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ORIGINAL ARTICLE

Comparison of effect of dexmedetomidine and lidocaine on intracranial and systemic hemodynamic response to chest physiotherapy and tracheal suctioning in patients with severe traumatic brain injury

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Abstract

Purpose Chest physiotherapy and tracheal suction cause sympathetic stimulation and increase heart rate (HR), mean arterial pressure (MAP) and intracranial pressure (ICP) which may have deleterious effect in the head injured. We planned to compare the effect of intravenous dexmedetomidine and lidocaine on intracerebral and systemic hemodynamic response to chest physiotherapy (CP) and tracheal suctioning (TS) in patients with severe traumatic brain injury (sTBI).

Methods Prospective, randomized study in patients with sTBI, 18–60 years of age, undergoing mechanical ventilation and intraparenchymal ICP monitoring. Patients were randomized to receive either iv dexmedetomidine 0.5 mcg/kg (group I; $n=30$) or iv lidocaine 2 mg/kg (group II; $n=30$) over 10 min. After infusion of test drug, CP with vibrator and manual compression was performed for 2 min and TS was done over next 15–20 s. The hemodynamic response was recorded before, during and at interval of 1 min for 10 min after CP and TS. A 20% change in hemodynamic parameters was considered significant.

Results The baseline hemodynamic (HR, MAP), intracranial (ICP, CPP) and respiratory (SPO_2, AWP_{peak}) parameters were normal and comparable in both the groups. After dexmedetomidine infusion, MAP and CPP decreased significantly from baseline value. In group II, there was no significant change in HR, MAP, ICP and CPP. At end of CP and TS, HR, MAP and CPP in group I was lower as compared to group II. During the 10-min observation period following CP and TS, MAP and CPP in group I remained significantly lower as compared to baseline and group II. There was no significant change in value of other measured parameters.

Conclusions Both dexmedetomidine and lidocaine were effective to blunt rise in HR, MAP and ICP in response to CP and TS in patients with sTBI. However, intravenous dexmedetomidine caused significant decrease in MAP and CPP as compared to the baseline and lidocaine.

Keywords Dexmedetomidine · Lidocaine · Hemodynamic response · Tracheal suctioning · Head injury

Introduction

Traumatic brain injury (TBI) results in a major portion of admissions to critical care unit. It is a major cause of death and disability worldwide [1]. Prevention of secondary brain injury by maintaining cerebral perfusion pressure (CPP) and intracranial pressure (ICP) is the corner stone of treatment in these patients for which sedation and mechanical ventilation are often required. Prolonged ventilation requirements make up to 80% of these patients prone to pulmonary complications [2]. Though the role of chest physiotherapy (CP) and tracheal suctioning (TS) in prevention of pulmonary complications is debatable, pulmonary toileting and bedside physiotherapeutic procedures are commonly performed procedures on mechanically ventilated patients [3]. Periodic CP and TS may help prevent mechanical and infectious complications, but may have deleterious effect on patient with

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severe TBI with compromised cerebral perfusion and intracranial compliance. CP causes sympathetic stimulation and increases the HR (heart rate), MAP (mean arterial pressure) and ICP [4]. The rise in ICP decreases CPP which leads to aggravation of cerebral ischemia and neurological tissue injury [1]. TS has shown to affect ICP, jugular oxygen saturation ($SjvO_2$) and CPP negatively in patients who cough or moved during TS [5]. These insults may result in secondary brain injury. Though the quantitative assessment of such injury has not been reported, cumulative burden of raised ICP worsens outcome [6].

Many methods and modalities are described to diminish or blunt the effect of TS on hemodynamic parameters [7–11]. But, there are few data on the cerebral effects of TS in the acute phase of head injury, when patients are at higher risk of intracranial detrimental events, and even a momentary increase in ICP may have potentially harmful effect [12]. The target for neuro-intensivist for such critically ill patients is to maintain normal cerebral and systemic hemodynamics. Lidocaine injected intravenously blunts the cough reflex in awake and anesthetized patients [13], and additionally has potential neuroprotective effects [14]. It has been used in various studies to blunt the pressor effect of CP and TS on ICP in head injured patients with equivocal results. There are no strong and definitive recommendations for its use. Dexmedetomidine is a selective α_2-agonist with sedative, anxiolytic, and analgesic properties. It has gained popularity among neuro intensivists for patient sedation. It produces a state of tranquility with minimal interference with neurological examination and respiratory efforts. However, there are not much data on its use to blunt systemic and cerebral pressure responses caused by CP and TS. Hence, we planned this study to compare the effects of intravenous lidocaine and dexmedetomidine on the systemic and intracranial pressure dynamics during CP and TS in head injured patients.

