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ORIGINAL ARTICLE

EFFECT OF DEXMEDETOMIDINE ON STRESS RESPONSE TO ENDOTRACHEAL INTUBATION

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ABSTRACT: Laryngoscopy as well as tracheal intubation cause changes in the hemodynamics of the patients. A similar set of hemodynamic events have been noticed by various studies during tracheal extubation also. These responses may produce myocardial ischemia or infarction in susceptible patients. Various agents like lignocaine, esmolol, sodium nitropruside, nitroglycerine etc. have been proved to be effective in attenuating these response. Dexmedetomidine, an alpha 2 agonist have been successfully used for attenuating the sympathetic response during endotracheal extubation. We conducted an observational study to examine the role of dexmedetomidine on hemodynamic response during endotracheal intubation. A bolus dose of Dexmedetomidine 0.7-1 mcg /kg over 10mts prior to endotracheal intubation provided hemodynamic stability than inj. lignocaine hydrochloride (Gold standard) .This can prove beneficial for patients where the stress response to intubation is highly undesirable.

KEYWORDS: Dexmedetomidine, lignocaine hydrochloride, endotracheal intubation.

INTRODUCTION: Laryngoscopy as well as tracheal intubation cause changes in the hemodynamics of the patient.(1) A similar set hemodynamic events have been noticed during tracheal extubation also.(2) These responses may produce myocardial ischemia or infarction in susceptible patients. Various agents like lignocaine, esmolol, sodium nitropruside, nitroglycerine etc have been proved to be effective in attenuating this response.(3) Dexmedetomidine an alpha 2 agonist have been successfully used for attenuating the sympathetic response during endotracheal extubation. We conducted an observational study to examine the role of dexmedetomidine on hemodynamic response during endotracheal intubation.

METHODOLOGY: After being approved by the board of studies, informed consent was obtained from 60 adult patients between the ages of 20-60 years of both sexes, conforming to ASA (American Society of Anesthesiologists) physical status I or II, weight 40-60 kg scheduled for elective surgical procedures lasting for 1-2 hours. Patients with cardiovascular, respiratory &renal diseases were excluded from the study. All patients were divided into two groups of 30 each.

Pre-operative evaluation and necessary investigations were done on the day before surgery. Investigations included heamogram, urine analysis, random blood sugar, chest x-ray, electro cardiogram. A baseline heart rate and blood pressure were recorded preoperatively on the day of surgery and after premedication. Premedication was done with Inj. Fentanyl 1mcg/body wt intravenously, Inj. Ondansetron 4mg, Inj.Midazolam.02mg/kg to all patients 1hour prior to anesthesia.

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Group A patients received Inj Dexmedetomidine 0.7mcg/kg diluted to10 ml in normal saline, over 10mnts time before laryngoscopy and intubation. Group B patients received Inj Xylocard (preservative free lignocaine hydrochloride) 1.5mg/kg body wt 2 minutes before intubation.

ASA standard monitors were used for monitoring during the procedure. Preinduction blood pressure and heart rate were recorded before the start of dexmedetomidine and xylocard. After pre-oxygenation for 3 minutes, induction of anesthesia was achieved with a sleep dose of thiopentone sodium (confirmed with loss of eye lash reflexes.) Endotracheal intubation was done after achieving muscle relaxation with suxamethonium. Pulse rate and Blood pressure were monitored at the start of bolus drug injection and subsequently at 3minutes, 5minutes, and 10 minutes after intubation. Maintenance of anesthesia was done using vecuronium bromide which is an intermediate acting muscle relaxant, relatively cardio stable in both groups.

We excluded the patients who required repeated attempts of laryngoscopy and intubation and cases of prolonged intubation time (more than 45 seconds). A fall in heart rate <50 is considered as brady cardia and > 90 is treated as tachy cardia. A systolic blood pressure >130 mmHg is considered as hypertension and <80 is as hypotension.

