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Dexmedetomidine: A Preliminary Exploration of its Safety and Efficacy in Pediatric Dental Setting

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Abstract

Objective: To report on safety and efficacy of intravenous usage of Dexmedetomidine for endodontic intervention in young and anxious pediatric patients.

Methods: This prospective pilot investigation enrolled 10 healthy ASA status I, 2-6 year old children who were anxious (Venham's score ≥ 4) and were scheduled to undergo primary molar pulpectomy under sedation. Sedation induction was done with 1 mg/kg of propofol bolus followed by 0.2-0.8 µg/kg of dexmedetomidine infusion for maintenance. Sedation was titrated to achieve Houpt's overall behavior score of ≥ 4. In case of insufficient sedation, rescue propofol boluses (1 mg/kg) were administered. Vitals were monitored every 5 minutes and recovery was evaluated using Alderete Modified Post Anesthesia Discharge Scoring System. Adverse events, i.e., ≥ ± 20% baseline fluctuations in vital signs, tachycardia, bradycardia, apnea, desaturation, stridor and/or laryngospasm were recorded.

Results: The procedure was successfully completed in all of the subjects with the current sedation regime as per the study protocol. Rescue propofol boluses were needed in 8 subjects. No untoward fluctuations in vital signs or adverse events were reported in either intra-operative phase or post-operatively.

Conclusion: Intravenous Dexmedetomidine is safe and efficient sedative for endodontic intervention in young and anxious pediatric patients.

Keywords: Behavior management; Deep sedation; Dexmedetomidine; Intravenous sedation; Pediatric dental sedation; Propofol

Introduction

Sedation has been available for decades to the pediatric dentists for optimizing the course of successful provision of efficient dental treatment to the difficult children. A plethora of sedative agents [1] have been in use in pediatric dental settings i.e. midazolam, ketamine, propofol, chloral hydrate, promethazine, hydroxyzine, nitrous oxide and sevoflurane. Each of these has its own sets of limitations [1]. Despite the voluminous literature, the search for efficient and safest sedative agent is yet in its 'ongoing phase' [1-3].

Dexmedetomidine is a recently introduced sedative agent with a stable respiratory drive [4]. It is a highly selective dose dependent α2 adrenergic agonist [4]. Thus, its primary mechanism of action is stimulation of parasympathetic outflow and inhibition of sympathetic outflow [5]. In healthy adult patients, its administration manifests as a biphasic effect, i.e., an initial increase in systolic blood pressure is followed by reflex decrease in blood pressure [6]. Bradycardia may also be observed [7,8]. The respiratory parameters usually remain stable, yet, a keen watch is required [9,10].

Although it is currently approved by Food and Drug Administration (FDA) for provision of short term sedation to adult patients in ICU settings [11], various reports describing its efficient and safe usage as a sedative for invasive and non-invasive procedures across various age groups have been published [4,5,12-15]. Dexmedetomidine has also earned its status as a potential sedative for dental procedures in adult as well as pediatric age group [15]. Few recent reports have described its safe and efficient use for moderate sedation in pediatric dental patients through a variety of routes [16-18]. But, no data has been published on its intravenous use as a deep sedative agent for invasive dental procedures in this age group. In light of these facts, the present pilot investigation was planned to explore the safety and efficacy of dexmedetomidine as a deep sedative agent when administered through intravenous route.

Material and Methods

Settings and recruitment

The present prospective clinical observation was carried out in department of Pediatric and Preventive Dentistry at Santosh Dental College and Hospital, Ghaziabad, Uttar Pradesh, India. A total of 10 subjects aged 2-6 years were recruited. Inclusion criteria were requirement of at least one pulpectomy, Venhams score ≥ 4 [19], ASA physical status I [20] and compliance to NPO instructions [20]. Exclusion criteria were previous exposure to general anesthesia or sedation, mental retardation or learning disabilities, and obstructed nasal passages. In case of history of upper respiratory tract infection (URTI) a time period of ≥ 4 weeks (after complete resolution of

symptoms) was kept as a waiting period for scheduling the subjects for sedation [21].