Methods

This study was carried out at the Level I, Apex Trauma Centre in India. After Approval from the Institutional Ethics Committee, written informed consent was obtained from close relatives of the patients. Trial was registered with Clinical Trial Registry of India, CTRI/2016/03/006770 [Registered on: 30/03/2016]. Out of a total of 176 TBI patients admitted to neurotrauma ICU during the study period (March 2016 to May 2016), 105 patients did not meet inclusion criteria and 11 were excluded due to unavailability of investigator (SS). A total of 60 patients with sTBI, between 18 and 60 years of age, undergoing mechanical ventilation and intraparenchymal ICP monitoring were enrolled for this prospective, randomized double blind study. Severe TBI was defined as Glasgow coma scale (GCS) score of ≤ 8. For inclusion in the study, stable ICP (< 20 mmHg) was required. Patients with spine injury, chest injury (fractured ribs, subcutaneous emphysema, hemo/pneumothorax, and chest wounds) interfering with effective chest physiotherapy were excluded from the study. Patients with history of severe cardio-respiratory disorders and those having hypotension (systolic blood pressure < 90 mmHg) or hypoxemia ($PaO_2 < 60$ mmHg) or oxygen saturation ($SpO_2 < 90\%$) were also excluded from the study.

According to a computer-generated randomization chart, the patients were assigned to one of the two treatment groups. Patients in group I received iv dexmedetomidine before CP and patients in group II received iv lidocaine before CP. The test drug was prepared and administered by a nurse who was blinded to drug assignment. Either dexmedetomidine 0.5 µg/kg or lidocaine 2 mg/kg was taken and diluted with NS to a volume of 10 ml in a 10 ml syringe and labeled as 'TEST DRUG'. Vitals were recorded by blinded treating clinician (SS). As per standard ICU protocol, all patients on mechanical ventilator were sedated using fentanyl (1 µg/kg/h) and midazolam (0.1 mg/kg/h). Head was kept in neutral position with 30° head end elevation. Mechanical ventilation was adjusted to maintain normocarbia ($PaCO_2 = 35 \pm 2$ mmHg). An intra-arterial cannula was inserted (if already not in place) under local anesthesia, to monitor the mean arterial pressure and blood gas analysis. Blood gas analysis was done prior to and after CP and TS.

Three consecutive readings of heart rate HR, MAP, peak airway pressure (AWP_{peak}), SpO_2 and ICP at interval of 1 min were recorded. Zero calibration and leveling of both ICP monitor and arterial transducer was done at the level of external auditory canal with head kept at 30° elevation. Cerebral perfusion pressure was calculated by subtracting ICP from MAP. Mean value of the three values was taken as baseline value. Thereafter, test drug was infused over 10 min. After completion of infusion of respective test drug, chest physiotherapy with vibro-compression/manual compression for 2 min was performed and tracheal suctioning was done over 15–20 s. CP was done by percussion method in which patient's chest and area under arms is vigorously shaken alternately with cupped hand over 2 min with a power to cause hollow sound and clinically judged to be painless if applied in awake patient. TS was done with a 14 French suction catheter passed just beyond the tip of the tracheal tube with negative pressure limited to 70–150 mmHg for less than 30 s in all patients. During chest physiotherapy inspired oxygen concentration was increased to 100%. Though the degree of stimulation was not measured, to remove bias all CP and TS were done by a single person using similar catheter size and suction pressure. During CP, HR, MAP, ICP, SpO_2, and AWP_{peak} were recorded at 1-min interval and continued till 10 min after tracheal suctioning. A 20% rise in HR, MAP and ICP was considered as hemodynamic

response to CP and TS. A 20% or more change vitals during the study period was considered significant. Hypotension was defined as ≥ 20% decrease in MAP from the average baseline value for more than 1 min was treated with intravenous bolus of 3 mg mephentermine hydrochloride. Bradycardia was defined as ≥ 20% decrease in HR from the baseline value and was treated if associated with hypotension or HR below 45 beats/min, with intravenous glycopyrrolate. If ICP values remained high (> 20 mmHg) even at end of 10 min after tracheal suctioning standard measures were taken to bring it down to baseline values on the discretion of treating neurocritical care team.

