A Comparison of Intravenous Sedation With Two Doses of Dexmedetomidine: 0.2 µg/kg/hr Versus 0.4 µg/kg/hr

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The present study investigated the physiologic and sedative effects between two different continuous infusion doses of dexmedetomidine (DEX). Thirteen subjects were separately sedated with DEX at a continuous infusion dose of 0.2 µg/kg/hr for 25 minutes after a loading dose of 6 µg/kg/hr for 5 minutes (0.2 group) and a continuous infusion dose of 0.4 µg/kg/hr for 25 minutes after a loading dose of 6 µg/kg/hr for 5 minutes (0.4 group). The recovery process was then observed for 60 minutes post infusion. The tidal volume, mean arterial pressure, and heart rate in both groups decreased significantly during infusion, but they were within a clinically acceptable level. A Trieger dot test plot error ratio in the 0.4 group was significantly higher than that in the 0.2 group until 15 minutes post infusion. Sedation appears to be safe at the infusion doses of DEX studied. However, increasing maintenance infusion doses of DEX from 0.2 µg/kg/hr to 0.4 µg/kg/hr delays some recovery parameters.

Key Words: Dexmedetomidine; Sedation; α_2 adrenoceptor; Amnesia; Trieger dot test.

Dexmedetomidine (DEX) is a sedative and analgesic agent that acts via the α_2 adrenoceptor,¹ which is associated with reduced anesthetic requirements and attenuated blood pressure and heart rate in response to stressful events.^{2–5} α_2 adrenoceptors within the spinal cord modulate pain pathways, thereby providing some degree of analgesia.^{6–8} In addition, DEX induces a sedative response that exhibits properties similar to natural sleep, without significant respiratory depression, unlike other anesthetics.

DEX, therefore, may be useful as a sedative agent in dental procedures. Ogawa et al⁹ studied the sedative, physiologic, and recovery responses to DEX infusion for sedation during dental procedures using the lowest recommended dose in Japan. Others have reported comparisons between sedation with high-dose DEX versus low-

dose DEX infusions.^{10,11} However, there have been few reports that have assessed effects due to an intermediate continuous infusion dose of DEX for proposed dental sedation. The present study investigated the effect on respiration, circulation, sedative level, recovery parameters, and amnesia due to 2 continuous infusion doses of DEX, 0.2 µg/kg/hr and 0.4 µg/kg/hr.

MATERIALS AND METHODS

Subjects

The subjects consisted of 13 ASA I volunteers who ranged from 24 to 37 years of age. Informed consent was obtained for this study approved by the institutional review board.

DEX Infusion

An intravenous catheter (Insyte 20-gauge, Becton Dickinson) was inserted in a medial cubital vein, and

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Figure 1. Time course of the investigation. The same subjects were sedated separately with dexmedetomidine (DEX) at a continuous infusion dose of 0.2 $\mu\text{g/kg/hr}$ for 25 minutes after a loading dose of 6 $\mu\text{g/kg/hr}$ for 5 minutes and a continuous infusion dose of 0.4 $\mu\text{g/kg/hr}$ for 25 minutes after a loading dose of 6 $\mu\text{g/kg/hr}$ for 5 minutes. Then, recovery process was observed for 60 minutes after the end of DEX infusion. (Baseline value was not measured in Ramsay score and one-leg standing with eyes closed test [O-L test] in the 0.4 group was observed for 90 minutes.)

an infusion of lactated Ringer solution was started at 2 mL/kg/hr. The subjects were kept in a supine position for 20 minutes. After stabilization of cardiovascular parameters (repeat vital signs within 10% or less; these were considered the baseline vital signs for the participants), subjects were given a Trieger dot test¹² and then sedated with 2 infusion methods of DEX (Figure 1) as follows:

- 0.2 group: subjects were sedated with DEX with a loading dose of 6 $\mu\text{g/kg/hr}$ for 5 minutes and a continuous infusion dose of 0.2 $\mu\text{g/kg/hr}$ for 25 minutes.
- 0.4 group: subjects were sedated with DEX with a loading dose of 6 $\mu\text{g/kg/hr}$ for 5 minutes and a continuous infusion dose of 0.4 $\mu\text{g/kg/hr}$ for 25 minutes.