Interventions

All subjects received topical application of EMLA at the dorsum of hand for cannulation an hour prior to the scheduled appointment. The induction of sedation was done with intravenous bolus of 1 mg/kg of propofol (Diprivan® Astra Zeneca Pharmaceuticals; 10 mg/mL) mixed with 2% of 1 ml lignocaine [22]. Maintenance of sedation was done with 0.2-0.7 μg/kg/h of dexmedetomidine (Dexem, Themis Medicare Ltd., India; 100 μg/mL) [11] titrated to achieve a Houpt's sedation score of ≥ 4. In case the desired sedation level could not be reached with this protocol, there was a provision to administer rescue sedation bolus of 1 mg/kg of propofol. Dental intervention included primary molar pupectomy.

Record keeping

A provision was made to record every subject's data on pre-printed case sheets. Demographic details including age, sex and weight were recorded. Vital signs including heart rate (HR), non-invasive blood pressure (NIBP), respiratory rate (RR) and oxygen saturation (SpO_2) were recorded every 5 minutes [20] from baseline till completion of the procedure. Houpt's sedation scores [23] for sleep, crying, movement and behavior were recorded at various pre-decided treatment steps, i.e. baseline, parental separation, administration of local anesthesia, rubber dam application, access cavity preparation, pulp extirpation, rubber dam removal and exit from operatory. Proceeding of procedure were recorded as 1=Smooth and completed, 2=Completed with interruptions and 3=Incomplete. Parental perception of child's pain and discomfort during procedure were recorded on Visual analog scale [24] where '0' meant no pain or discomfort and '10' meant the highest pain or discomfort ever possible. Three time period were recorded, i.e., induction time, procedure time, recovery time. Induction time was defined as time from intravenous administration of induction bolus till the adequate sedation level was reached for starting the procedure. The procedure time was defined as time period from injection of local anesthesia till removal of rubber dam. Recovery time was defined as time period needed to achieve Alderete recovery score [22,25] of 8 after exit from operatory. Recovery was assessed every 5 minutes for first 15 minutes and every 15 minutes thereafter.

Observation parameters

These included vital signs (HR, NIBP, RR, SpO_2), Houpt's sedation scores, proceedings of procedure, VAS scores for parental perception of child's pain and discomfort during the procedure, induction time, procedure time, recovery time, total dose of dexmedetomidine, requirement for additional drug boluses. The most important outcome measure for this pilot observation was intra-operative and/or post-operative adverse events. These were recorded as tachycardia (HR ≥ 140), bradycardia (HR ≤ 60) and respiratory depression. Later was recorded as desaturation (SpO_2 ≤ 94%), apnea (cessation of breathing for ≥ 15 seconds) and requirement of airway manipulation as in cases of stridor, coughing, laryngospasm (Table 1).

Statistical analysis

Descriptive statistics were expressed as mean ± SD and/or number (percentage). Analytic statistics were calculated using repeated measures of ANOVA.

Parameter	Score
Sleep	
Awake but responsive	4
Drowsy, disoriented	3
Asleep, easily aroused	2
Asleep, difficult to arouse	1
Movement	
No movements	4
Intermittent movement affecting treatment	3
Continuous movement affecting treatment	2
Violent movement that interrupted or prevented the treatment	1
Crying	
No crying	4
Intermittent crying	3
Continuous crying	2
Hysterical crying	1
Overall Behavior	
Excellent, no disruption	6
Very good, limited disruption	5
Good, some difficulty	4
Fair, much difficulty but treatment done	3
Poor,partial treatment done	2
Aborted	1

Table 1: Houpt's sedation rating score

Results

Mean age of the subjects was 52.00 ± 11.09 months and mean weight was 16.00 ± 4.55 kg. No significant fluctuations ($p>0.05$, calculated by repeated measures of ANOVA) compared to baseline were seen in vital signs throughout the procedure (Table 2). Targeted sedation levels were achieved soon after induction at parental separation (Table 3and Figures 1a-1d). Rescue boluses of propofol were required by 4 subjects. Mean dose of dexmedetomidine was 9.4 ± 5.3 μg. Mean induction time, procedure time and recovery time were 5.00 ± 2.83 minutes, 32.60 ± 8.58 minutes and 19.00 ± 8.43 minutes respectively. No adverse events were reported in any of the subjects either intra-operatively or during post-operative follow-up. Mean parental VAS scores for child's discomfort and pain during the procedure were 1.90 ± 0.99. The endodontic procedure was completed without interruptions in all of the subjects.