Statistical analysis

Assuming the effect size of 0.3, level of significance set as 0.05, power of the study 80%, number of groups 2 and number of measurements 10, the total sample size was calculated to be 24 in each group. However, we enrolled 30 patients in each group to compensate for the dropouts. There was no drop out. Power analysis was done for the estimated effect size and sample size recruited, the power of the study was 90%. Results are expressed as mean ± SD. Two ways repeated measures ANOVA was performed to find association between and within the groups. The differences in the each monitored variable (HR, MAP, CPP, ICP, AWP_{peak} and SpO_2) between the groups induced by CP and TS were analyzed with unpaired '*t*' test (intergroup) and paired '*t*' test (intragroup). Statistical significance was set at less than 0.05 level. Bonferroni correction was used when the result of repeated measures was statistically significant.

Results

Effect of dexmedetomidine and lidocaine on intracranial and systemic hemodynamics was studied at the time of CP and TS in 60 patients with severe TBI between March 2016 to May 2016. Both the study groups had 30 patients each. All patients were admitted in neurotrauma ICU and received mechanical ventilation and ICP monitoring. Demographic parameters and clinical characteristics were comparable between the groups (Table 1). Majority of the patients were male under the age of 40 years. The median GCS score of the patients was 5 in both the groups.

The baseline hemodynamic (HR, MAP), intracranial (ICP, CPP) and respiratory (SPO_2, AWP_{peak}) parameters were normal and comparable in both the groups (Table 2). After test drug infusion MAP and CPP decreased significantly from baseline values in dexmedetomidine group I as compared to group II (Table 2). In group II ($n = 30$) there was no significant change in HR, MAP, ICP and CPP. (Table 2,3). At the end of CP and TS, MAP and CPP continued to be lower in group II as compared to the baseline as well as group I (Table 2). A significant decrease in HR was also seen in group (I) The value of measured parameters during 10-min observation period following CP and TS is tabulated (Table 3). The MAP and CPP in group I were

Table 2 Systemic and intracranial hemodynamic parameters (values expressed as mean ± SD or number) at various time points in two groups

	HR	MAP	ICP	CPP
Baseline				
Group I	**92 ± 15**	**94 ± 12**	**13 ± 4**	**82 ± 12**
Group II	**92 ± 15**	**91 ± 12**	**12 ± 5**	**79 ± 13**
	0.99**	0.22**	0.65**	0.23**
F1				
Group I	**88 ± 15**	**80 ± 12**	**12 ± 5**	**68 ± 12**
	0.33*	0.001*	0.37*	0.0001*
Group II	**92 ± 15**	**91 ± 13**	**12 ± 6**	**79 ± 13**
	0.88*	< 0.001*	> 0.99*	0.85*
	0.41**	0.001**	0.71**	0.00**
F2				
Group I	**88 ± 14**	**79 ± 13**	**11 ± 4**	**68 ± 12**
	0.39*	< 0.0001*	0.13*	0.0001*
Group II	**99 ± 17**	**97 ± 13**	**13 ± 6**	**84 ± 14**
	0.16*	0.07	0.52*	0.19*
	0.02**	0.00**	0.14**	0.0001**

Bold value indicates of parameters

F1 at the end of test drug infusion, *F2* at the end of CP and TS

*'*p*' value on intra-group comparison of the concerned value with that at the baseline

**'*p*' value on inter-group comparison of the concerned value at the particular time-point

Table 1 Demographic profile and baseline clinical characteristics of patients in both the groups