Review of Literature: DEXMEDETOMIDINE -is a highly selective α2 adrenergic agonist, most often used for short term sedation in patients in intensive care, for short surgical procedures, to maintain the hemodynamic stability during extubation etc. The main advantage of this drug is it does not produce serious respiratory side effects, in addition it has got an opioid –sparing effect. The analgesic, sedative/hypnotic effect, and anxiolytic properties of dexmedetomidine make this drug potentially useful for pain full procedures. Systemic administration of dexmedetomidine and its congener clonidine has been reported to have their effects by both supraspinal as well as spinal mechanisms. It is thought that the central adrenoreceptors in the locus ceruleans and the dorsal horn of the spinal cord are involved in this activity. This drug enhances the effects of analgesics without, increasing the incidence of side effects.[4]

Mechanism of action- From anesthesiologist view point, neuronal hyperpolarisation is a key element in the mechanism of action of alpha-2 adrenergic receptor agonists. In general, presynaptic activation of alpha-2 adrenergic receptor inhibits the release of norepinephrine, terminating the propagation of pain signals and inhibits sympathetic activity and thus can decrease blood pressure and heart rate. Alpha 2 receptors are found in the peripheral and central nervous systems, platelets, and other organs including the liver, pancreas, kidney, and eyes. Stimulation of receptors in the brain and spinal cord decreases neuronal firing, causing hypotension, bradycardia, sedation, and analgesia. The responses from other organs include decreased salivation, decreased secretion, and decreased bowel motility, inhibition of rennin. reduction in intraocular pressure, decreased insulin release from pancreas.[5]

The mechanism of action of dexmedetomidine differs from clonidine as it posses selective alpha-2 adrenoceptor agonism especially for 2A subtype of this receptor, which causes it to be much more effective and analgesic agent than clonidine. A biphasic effect is seen after administration of dexmedetomidine.[6] Majority of patients receiving dexmedetomidine are effectively sedated but are easily arousable unlike other agents.[7] It does not appear to have any direct effect on heart.[8] A bolus dose if 1mcg/kg results in transient increase in BP, and reflex fall in heart rate. But Later reduction in BP occurs due to central sympathetic flow reduction.[9,10]

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The reduction in noradrenaline release caused by presynaptic alpha2 receptor stimulation result in reduction in BP and heart rate.[11] The respiratory depression caused by dexmedetomidine has been reported to be much less than other sedatives. Dexmedetomidine, a short acting alpha 2 agonist was approved by the U.S Food and Drug Administration (FDA) in 1999. It possesses anxiolytic, anesthetic, hypnotic and analgesic properties. Patients receiving Dexmedetomidine infusions are easily aroused yet appear calm and comfortable. When they remain unstimulated, patients return to a hypnotic state.

The primary effect of dexmedetomidine on heart rate is negative chronotropy, effected by blocking the cardio accelerator nerves as well as by augmenting vagus nerve. The alpha-2 agonist action of dexmedetomidine on the autonomic ganglia includes decreasing sympathetic out flow which leads to hypotension and bradycarcia. Action on the peripheral vasculature depends on dose of dexmedetomidine: vasodilatation is the result of sympatholysis which occurs at low doses, and vasoconstriction is the result of direct action on smooth muscle at high doses. The pre-synaptic and post-synaptic effects of alpha-2 agonist diminish nor-epinephrine release and inhibit sympathetic activity.

Adverse Effects: The most notable effects observed are first degree heart block and second degree heart block. No hemodynamic compromise was noted with the AV block and the heart block resolved spontaneously within one minute. Rarely observed adverse effects include pyrexial reactions, agitation, dizziness, hypotension, hypertension, nausea, bradycardia, fever, vomiting, hypoxia, tachycardia and anemia Dexmedetomidine , a short acting alpha 2 agonist was approved by the U.S Food and Drug Administration (FDA) in 1999.It possesses anxiolytic, anesthetic, hypnotic and analgesic properties. Patients receiving Dexmedetomidine infusions are easily aroused yet appear calm and comfortable. When they remain unstimulated, patients returned to a hypnotic state.

LIGNOCAINE HYDROCHLORIDE: Preservative free lignocaine is used as an adjuvant in anesthetic practice.[12.13]
It is an intermediate acting local anesthetic agent.

