Comparative Evaluation of Dexmeditomidine & Fentanyl in Terms of Cardiovascular Stress Response During Anesthetic Airway Management in Major Surgical Procedures

Niraj Rathod[1], Sunil Valand[1], Seema Rawat[2], Komal Makwana[3]

[1]Assistant Professor, SBKS Medical Institute & Research Centre, Waghodiya, Pipariya, Gujarat, [2]Professor, C.U. Shah Medical College and Hospital Dudhrej Rd, Laxminarayan Society, Surendra Nagar, Gujarat , [3]Assistant Professor, GMERS Medical College Gotri, Old TB hospital Campus, Gotri Rd, Gotri, Vadodara, Gujarat

Abstract

Background- airway management both in operation theatre and during emergencies remains challenge because of cardiovascular stress response & inflammatory mediators during procedure exhilarating the stress response itself leading to catastrophic events. This study is aimed to evaluate comparative efficacy of dexmedetomidine over fentanyl because of it have not only as sympatholytic also as anti-inflammatory properties. Study was orchestrated at tertiary care centre in western India after approval of institutional scientific & ethical committee. Methodology Study group include 50 patients of either sex aged between 18 to 55 years who were admitted for major surgical procedure and given consent for inclusion. Study group divided in two group for record & statistical analysis of parameters like heartrate, mean arterial pressure at various interval during surgery to ascertain the superiority of dexmedetomidine vs fentanyl in stabilizing cardiovascular stress response.

Keywords: *Airway management, Anaesthesia, cardiovascular stress, Dexmedetomidine, inflammatory mediators, fentanyl*

Introduction

An airway management is first and very essential part of anesthetic management and critical care of the patient that why it's core in competency based medical education. The medical science has been fighting against the challenges of cardiovascular stress response to tracheal intubation for long time. Airway maneuvers like Laryngoscopy, tracheal intubation & extubation and inflammatory mediators released during these all are to blame for incitement to cardiovascular instability & stress. This is sympathetic stress response which results in raised blood pressure and heart rate due to rise in plasma concentration of catecholamine and other mediators. Extensive research work is done indicating that increase in sympathoadrenal activity with inflammatory substance release due to airway manipulation may result in hypertension, tachycardia and arrhythmias which can be minimized by use of dexmedetomidine [1,2,3] Anesthetists for many years trying to maintain stability of cardiovascular system in vivo. [4] Laryngoscopy and tracheal intubation are

Corresponding Author:
Komal Makwana
(MD Physiology, Assistant Professor, GMERS Medical College Gotri, Old TB hospital Campus, Gotri Rd, Gotri, Vadodara, Gujarat 390021
Mobile no- 7984288337, 8128652117,
mail: drkomalmakwana@gmail.com

associated with a sympathetically driven increase in blood pressure by 40-50% and heart rate by 20% which is threatful for patients having cardiovascular and cerebrovascular disease [4,5,6] already so much research work done in defining role of drug regimens like opioids, barbiturates, benzodiazepines, beta blockers, calcium channel blockers, vasodilators have been used from time to time for attenuating the stress response to laryngoscopy and intubation. [4,5]

Aim of the Study

comparative evaluation of dexmedetomidine & fentanyl in terms of cardiovascular stress response during anesthetic airway management in major surgical procedures to ascertain superiority of any drug.

Material and Methods

This study was carried out at C.U. Shah Medical College and Hospital, Surendra Nagar, after obtaining scientific & ethical committee approval. Informed written consent was taken from all patients. 50 patients in the age group 18-55 year of either sex, belonging to (American society of anesthesiologists) ASA grade I and II scheduled for elective surgical procedures under General anesthesia were included. Group F: Inj Fentanyl citrate 50 µg /ml - 2ml ampoule & for Group D: Dexmedetomidine (100µg/ml- 2ml ampoule) Normal saline (25 ml)

Inclusion criteria were 1. Patients aged between 18-55 years 2. Patients of either sex male or female 3. Patients with ASA grade I & II 4. Patients scheduled for elective surgical procedure under general anesthesia.