After the DEX infusion was stopped in both groups, the identical recovery parameters were recorded for 60 minutes in both groups with additional parameters studied on the 0.4 group at 90 minutes.

A repeated measures design was used with subjects randomly sedated initially with DEX infusion at either the 0.2 group or the 0.4 group. Two weeks later, the same subjects were sedated with the other dose of DEX infusion.

The following physiologic parameters were measured during sedation: tidal volume (TV), respiratory rate (RR), minute volume (MV), end-tidal carbon dioxide (E_TCO₂), mean arterial pressure (MAP), heart rate (HR), bispectral index (BIS), and Ramsay score (RS).¹³ The respiratory parameters were measured with a MAGTRAK (IMI) with a tight-fitting mask; E_TCO₂ was measured with a Capnomac Ultima (Datex); MAP and

HR were measured with a DINAMAP 8100 (CRITIKON); and sedative level was evaluated with BIS A-2000 (Aspect Medical System).

Amnesia was measured by a pinprick test with a 27-gauge needle in the labial gingival mucosa, which was performed at 21 minutes after the loading infusion was started (16 minutes after maintenance infusion) and assessing recall of the needle prick.

Recovery parameters in both groups for 60 minutes post infusion included the Trieger dot test¹² plot error ratio (TDT p.e.r.) to determine psychomotor function, and a one-leg standing test with eyes closed (O-L test; keep standing with eyes closed for 15 seconds) to determine recovery of equilibrium. The O-L test was also administered to the 0.4 group at 90 minutes post infusion. Additionally, the O-L test was determined to be successful in all subjects before DEX infusion.

Statistical Analysis

In comparing each group with baseline recordings, Friedman's test was applied for the statistical analysis except for RS, followed by the Wilcoxon *t* test with Bonferroni correction. In a comparison between the 0.2 group and the 0.4 group, the Wilcoxon *t* test was applied for the statistical analysis except for amnesia. The chi-square test was applied for the statistical analysis of amnesia. *P* values < .05 were considered to be statistically significant. O-L test results were reported without statistical analysis.

Table 1. Age, Weight, and ASA Physical Status of 13 Healthy Adult Volunteers

Number	13
Age (yr)	28.8 ± 3.3
Weight (kg)	69.3 ± 8.1
ASA physical status	1

RESULTS

Subjects

The subjects were on average 28.8 ± 3.3 years of age and weighed 69.3 ± 8.1 kg (Table 1).

Respiration

In RR, MV, and $E_T\text{CO}_2$, no significant changes were seen in comparison with baseline recordings in each group, or between the 0.2 group and the 0.4 group (Figure 2, Table 2). In the comparison to baseline recordings in each group, however, TV in the 0.2 group decreased significantly at 5, 10, 15, 20, 25, and 30 minutes after the start of the DEX infusion from an average of 560 mL to 430–470 mL ($P < .05$). Similarly, TV in the 0.4 group decreased significantly at 5, 10, 15, 20, 25, and 30 minutes after the start of the DEX infusion from an average of 550 mL to 413–463 mL ($P < .05$). No significant changes in TV were seen in the comparison between the 0.2 group and the 0.4 group.

Cardiovascular

After a brief increase in the MAP of both groups following the initiation of infusion, the MAP decreased significantly from 10 minutes after initiation of DEX infusion through the 60 minutes post infusion time period. The MAP decreased from an average of 86 mm Hg to 70–77 mm Hg (0.2 group) and 83 mm Hg to 67–75 mm Hg (0.4 group) over this 80-minute time period. In both groups, HR decreased significantly from 5 minutes after DEX infusion through the 60 minutes post infusion time period (the low 60s beats per minute to the low to mid 50s beats per minute range) (Figure 3, Table 2).

