & blood pressure during laryngoscopy and tracheal intubation but it was significant when compared with the baseline value of that Group.

Rise in mean heart rate was maximum upto 23% in Group 2(Fentanyl) and mean systolic blood pressure was 8% and mean diastolic pressure was 1.51% when compare to the baseline value, but the rise was not significant when compare with the control group of the other studies where the rise in mean heart rate was approximately 29%,mean systolic blood pressure was 21% and mean diastolic blood pressure was 46%.

So it was inferred that Fentanyl can also helps to attenuate laryngoscopic stress response, because the rise in hemodynamics after laryngoscopy and intubation was within the normal limits of heart rate and blood pressure thus may be recommended in patients' with cardiovascular instability, ischemic heart disease and hypertension.

CONCLUSION

- From our study we concluded that :-

1) A single pre-operative dose of Dexmedetomidine provides better hemodynamic stability during laryngoscopy and in the perioperative period as compared to Fentanyl by attenuation of sympathoadrenal response.
2) Dexmedetomidine and Fentanyl when used with BIS monitoring, provide adequate depth of anesthesia during surgery.
   i.Dexmedetomidine reduces the usage of anesthetic agents required during surgery as compared to Fentanyl, Hence it is more cost-effective.
   ii.By reducing requirement of inhalational agents, Dexmede tomidine helps to reduce theatre pollution as compare to Fentanyl, when there is poor scavenging system.
3) Dexmedetomidine provides smooth recovery without undue sedation with better analgesia compare to Fentanyl in post-operative period, thus reduces the requirement of analgesics.

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