Exclusion criteria: were 1. Patients with anticipated difficult airway 2. Patients with cardiac, coronary, renal, hepatic, cerebral diseases and peripheral vascular diseases. 3.Obese patients (BMI>30) or malnourished 4. Patients on drugs like antihypertensive, sedative, antidepressant

Technique of anesthesia/Procedure: 50 patients aged between 18 to 55 yrs belonging to ASA grade I & II were randomly divided into 2 groups, each group consists of 25 patients Group F [Fentanyl group] Group D [Dexmedetomidine group]. After confirmation of NBM status an intravenous line was secured with 18G cannula & preloading with 10 ml/kg of Ringer lactate done over 30 min for all patients. In premedication Inj Glycopyrrolate 0.2 mg, Inj Ondansetron 4 mg & Inj Ranitidine 150 mg IV was given. Basal systolic blood pressure (SBP)(T0), diastolic blood pressure (DBP) (T0), Mean arterial pressure (MAP)(T0), heart rate and SpO2 (T0) were recorded after 5 min of settling in the OR. Group F [Fentanyl group] patients received IV.Inj Fentanyl 2 µg/kg in 10ml normal saline. Group D [Dexmedetomidine group] patients received IV. Inj Dexmedetomidine 1µg/ kg in 25 ml normal saline infused over 10 mins with the help of syringe pump.

Systolic blood pressure (SBP)(T1), Diastolic blood pressure (DBP)(T1), Mean arterial pressure (MAP)(T1), heart rate and SpO2 (T1) were recorded. All patients were pre- oxygenated for 3 mins with 100% oxygen & patients were induced with Inj Propofol 2mg/kg (1%) IV. After successful check ventilation with 100% oxygen, Intravenous Inj succinylcholine 2mg/kg given to facilitate laryngoscopy & intubation. Oxygenation continued by positive pressure mask ventilation using Bains circuit.

After induction, endotracheal intubation was done. SBP, DBP, MAP, Heart rate, SpO2 were recorded. Anesthesia maintained with 50% N2O, 50% O2, Isoflurane, controlled ventilation with intravenous atracurium 0.5 mg/kg as loading dose and 0.1 mg/kg as maintenance dose. SBP, DBP, MAP, Heart rate, SpO2 were recorded at 1 (T2), 3 (T3), 5 (T4), & 10min (T5) after laryngoscopy & intubation.

Table 1 parameters coding explained

Sequence of SBP, DBP, MAP, HeartRate, spo2 Recording	CODING: T- time, 0to5 numerical codes minutes as below mentioned
Basal reading when the patient is shifted to OT,	T0
At Induction (with propofol + succinyl choline)	T1
At 1 min after intubation	T2
At 3min after intubation	T3
At 5min after intubation	T4
At 10min after intubation	T5

Results: Statistical analysis was performed by descriptive and inferential statistics using the student's unpaired *t*-test, Graph Pad Prism (version 5.0; Graph Pad Software Inc., California, USA). All data are presented as mean ± SD (standard deviation). Demographic data analysis and justification of study population was inferred by student's t test. ($p<0.01$) – Statistically highly significant, ($p<0.05$) – Statistically significant, ($p> 0.05$) – Statistically Not Significant (NS),

Table 2: Age and sex wise distribution

AGE GROUPS IN YEARS	FENTANYL			DEXMEDETOMIDINE		
	Male M	Female F	Total M & F	Male M	Female F	Total M & F
18-36	6	6	12	6	6	12
37-55	7	6	13	6	7	13
total subjects 50	13	12	**25**	12	13	**25**

Table 3: Comparison of demographic parameters in Group F(Fentanyl) and Group D(Dexmedetomidine) and results of t-test:

Parameters	Group F Mean ± SD	Group D Mean ± SD	T	P
Weight (kilograms)	55.160±5.836	53.880±5.805	0.7775	0.4407 NS
AGE (years)	38.000±13.143	37.08±12.747	0.2512	0.8027 NS

Table 4: Showing the intergroup comparison of mean heart rate (bpm) changes in response to laryngoscopy and intubation between Fentanyl Group F and Dexmedetomidine Group D

TIME	Group F	Group D	p- value	t-value	Remarks
T0 (Basal)	89.560 ± 11.612	88.320± 12.058	0.7127	0.3704	NS
T1Induction	85.92±10.234	71.320±11.721	<0.0001	4.691	S
T2 (1 min)	103.08±11.637	81.020±12.021	<0.0001	6.599	S
T3 (3min)	101.24±11.773	78.600±11.284	<0.0001	6.942	S
T4(5 min)	97.600±11.77	76.400±10.468	<0.0001	6.922	S
T5 (10 min)	94.160±10.16	76.080±11.083	<0.0001	6.013	S