Time point of observation	Heart rate (Beats/min)	p value*	NIBP (mm Hg)	p value*	Respiratory rate (times/min)	p value*	SpO_2 (%)	p value*
Baseline	106.8 ± 11.47		98.40 ± 18.40		20.00 ± 4.40		97.90 ± 1.66	
5 minutes	106.70 ± 8.99	1.00	96.30 ± 16.32	0.87	20.30 ± 2.54	1.00	98.50 ± 1.27	1.00
10 minutes	108.10 ± 8.88	1.00	98.00 ± 17.28	1.00	21.70 ± 3.65	1.00	98.10 ± 1.79	1.00
15 minutes	103.60 ± 9.26	1.00	93.90 ± 12.97	0.71	21.70 ± 4.47	1.00	95.80 ± 7.13	1.00
20 minutes	105.20 ± 9.58	1.00	93.60 ± 14.51	0.69	21.90 ± 4.09	1.00	98.40 ± 1.43	1.00
25 minutes	106.13 ± 9.43	1.00	88.00 ± 10.69	0.09	20.25 ± 2.82	1.00	98.75 ± 1.49	1.00
30 minutes	104.63 ± 15.54	1.00	89.38 ± 13.19	0.1	20.63 ± 3.02	1.00	98.63 ± 2.00	1.00
35 minutes	117.25 ± 12.89	0.944	98.75 ± 11.59	1.00	23.75 ± 1.26	1.00	97.75 ± 3.86	1.00
40 minutes	113.00 ± 15.39	0.935	96.67 ± 8.02	0.94	21.67 ± 2.08	1.00	99.00 ± 1.00	1.00
45 minutes	90.00 ± 0.00	1.00	98.00 ± 0.00	1.00	20.00 ± 0.00	1.00	100.00 ± 0.00	1.00

Table 2: Variations in Vital signs during treatment progression at 5 minute intervals; *calculated on the basis of repeated measures of ANOVA.

Discussion

The present study is the first report on intravenous dexmedetomidine as a deep sedative in pediatric dentistry. This pilot investigation reported the successful safe and efficient use of dexmedetomidine in pediatric dental patients as intravenous deep sedative agent. The results of this investigation corroborate with few recent reports on dexmedetomidine where safe successful usage of this drug in pediatric dental settings have been reported [16-18]. However, a direct comparison should be drawn with caution because of a variety of routes [16,17] and dosages [18] employed in these reports. Also, previous authors [16-18] employed this agent for moderate sedation while we targeted deep sedation. We targeted deep sedation instead of moderate sedation as subjects were young, i.e., 2-6 years old and for this age group levels of sedation consistent with deep sedation are considered to be more reliable [1,26].