Baseline characteristics	Group I ($n = 30$)	Group II ($n = 30$)	*p* value
Age (years)	33.3 ± 10.9	29.3 ± 10.7	0.15
Gender (male/female)	22/8	21/9	0.08
Body weight (kgs)	67.8 ± 6.8	68.8 ± 8.2	0.62
GCS (median/range)	5 (3–6)	5 (3–8)	
Patients with associated injuries	13	11	

All values expressed as mean ± SD or as expressed otherwise

Table 3 Systemic and intracranial hemodynamic parameters (values expressed as mean ± SD or number) during 10 min observation period in two groups

Value	T1	T2	T3	T4	T5	T6	T7	T8	T9	T10	*p* value
HR											
Group I	88 ± 15	88 ± 16	88 ± 15	89 ± 15	89 ± 15	88 ± 15	88 ± 15	88 ± 15	88 ± 15	88 ± 15	0.61
Group II	98 ± 14	96 ± 16	95 ± 15	96 ± 16	94 ± 16	95 ± 16	95 ± 16	94 ± 17	94 ± 17	95 ± 16	
MAP											
Group I	81 ± 12	79 ± 11	78 ± 11	78 ± 12	77 ± 11	77 ± 11	77 ± 11	77 ± 11	77 ± 11	77 ± 11	0.0*
Group II	96 ± 13	94 ± 12	93 ± 12	93 ± 12	92 ± 12	91 ± 12	90 ± 12	91 ± 12	91 ± 13	91 ± 13	
ICP											
Group I	15 ± 6	14 ± 6	15 ± 4	15 ± 6	15 ± 6	14 ± 5	15 ± 5	14 ± 5	15 ± 5	14 ± 5	0.68
Group II	16 ± 8	15 ± 8	14 ± 7	14 ± 6	14 ± 6	14 ± 6	14 ± 7	14 ± 7	13 ± 6	13 ± 6	
CPP											
Group I	67 ± 13	63 ± 12	63 ± 12	63 ± 12	62 ± 12	62 ± 12	62 ± 13	63 ± 12	62 ± 12	63 ± 11	0.00*
Group II	79 ± 16	78 ± 15	78 ± 14	79 ± 14	78 ± 13	78 ± 13	76 ± 13	77 ± 13	77 ± 13	78 ± 12	

CS chest physiotherapy, *TS* tracheal suctioning, *Group I* dexmedetomidine group, *Group II* lidocaine group, *HR* heart rate (per min), *MAP* mean arterial pressure (mmHg), *ICP* intracranial pressure (mmHg), *CPP* cerebral perfusion pressure (mmHg)

*Bonferroni test was significant at *p* value of 0.0015

significantly low as compared to group (II) (Table 3). There was no significant change in value of HR, ICP, AWP_{peak} and SpO_2 in both the groups. SpO_2 was 100% throughout the study period. AWP_{peak} in both the groups was maintained between 15 and 20 mmHg.

Five patients who received Dexmedetomidine developed hypotension during the study period and were treated with fluid and mephentermine bolus, but one patient required noradrenaline infusion in addition. No patient in lidocaine group developed hypotension. One patient in each group developed restlessness after TS, however, no drug intervention was required in either patient.