Table 5: table 5 showing the intergroup comparison of Systolic (SBP), diastolic (DBP) & Mean arterial Blood Pressure (MABP) changes (mmhg) in response to laryngoscopy and intubation between fentanyl Group F and Dexmedetomidine Group D

parameter	TIME	Group F	Group D	p- value	t-value	Remark
SBP	T0 (Basal)	122.40 ± 9.412	122.56± 9.996	0.9538	0.05827	NS
	T1 (Induction)	118.56±7.906	112.28±10.386	0.0200	2.406	S
	T2 (1 min)	126.72±7.602	113.28±8.615	<0.0001	5.849	S
	T3 (3min)	123.32±7.353	112.04±8.890	<0.0001	4.889	S
	T4(5 min)	120.0±6.758	111.52±9.184	0.0005	3.719	S
	T5 (10 min)	118.84±7.341	111.36±8.190	0.0014	3.401	S
DBP	T0 (Basal)	78.120± 8.151	78.000± 9.443	0.9618	0.04810	NS
	T1 (Induction)	74.440±7.638	67.440±9.845	0.0072	2.809	S
	T2 (1 min)	82.560±5.817	70.560±10.666	<0.0001	4.939	S
	T3 (3min)	78.880±6.900	66.800±8.602	<0.0001	5.477	S
	T4(5 min)	76.120±6.888	65.160±8.004	<0.0001	5.190	S
	T5 (10 min)	75.920±7.164	63.920±8.597	<0.0001	5.361	S
MABP	T0 (Basal)	92.88± 7.884	92.360± 9.092	0.8295	0.2165	NS
	T1 (Induction)	89.160 ±7.128	81.880 ± 9.597	0.0038	3.045	S
	T2 (1 min)	96.720± 5.997	84.240 ±9.558	<0.0001	5.530	S
	T3 (3min)	93.040± 6.419	81.320± 8.148	<0.0001	5.649	S
	T4(5 min)	90.000 ± 6.158	80.120 ±7.732	<0.0001	4.998	S
	T5 (10 min)	89.64 ± 6.903	79.160 ±7.930	<0.0001	4.984	S

Discussion

Airway management which includes llaryngoscopy and tracheal intubation are considered as the most critical events during administration of general anesthesia in major surgeries as they provoke transient but marked sympathoadrenal response manifesting as hypertension and tachycardia. [7,8]

These responses are transitory, variable and may not be significant in otherwise normal individuals but in patients with cardiovascular compromise like hypertension, Ischemic heart disease, Cerebrovascular disease even these transient changes or stress can provoke ventricular failure, pulmonary edema, myocardial ischemia, ventricular dysrhythmias and cerebral haemorrhage[3]. Not only airway maneuvers but also the inflammatory mediators released during it threat to such patient which indicates the need of sympatholytic and anti-inflammatory drug in such procedures. [3,7,8].

Methods like use of inhalational anesthetic agents, lidocaine, opioids, direct acting vasodilators, calcium channel blockers and β-blockers have been tried for blunting cardiovascular stress because of laryngoscopy and intubation. [9,10,11]

Each has its pros & cones for example: opioids respiratory depression and chest wall rigidity were potential problems, use of halothane was associated with dysrhythmia, calcium channel blockers lead to reflex tachycardia, direct acting vasodilators needed invasive hemodynamic monitoring and lidocaine showed in consistent results in blunting the hemodynamic responses to laryngoscopy and intubation [12,13,14,15]

Beta blockers are administered for blunting sympathoadrenal stress response to airway manipulation, but their action is more targeted on heart rate rather than blood pressure stability. So, we need a drug which can is effective not only in stabilizing cardiovascular reflexes but also can control inflammation, post-operative nausea and vomiting (PONV) [16,17,18,19,20]

The search for the ideal technique or agents which can control all the side effect of airway manipulation stated above resulted in this study where we are checking supremacy of dexmedetomidine vs fentanyl as anesthetic agent in cardiovascular domain affected by airway manipulation.