Mechanism of Action:

1. Membrane stabilizing effect.
2. Central analgesic effect
3. Mild sedative effect.

Lignocaine –uses:

1. Local anesthetic agent in topical anesthesia.
2. In central neuraxial block
3. As an antiarrythmic agent to treat ventricular arrhythmias
4. Agent to decrease ICP, IOP etc.
5. To abate the sympathetic stimulation during laryngoscopy &Intubation.

I/V –Lignocaine-used in anesthesia practice as an adjuant to opiods to attenuate sympathetic stimulation during laryngoscopy & intubation. However smaller dose 1.5-2mg/kg body weight, donot appear to be effective in abating the hemodynamic response during laryngoscopy &intubation.

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Adverse effect- over dosage can produce CNS & CVS toxicity.

CNS-Dizziness, drowsy, Euphoria, psychosis, convulsions.

CVS-Heart block, bradycardia etc.

Various studies are available in view of the effectiveness of Dexmedetomidine: It's effect in abating the hemodynamic response during extubation. To increase the analgesic effect of anesthetic agents dexmedetomidine is widely used in perioperative period. Use of dexmedetomidine in intraoperative period has got excellent opiod sparing effect in the post-operative period also.[14] Dexmedetomidine is widely used in ICU as a sedative agent in ventilator patients.

By considering the above facts we are expecting that they can prove beneficial for cardiac patients where the stress response to intubation is highly undesirable.

All most all studies regarding dexmedetomidine is done in groups of 20-25 patients and they showed excellent results. So we conducted the study in a sample size of 30 each.

RESULTS: Patients in-group I were compatible with group II with regard to age (45±8vs50±3) and weight (55±5 vs52±4). Comparison of BP of the two different groups who were exposed to two different treatment was done by using independent t-test. In each measurement time there exists significant difference in BP at P=0.01. Before treatment, BP was higher in the case of group I (Those who were treated with Dexmedetomidine) than group II (Those were treated with Xylocard). However after treatment, BP is significantly lower in the case of group I than group II. There was an increase noted in the case of group II. The reduction in Bp was noted in the case of subjects who were treated with Dexmedetomidine

Comparison of pulse rate of the two different groups who were exposed to two different treatment was done by using independent t-test. In each measurement time there exists significant difference in pulse rate at P=0.01. Before treatment, pulse rate was higher (p=0.024) in the case of group 1 (Those who were treated with Dexmedetomidine) than group II (Those were treated with Xylocard). However after treatment, pulse rate is significantly lower in the case of group I than group II.

Comparison of BP:

BP	Treatment	Mean	Std. Error	t-value	p-value
Pre-op	Dexmedetomidine	125.3	2.1	3.064**	0.003
	Xylocard	115.8	2.3		
3'	Dexmedetomidine	121.7	2.0	12.381**	< 0.001
	Xylocard	156.6	2.0		
5'	Dexmedetomidine	118.6	1.6	13.668**	< 0.001
	Xylocard	154.0	2.1		
10'	Dexmedetomidine	110.2	1.7	13.794**	< 0.001
	Xylocard	146.2	2.0		

Table 1

** significant at 0.01 levels;

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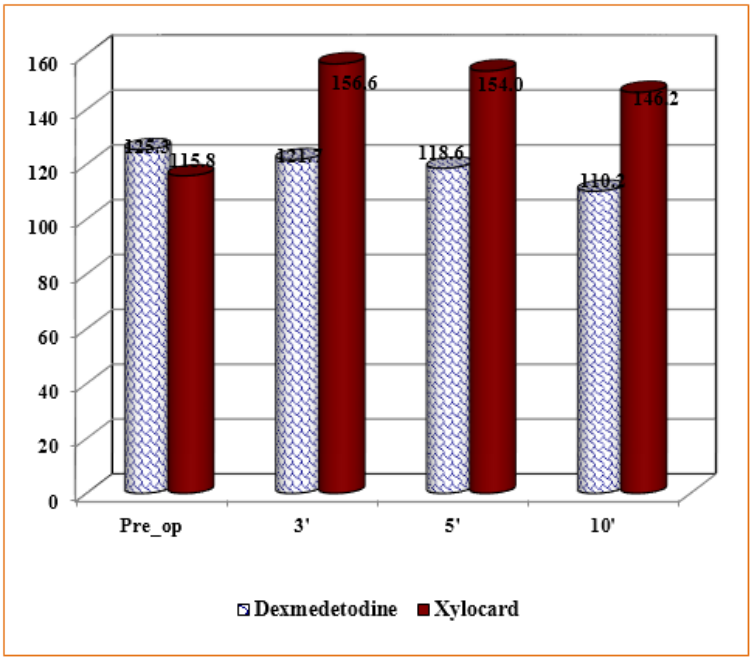