BIS

BIS decreased significantly from 10 minutes after the start of the DEX infusion to 30 minutes after the end of the DEX infusion in both groups. In addition, BIS

Figure 2. Changes in tidal volume (TV), respiratory rate (RR), minute volume (MV), and end-tidal carbon dioxide ($E_T\text{CO}_2$). TV in both groups decreased significantly from 5 minutes to 30 minutes after the start of dexmedetomidine (DEX) infusion in spite of no significant changes in RR, MV, and $E_T\text{CO}_2$. TV in the 0.2 group decreased significantly from an average of 559 mL (baseline value) to 430–470 mL ($P < .05$). TV in the 0.4 group decreased significantly from an average of 551 mL (baseline value) to 410–460 mL ($P < .05$). However, there was no significant change in TV, RR, MV, and $E_T\text{CO}_2$ between both groups.

showed the lowest average at 30 minutes after the start of the DEX infusion in both groups, which were 73.6 (0.2 group) and 69.8 (0.4 group). No significant changes were seen in the comparison between both groups (Figure 4, Table 2).

RS

Statistical analysis in RS was not performed in the comparison in each group. In the 0.2 group, the RS was within the optimal sedative score (3–4) at 15, 20, 25, and 30 minutes after the start of the DEX infusion. In the 0.4 group, these same RS occurred at the same time intervals as the 0.2 group but also included

Table 2. Physiologic parameters. Summary of the Results in Respiration, Cardiovascular, and Sedative Level (Mean $\pm$ SD)*