Fentanyl

Fentanyl is advocated attenuation of sympathetic response to laryngoscopy and intubation [21]. But blunting of sympathetic response is highly dose dependent which results in to undesirable respiratory depression [22,23]. Fentanyl at 6 μg/kg completely abolishes sympathetic response, whereas at 2 μg/kg significantly attenuates the hemodynamic response, during laryngoscopy and intubation [24]. In this study Intravenous fentanyl was given at the dose of 2 μg/kg diluted in 10 ml normal saline 10 min before induction [24,25].

Dexmedetomidine

In our study we have given dexmedetomidine as I.V. infusion 1 μg/kg in 25 ml normal saline over 10 min. If Bolus dose of Dexmedetomidine is given rapidly, it leads to an initial transient increase in blood pressure and reflex decrease in HR because of peripheral α-2 adrenoceptor stimulation of vascular smooth muscle. So, in the present study we have given dexmedetomidine administration slowly over 10 min[25]. It has been proven that dexmedetomidine and fentanyl as premedication attenuates the sympathoadrenal response to laryngoscopy and endotracheal intubation.

The statistical analysis of outcomes shows that the population in groups are standardized in age, sex & weight distribution (table 2,3)

Heart rate variation analysis in the two groups (table 4) demonstrated that there was no statistically significant difference until induction of anesthesia ($P > 0.05$). The increase in mean HR after administration

of Propofol was statistically lower in Group D as compared with Group F. Analysis of the postinduction, postintubation values of the mean HR variation from the baseline values of the two groups showed a statistically significant difference until 10 min ($P < 0.05$).

Kharwar *et al*. [26] observed that there was a decrease in pulse rate from baseline by 17.80% in the dexmedetomidine Group Fs compared with the fentanyl group, in which the decrease was 6.99% from baseline after induction.

Statistical analysis showed that there was no significant change in Systolic & diastolic blood pressure between the two groups at Basal level-significant at T1 (Induction) level, but highly significant At T2 (1 min), At T3 (3min), At T4(5 min), At T5 (10 min) level. Mean arterial BP also follow the same discourse.

Gandhi *et al*. [25]observed that Dexmedetomidine produces more significant attenuation of increase in SBP & DBP during laryngoscopy and intubation as compared with fentanyl, which is in concordance with our study. With respect to MAP, our findings are confirming the statements of previous researchers [25,26,]

The above observations can be justified by ability of dexmedetomidine to reduce sympathetic nerve activity, inhibit the release of sympathetic impulses, and relieve nerve tension primarily according to the highly selective nature of the drug [3]

On using equipotent doses of fentanyl and dexmedetomidine, we found that Dexmedetomidine significantly depressed sympathetic response to laryngoscopy and intubation in terms of HR, SBP, DBP, and MAP compared with fentanyl. There are studies done previously which can justify the superiority of dexmedetomidine over fentanyl in cardiovascular domain. Hyperinflammatory responses damage organs like lung, heart and kidney paving for unfavourable pathological changes, including tissue and cell degeneration, necrosis, changes in hemodynamic like inflammatory hyperaemia, increased vascular permeability (inflammatory exudation), fluid exudation and cellular exudation (inflammatory infiltration) resulting in systemic inflammatory response syndrome: which facilitates secondary multiple organ injury and dysfunction, affecting postoperative outcomes like prolonged hospitalization and increased medical costs. [27,28,29,30,31,32,33,34] Previous researchers proves efficacy of dexmedetomidine as anti-inflammatory agent & potent sedative also because it suppresses the production of lipopolysaccharide-induced proinflammatory mediators, including Tumour necrosis facto-α, Interleukin-6, and CRP, both in vivo and in vitro [31,32,33,34]. Interleukin-10 is a cytokine that inhibits the production of IL-6 and TNF-α decreasing intra & postoperative inflammation [35]. Yang and Hong also suggested that dexmedetomidine could inhibit nuclear factor-κB activity and activate cholinergic anti-inflammatory pathways [36].

The conclusion is the dexmedetomidine should be preferred for administration during airway management over traditional optional like fentanyl because it has versatile properties which benefit the patients not only intraoperatively to minimize cardiovascular risks but also postoperatively as potent anti-inflammatory properties.

Ethical Clearance- was Taken from Institutional Ethics Committee – Human Research: C. U. Shah Medical College. **Source of funding**- Self. **Conflict of Interest** - Nil

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