Graph 1

Comparison of BP of the two different groups who were exposed to two different treatment were done by using independent t-test. In each measurement time there exists significant difference in BP at P=0.01. Before treatment, BP was higher in the case of group 1 (Those who were treated with Dexmedetomidine) than group II (Those were treated with Xylocard). However after treatment, BP is significantly lower in the case of group I than group II. There was an increase was noted in the case of group II. The reduction in Bp was noted in the case of subjected who were treated with Dexmedetomidine.

Comparison of pulse rate:

Pulse rate	Treatment	Mean	Std. Error	t-value	p-value
Pre-op	Dexmedetomidine	80.3	1.3	2.315*	0.024
	Xylocard	75.7	1.5		
3’	Dexmedetomidine	80.6	1.2	10.971**	< 0.001
	Xylocard	102.9	1.6		
5’	Dexmedetmiodine	77.5	1.4	11.590**	< 0.001
	Xylocard	99.5	1.3		
10’	Dexmedetomidine	73.2	1.1	11.463**	< 0.001
	Xylocard	97.5	1.8		

Table 2

** significant at 0.01 levels; * significant at 0.01 levels.

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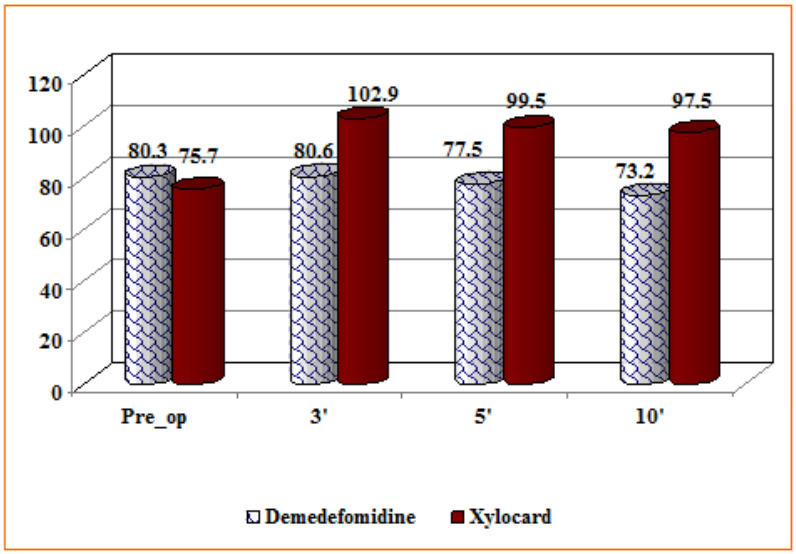

Graph 2

Comparison of pulse rate of the two different groups who were exposed to two different treatment were done by using independent t-test. In each measurement time there exists significant difference in pulse rate at P=0.01. Before treatment, pulse rate was higher (p=0.024) in the case of group 1 (Those who were treated with Dexmedetomidine) than group II (Those were treated with Xylocard). However after treatment, pulse rate is significantly lower in the case of group I than group II.

CONCLUSION: A bolus dose of Dexmedetomidine 0.7-1 mcg /kg body wt over 10mts prior to endotracheal intubation provided hemodynamic stability than inj .Lignocaine hydrochloride (gold standard) .This can prove beneficial for patients where the stress response to intubation is highly undesirable.

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