Discussion

Respiratory physiotherapeutic interventions are commonly performed on critically ill patients with TBI [15]. The effects of these maneuvers on cerebral and cardiovascular dynamics are reported in the literature. These interventions are likely to increase intra-thoracic pressure and alveolar pressure [14], and thus reduce venous return to the heart causing decreased cardiac output (CO) and MAP. It may also jeopardize cerebral venous drainage leading to increased ICP. Studies attribute increase in ICP after TS to vasodilatation and increase in cerebral blood flow [16]. Increase in MAP, ICP, HR, pulmonary arterial pressure and pulmonary capillary pressure are described during airway suctioning [14, 17]. In a study by Gemma et al., TS in acute phase of head injury caused increase in ICP, CPP and $SjvO_2$ without evidence of ischemia in well-sedated patients. However, in patients who coughed or moved in response to TS, there was significant decrease in CPP and $SjvO_2$ [5]. Fentanyl and Midazolam in the mentioned doses might be sufficient to promote deep sedation, but noxious stimuli like TS are known to produce stressful stimuli resulting in increase in endogenous catecholamine levels resulting in tachycardia, hypertension, etc. [18, 19]. Therefore, deepening the level of sedation or use of additional drugs to suppress the response to TS is rational. In literature hyperventilation, muscles relaxants and sedative drugs have been used to avoid hemodynamic and cerebral response to CP and TS. Lidocaine and sedative drugs are among the popular choices. Lidocaine in a dose of 2 mg/kg has been widely used for attenuation of ICP response to suctioning and similar stimuli [10, 20, 21]. Lidocaine acts by blocking fast voltage-gated Na^+ channels by neuronal blockade of vagal reflex pathways and by direct effect on smooth muscle cells of respiratory pathway [18]. Its onset of action is within minutes and lasts for half an hour to 3 h. It is metabolized mostly in the liver and eliminated in around 90–120 min in most patients. At author's institute lidocaine is used before tracheal suctioning. The evidence regarding impact of lidocaine to prevent such response is equivocal. There is no strong and definitive recommendation on usefulness of lidocaine on attenuation of ICP spikes during stimulation [22]. Our results supported the use of lidocaine for blunting the cerebral and systemic hemodynamic response to CP and TS. The HR, MAP, CPP remained comparable to baseline values throughout the study period. Maximum ICP (15.2 ± 7.6) was observed at 2 min following TS.

The alpha-2 agonist property of dexmedetomidine has gained popularity in neurocritical care units owing to hemodynamic stability, ease of neurological examination and minimal respiratory depression [23]. It exhibits rapid

distribution half-life of approximately 6 min and a terminal elimination half-life of 2 h after an iv dose. It is 94% protein bound, metabolized mostly in liver and majority of metabolites are excreted in urine. In addition the drug has been shown to have favorable effects on cerebral blood flow in critically ill patients with TBI [24]. Preliminary studies have described its role in management of refractory intracranial hypertension [25]. Many critically ill patients receive dexmedetomidine infusions for sedation, but the role of dexmedetomidine to prevent response to TS is poorly defined. The recommended dose for Dexmedetomidine is 1.0–2.0 mcg kg^{-1}, but this dose is associated with development of significant hypotension and bradycardia [26]. We studied the effect of intravenous dexmedetomidine 0.5 mcg/kg over 10 min to avoid the adverse effects like hypotension and bradycardia described with higher dose of drug [27]. Though there was no bradycardia with this dose of dexmedetomidine, a significant decrease in MAP was observed. After the infusion of dexmedetomidine, MAP and CPP significantly decreased from baseline values; however, it remained within normal limits. Five patients developed significant hypotension following drug infusion and required active management. Hypotension refractory to fluid and mephentermine was seen in one patient, who was treated by noradrenaline infusion. ICP was maintained within normal limits throughout, the highest values were recorded at 4 min. Since ICP was normal in all the patients, we believe that significant fall in MAP led to statistically significant decrease in CPP but were still in acceptable clinical range. This may not be so in patients with raised ICP. A decrease in HR was seen with dexmedetomidine infusion, but was not significant as observed in other clinical studies, due to lesser dose of drug used in our study. No changes in SpO_2 and AWP_{peak} pressure were seen during the study period.

Limitations

Patient included in this study had normal ICP. It limits applicability and generalizability of results to patients with higher ICP who nevertheless require TS and CP. Impact of these transient but significant hemodynamic and cerebrovascular changes on overall patient outcome is not evaluated. Use of only single concentration of drugs is reported. Study objective did not include measurement of sedation score. A preliminary study to see hemodynamic response to TS without dexmedetomidine or lidocaine should have been done but could not be performed due to ethical issues.

To conclude, both dexmedetomidine and lidocaine are effective in blunting systemic and cerebrovascular response (rise in HR, MAP, ICP) to CP and TS in mechanically ventilated patients with severe TBI, but potential deleterious effects like fall in MAP and CPP compared to baseline and lidocaine group makes dexmedetomidine undesirable in TBI patients for TS and CP. Studies using smaller dose of dexmedetomidine and enrollment of patients with raised ICP are required.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

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