Group	Baseline	5	10	15	20	25	30	After 30	After 60
TV (ml)	559 $\pm$ 71	466 $\pm$ 54 $\ddagger$	439 $\pm$ 101 $\ddagger$	430 $\pm$ 88 $\ddagger$	446 $\pm$ 82 $\ddagger$	452 $\pm$ 97 $\ddagger$	447 $\pm$ 66 $\ddagger$	495 $\pm$ 117	531 $\pm$ 124
RR (/min)	551 $\pm$ 89	463 $\pm$ 60 $\S$	414 $\pm$ 37 $\S$	420 $\pm$ 55 $\S$	432 $\pm$ 79 $\S$	416 $\pm$ 58 $\S$	434 $\pm$ 80 $\S$	467 $\pm$ 66	512 $\pm$ 90
MV (l/min)	14.2 $\pm$ 2.2	15.5 $\pm$ 3.2	14.8 $\pm$ 2.4	16.2 $\pm$ 2.3	15.1 $\pm$ 2.5	15.6 $\pm$ 2.4	15.8 $\pm$ 2.4	14.4 $\pm$ 2.7	14.8 $\pm$ 2.4
E _T CO ₂ (mmHg)	14.5 $\pm$ 1.6	15.4 $\pm$ 2.3	15.5 $\pm$ 2.8	15.8 $\pm$ 2.3	16.3 $\pm$ 2.6	16.2 $\pm$ 2.4	15.4 $\pm$ 2.3	15.0 $\pm$ 1.4	14.3 $\pm$ 2.9
MAP (mmHg)	7.9 $\pm$ 1.3	7.1 $\pm$ 1.7	6.5 $\pm$ 1.5	6.9 $\pm$ 1.5	6.7 $\pm$ 1.7	7.1 $\pm$ 1.2	7.1 $\pm$ 1.4	7.0 $\pm$ 1.7	7.9 $\pm$ 2.2
HR (bpm)	7.9 $\pm$ 1.3	7.2 $\pm$ 1.1	6.4 $\pm$ 1.4	6.6 $\pm$ 1.0	7.0 $\pm$ 1.5	6.6 $\pm$ 0.9	6.6 $\pm$ 1.3	7.0 $\pm$ 0.9	7.7 $\pm$ 2.1
BIS	40.7 $\pm$ 3.5	40.0 $\pm$ 3.4	40.0 $\pm$ 2.9	39.4 $\pm$ 4.1	40.5 $\pm$ 4.8	40.2 $\pm$ 4.5	41.0 $\pm$ 4.7	39.8 $\pm$ 4.0	38.9 $\pm$ 3.2
RS	40.2 $\pm$ 3.6	40.5 $\pm$ 4.4	40.3 $\pm$ 4.4	40.7 $\pm$ 4.1	39.6 $\pm$ 3.9	39.9 $\pm$ 4.6	39.6 $\pm$ 4.2	40.8 $\pm$ 3.1	40.1 $\pm$ 3.1
TV (ml)	85.7 $\pm$ 6.3	88.8 $\pm$ 9.6	77.0 $\pm$ 70.7	75.6 $\pm$ 51.1 $\ddagger$	74.6 $\pm$ 51.1 $\ddagger$	72.5 $\pm$ 60.1 $\ddagger$	72.7 $\pm$ 62.2 $\ddagger$	70.0 $\pm$ 51.1 $\ddagger$	70.8 $\pm$ 70.7
HR (bpm)	83.2 $\pm$ 5.4	86.3 $\pm$ 9.9	74.9 $\pm$ 8.9 $\S$	74.3 $\pm$ 7.4 $\S$	73.6 $\pm$ 7.8 $\S$	73.5 $\pm$ 7.9 $\S$	71.4 $\pm$ 9.1 $\S$	67.3 $\pm$ 8.5 $\S$	68.9 $\pm$ 71.1 $\S$
BIS	65.2 $\pm$ 11.1	54.4 $\pm$ 10.3 $\ddagger$	57.1 $\pm$ 9.6 $\ddagger$	56.8 $\pm$ 8.9 $\ddagger$	55.1 $\pm$ 9.3 $\ddagger$	55.5 $\pm$ 9.2 $\ddagger$	55.1 $\pm$ 8.6 $\ddagger$	53.4 $\pm$ 8.2 $\ddagger$	54.4 $\pm$ 9.6 $\ddagger$
RS	65.3 $\pm$ 6.5	53.1 $\pm$ 6.0 $\S$	56.3 $\pm$ 7.4 $\S$	56.4 $\pm$ 8.3 $\S$	55.7 $\pm$ 7.7 $\S$	56.3 $\pm$ 8.4 $\S$	55.5 $\pm$ 7.9 $\S$	54.4 $\pm$ 8.1 $\S$	54.2 $\pm$ 8.5 $\S$
TV (ml)	96.6 $\pm$ 2.4	91.9 $\pm$ 8.1	81.6 $\pm$ 15.6 $\ddagger$	80.6 $\pm$ 8.2 $\ddagger$	77.6 $\pm$ 11.3 $\ddagger$	79.1 $\pm$ 13.4 $\ddagger$	73.6 $\pm$ 13.0 $\ddagger$	84.5 $\pm$ 11.3 $\ddagger$	94.5 $\pm$ 3.5
HR (bpm)	96.9 $\pm$ 1.9	92.1 $\pm$ 9.0	79.3 $\pm$ 15.1 $\S$	74.6 $\pm$ 13.2 $\S$	69.9 $\pm$ 14.8 $\S$	74.2 $\pm$ 13.4 $\S$	69.8 $\pm$ 17.4 $\S$	79.8 $\pm$ 7.0 $\S$	93.5 $\pm$ 3.9
BIS	2.1 $\pm$ 0.3	2.1 $\pm$ 0.3	2.7 $\pm$ 0.6	3.4 $\pm$ 1.0	3.6 $\pm$ 1.0	3.6 $\pm$ 0.7	3.9 $\pm$ 0.9	2.1 $\pm$ 0.3	2.0 $\pm$ 0.0
RS	2.1 $\pm$ 0.3	2.1 $\pm$ 0.3	3.2 $\pm$ 0.6	4.1 $\pm$ 0.9	4.2 $\pm$ 0.9	4.3 $\pm$ 0.6 $\ddagger$	4.4 $\pm$ 0.9 $\ddagger$	2.2 $\pm$ 0.3	2.0 $\pm$ 0.0

* TV indicates tidal volume; RR, respiratory rate; MV, minute volume; E_TCO₂, end-tidal carbon dioxide; MAP, mean arterial pressure; HR, heart rate; BIS, bispectral index; and RS, Ramsay score.