Time point of observation	Houpt's sleep scores	p value*	Houpt's movement scores	p value*	Houpt's crying scores	p value*	Houpt's overall behavior scores	p value*
Induction	3.20 ± 0.42		2.30 ± 1.06		2.40 ± 0.84		4.00 ± 0.82	
Parental separation	3.30 ± 0.48	1.00	3.30 ± 1.06	0.01†	3.10 ± 0.99	0.98	5.20 ± 0.92	0.65
Administration of local anesthesia	2.00 ± 0.82	0.01†	3.10 ± 1.29	0.004†	3.60 ± 0.52	0.74	5.00 ± 1.25	0.89
Rubber dam application	1.50 ± 0.71	0.00†	3.20 ± 1.03	0.004†	3.80 ± 0.42	0.04†	5.30 ± 1.16	0.48
Access cavity preparation	1.20 ± 0.42	0.00†	4.00 ± 0.00	0.003†	4.00 ± 0.00	0.01†	5.80 ± 0.52	0.003†
Pulp extirpation	1.20 ± 0.42	0.00†	4.00 ± 0.00	0.003†	4.00 ± 0.00	0.01†	5.90 ± 0.32	0.003†
Rubber dam removal	1.60 ± 0.84	0.01†	4.00 ± 0.00	0.01†	3.90 ± 0.32	0.01†	6.00 ± 0.00	0.001†
Exit from operatory	2.20 ± 0.79	0.00†	4.00 ± 0.00	0.01†	3.90 ± 0.32	0.01†	6.00 ± 0.00	0.001†

Table 3: Variations in Houpt's sedation scores during treatment progression at various treatment steps; *calculated on the basis of repeated measures of ANOVA; †significant p-value.

One fact that merits discussion here is the technique of administration of dexmedetomidine. As per manufacturer's recommendation this drug is administered as 1 μg/kg infused over 10 minutes followed by maintenance infusion of 0.2-0.8 μg/kg/hr [11]. Originally, this was recommended for short term ICU sedation. However, this technique may not be suitable in pediatric dentistry set up owing to long induction time of 10 minutes. In a young child, the event of venous cannulation exacerbates the anxiety and further increases the uncooperation. In such a setup, in order to control the young child a faster sedative agent is desirable. Thus a faster acting induction agent, i.e., propofol [27] may be more suitable. On the other hand, dexmedetomidine offers stable respiratory drive. Bearing these facts, we employed a modification of manufacturer's recommended technique. Here, induction of sedation was done with 1 mg/kg of

propofol bolus followed by sedation maintenance with 0.2-0.8 µg/kg/hr of dexmedetomidine. In this way, we were able to overcome the slow onset of dexmedetomidine sedation.