$\ddagger$ $P < .05$, 0.2 group vs 0.4 group.

$\S$ $P < .05$, vs control in the 0.2 group.

$\S$ $P < .05$, vs control in the 0.4 group.

Figure 3. Changes in mean arterial pressure (MAP) and heart rate (HR). In both the 0.2 group and the 0.4 group, the transient increase in MAP was observed at 5 minutes after the start of dexmedetomidine (DEX) infusion (not significant). MAP in the 0.2 group decreased significantly from an average of 86 mm Hg (baseline value) to 70–77 mm Hg over an 80-minute time period since 10 minutes after the start of DEX infusion ($P < .05$). MAP in the 0.4 group decreased significantly from an average of 83 mm Hg (baseline value) to 67–75 mm Hg over an 80-minute time period since 10 minutes after the start of DEX infusion ($P < .05$). HR in both groups decreased significantly since 5 minutes after the start of DEX infusion, and from an average of 65 beats per minute (baseline value) to 53–57 beats per minute ($P < .05$). However, there was no significant change in MAP and HR between both groups.

Figure 4. Changes in bispectral index (BIS) and Ramsay score (RS). BIS in both groups decreased significantly from 10 minutes after the start of dexmedetomidine (DEX) infusion to 30 minutes after the end of DEX infusion ($P < .05$). However, there was no significant change on the BIS monitor between both groups. RS in the 0.4 group reached the optimal sedation level earlier than in the 0.2 group, and there were significant differences between groups at 25 and 30 minutes after the start of DEX infusion ($P < .05$).

Figure 5. Changes in Trieger dot test plot error ratio (TDT p.e.r.). TDT p.e.r. in the 0.2 group increased significantly at 5 and 10 minutes from the end of dexmedetomidine (DEX) infusion ($P < .05$), and that in the 0.4 group increased significantly at 5, 10, and 15 minutes from the end of DEX infusion ($P < .05$). TDT p.e.r. in the 0.4 group was significantly higher than that in the 0.2 group at 5, 10, and 15 minutes from the end of DEX infusion ($P < .05$).

10 minutes after the start of the DEX infusion. In the comparison between groups, RS in the 0.4 group increased significantly more than that in the 0.2 group at 25 and 30 minutes after the start of the DEX infusion (Figure 4, Table 2).

TDT p.e.r.

In the comparison in each group, TDT p.e.r. in the 0.2 group increased significantly at 5 and 10 minutes from the end of the DEX infusion. Those were 37.5% and 25.4%, respectively ($P < .05$) in comparison with the baseline value 12.4%. TDT p.e.r. in the 0.4 group increased significantly at 5, 10, and 15 minutes from the end of the DEX infusion. Those were 54.3%, 37.6%, and 29.1%, respectively ($P < .05$) in comparison with the baseline value 11.5%. In the comparison between groups, TDT p.e.r. in the 0.4 group increased significantly in comparison with that in 0.2 group at 5, 10, and 15 minutes from the end of the DEX infusion (Figure 5, Table 3).

Figure 6. One-leg standing with eyes closed (O-L) test. In the 0.2 group, all subjects passed the O-L test at 60 minutes after the end of DEX infusion. However, all subjects in the 0.4 group passed the O-L test at 90 minutes after the end of DEX infusion.

O-L Test

All subjects were successful at 60 minutes post infusion in the 0.2 group, but 40% of the 0.4 group required more time to successfully complete the test. All participants in the 0.4 group could complete this test at 90 minutes post infusion (Figure 6, Table 3).

Amnesia

Amnesia of the 27-gauge needle prick test occurred in 69% of subjects in the 0.2 group and 85% of them in the 0.4 group at 21 minutes after the start of the DEX infusion. No significant difference in amnesia was recognized in the comparison between both groups (Figure 7).

DISCUSSION

Respiration

In comparison with baseline values in TV, RR, MV, and $E_T\text{CO}_2$, only TV in both groups decreased significantly from baseline with no statistically significant changes

Table 3. The Results of Trieger Dot Test Plot Error Ratio (TDT p.e.r.) and O-L Test (Mean $\pm$ SD)*

	Group	Baseline	After 5	After 10	After 15	After 30	After 60	After 90
TDT p.e.r. (%)	0.2	12.4 $\pm$ 10.4	37.5 $\pm$ 13.9	25.4 $\pm$ 14.5‡	17.0 $\pm$ 19.1	20.1 $\pm$ 13.0	13.8 $\pm$ 11.6	
	0.4	13.1 $\pm$ 7.1	54.3 $\pm$ 27.9¶†	37.6 $\pm$ 25.4¶†	29.1 $\pm$ 17.5§†	24.2 $\pm$ 15.7	17.0 $\pm$ 10.2	
O-L test (%)	0.2	100	0	0	31	85	100	
	0.4	100	0	0	0	23	77	100

* O-L test indicates one-leg standing test with eyes closed.

† $P < .05$, 0.2 group vs 0.4 group.

‡ $P < .05$, vs control in 0.2 group.

§ $P < .05$, vs control in 0.4 group.

|| $P < .01$, vs control in 0.2 group.

¶ $P < .01$, vs control in 0.4 group.

Figure 7. Amnesia of 27-gauge needle prick test at 21 minutes after the start of dexmedetomidine (DEX) infusion was recognized in 69% of subjects in the 0.2 group and in 85% of them in the 0.4 group. In the comparison between both groups, no significant difference was recognized in amnesia of 27-gauge needle prick test.

in RR, MV, and $E_T\text{CO}_2$. This respiratory change is similar to that seen in other studies using other α_2 agonists.^{14,15} Belleville et al¹⁶ have reported a small, but statistically significant, decrease in MV caused by DEX, thus reflecting a reduction in TV. The significant decrease in TV was consistent with Belleville's report, though MV did not show a significant change in the current study. This suggests that the decrease in TV occurred due to an inhibition in the central respiratory drive. Because α_2 adrenoceptors are ubiquitous throughout the central nervous system, including in the brainstem regions, and are instrumental in the control of breathing,¹⁷ it is likely that α_2 adrenoceptor activation of this region was responsible. However, the mechanism of α_2 adrenoceptors in the control of respiration has not yet been elucidated.

In clinical situations, the decrease in TV may be affected not only by an inhibition in the central respiratory drive but may also be due to an upper airway obstruction. However, the current results indicate that a significant decrease in TV has no influence on MV and $E_T\text{CO}_2$ in both groups, so that the two continuous infusion doses of DEX can be used without producing hypercapnia.

Cardiovascular

Though MAP in both groups increased nonsignificantly at 5 minutes following the loading dose of DEX, it decreased significantly after 10 minutes. This transient increase is thought to be due to the activation of peripheral α_{2B} adrenoceptors, which appeared earlier than the activation of central α_2 adrenoceptors.¹¹ At the same time as the early transient increase in MAP

in both groups, HR showed significant decreases from 65.2 ± 11.1 (baseline value) to 54.4 ± 10.3 in the 0.2 group, and from 65.3 ± 6.5 (baseline value) to 53.1 ± 6.0 in the 0.4 group. This bradycardiac effect is postulated to be a baroreceptor-mediated reflex event secondary to the MAP increase caused by an activation of α_{2B} adrenoceptor on the peripheral vasculature.¹⁸ With regard to the early effect, Hall et al¹¹ suggested that this might be an unavoidable effect of infusing α_2 agonists because the time differential between direct binding to the peripheral vascular receptors and diffusion into the central nervous system, which decreases the sympathetic outflow during intravenous infusions, is difficult to control. In addition, MacDonald et al¹⁸ reported that the bradycardiac effect induced by α_2 adrenoceptor agonists is partly mediated by α_2 adrenoceptors and partly by the baroreflex.