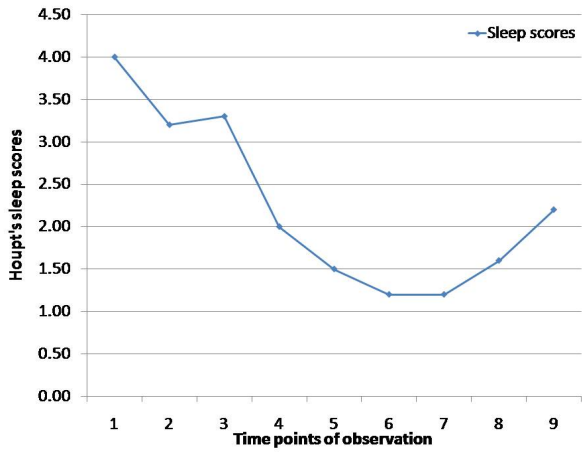

Figure 1a: Variation in Houpt's sleep scores at various treatment steps

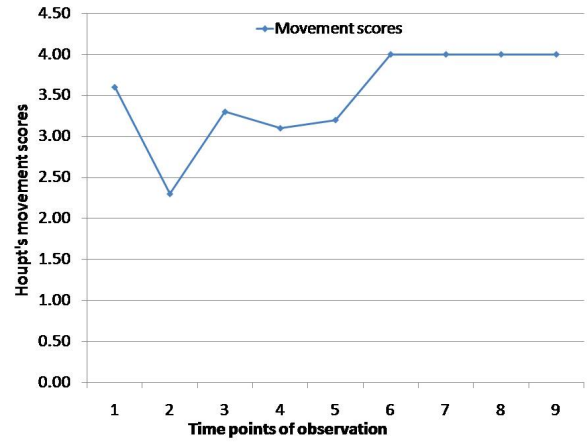

Figure 1b: Variation in Houpt's movement scores at various treatment steps

Previously concerns have been raised about cardio-depressant properties [6-8] of dexmedetomidine and bradycardia [7,8] has been the most feared adverse effect associated with this agent. However, in the present study no such effect was noted at any time point of observation in any of the subjects. The protocol of the present study permitted administration of rescue sedation boluses of propofol to reach the desired sedation end point, i.e., Houpt's overall behaviour score ≥ 4. In contrast to cardio-depressant properties of Dexmedetomidine, effects of this agent on respiration are minimal [9,10] while the rescue sedation agent, i.e., propofol, has been reported to have respiratory depressant effects [27]. Fortunately in the present observation, no adverse respiratory events were reported. In fact, no untoward fluctuations in vital signs were reported throughout the procedure. Thus, on the basis of results in this study it can be concluded that dexmedetomidine is a safe sedative agent even in combination with cardio-respiratory depressants like propofol.

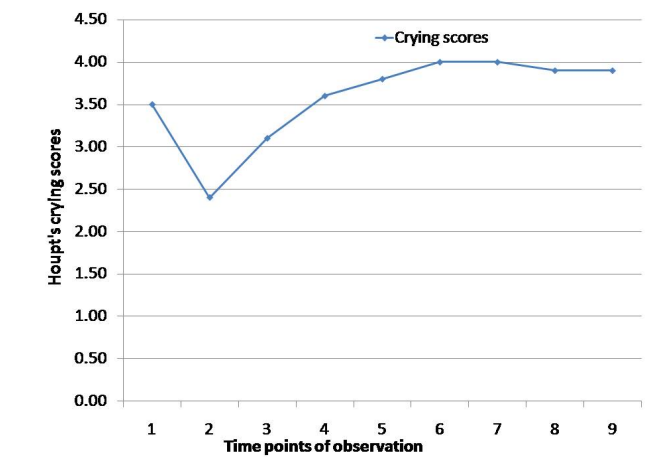

Figure 1c: Variation in Houpt's crying scores at various treatment steps

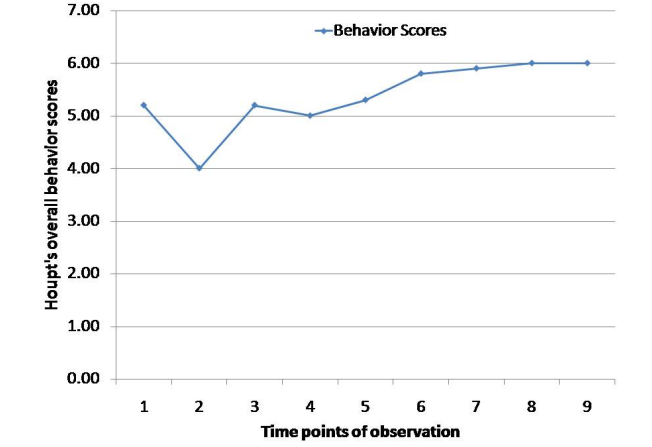

Figure 1d: Variation in Houpt's overall behavior scores at various treatment steps

Stable desired sedation end points were achieved with the sedation technique employed in present study. The sedation peak was achieved soon after parental separation at the very first treatment step, i.e., during administration of local anesthesia. The desired sedation levels were maintained throughout the procedure in all of the subjects. Furthermore, short procedure time of 32.60 ± 8.58 minutes highlights the smooth accomplishment of even invasive dental procedure like pulpectomy. Additionally, the shorter recovery time of 19.00 ± 8.43 minutes allowed faster evacuation of patients from recovery area which extrapolated into fewer burdens on staff personnel for post-operative care and monitoring.

In conclusion, dexmedetomidine administered through intravenous route for provision of deep sedation for endodontic procedures in young and anxious subjects provided safe and efficient deep sedation.

Conclusion

Intravenous dexmedetomidine in combination with propofol is safe and efficient alternative for provision of deep sedation in young and anxious pediatric patients. However, owing to its potential for cardio-depression an ardent vigilance of vital signs by dedicated team, i.e., anesthesia personnel is advised. Future research should explore modification of this technique to reduce the dose of propofol.

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