MAP in both groups showed significant decreases from the 10-minute time point following start of infusion throughout the 60 minutes post infusion time period. MAP decreased from an average of 86 mm Hg to 70–77 mm Hg (0.2 group) and 83 mm Hg to 67–75 mm Hg (0.4 group) over this 80-minute time period. In both groups, the decrease in MAP from 10 minutes until 60 minutes post infusion likely reflects an inhibition of the sympathetic outflow that overrode the direct peripheral effects of DEX on the vasculature.¹¹ Generally, local anesthesia including epinephrine is clinically used in dental procedures or oral surgery, and the use of the local anesthesia with epinephrine can lead to an increase in blood pressure.^{19,20} Therefore, its use should be evaluated during the loading of a DEX infusion of 6 $\mu\text{g}/\text{kg}/\text{hr}$ based on individual patient parameters to help ensure cardiovascular stability.

The difference between 2 continuous infusion doses of DEX had no differential effects on cardiovascular system because no significant difference was statistically recognized in the comparison between both groups.

Sedative Level

In both groups, a sedative level was observed on the BIS monitor from 10 minutes after the start of the DEX infusion to 30 minutes after the end of the DEX infusion. RS in both groups was not within the optimal sedative score at 5 minutes after the start of the DEX infusion. This result means the initial continuous infusion will likely need to be continued for a longer period, presumably for 10 minutes prior to starting the procedure, as is recommended in the US FDA labeling. This suggests that combining DEX with other sed-

atives such as a benzodiazepine to improve onset time may be clinically necessary.

RS in the 0.2 group did not reach the optimal sedative score at 10 minutes after the start of DEX infusion despite no significant changes between both groups. This result suggests that the loading dose should continue more than at least 5 minutes, or the continuous infusion dose should increase more than at least 0.4 $\mu\text{g}/\text{kg}/\text{hr}$ when sedation is induced with only DEX.

RS in the 0.4 group increased significantly relative to the 0.2 group at 25 and 30 minutes after the start of DEX infusion. It may be that RS may increase gradually if a continuous infusion dose of 0.4 $\mu\text{g}/\text{kg}/\text{hr}$ were continued past 30 minutes.

In both groups, a sedative state based on the BIS monitor was recognized despite no demonstration of a sedative condition on RS at 30 minutes post infusion. This result suggests that the DEX infusion needs to discontinue before completion of the dental procedure when sedation is maintained with a continuous infusion dose of 0.2–0.4 $\mu\text{g}/\text{kg}/\text{hr}$ DEX in the present study.

Amnesia

A 27-gauge needle prick test was used in the present study to assess for amnesia. Other studies have concluded no significant difference in the perception of pain produced by penetrations of 25-, 27-, and 30-gauge needles.²¹ There was no significant difference between the 0.2 group and the 0.4 group with regard to amnesia. However, the incidence of amnesia with DEX infusion (either the 0.2 group or the 0.4 group) may not be as likely during dental or oral surgery as these are more invasive than the 27-gauge needle prick. Therefore, to improve the incidence of amnesia during sedation for oral surgery and dental procedure, a sedative such as benzodiazepine may have to be added during sedation with DEX.

Recovery Period

In TDT p.e.r., the subjects in the 0.2 group regained their orientation from 15 minutes after the end of the DEX infusion, and the subjects in the 0.4 group regained their orientation from 30 minutes after the end of the DEX infusion, based on comparison to baseline recordings. However, the sedative level based on BIS levels was obtained in both groups at 30 minutes after the end of the DEX infusion. This demonstrates that DEX has a unique property¹¹ which allows the subjects to arouse easily with cognition from a sedative state. In TDT p.e.r. at 5, 10, and 15 minutes, but

not at 30 minutes, after the end of the DEX infusion, there were significant differences in the comparison between both groups. Recovery based on TDT was therefore within an acceptable range for both infusion groups.

While elimination half-life does not always equate to clinically effective sedation duration, the elimination half-life of DEX (2 hours²²), presented some concern regarding delayed return of recovery parameters with this agent. Nevertheless, all subjects in the 0.2 group could perform on O-L test at 60 minutes after the end of the DEX infusion, and all subjects in the 0.4 group could perform at 90 minutes post infusion. All subjects in the 0.2 group succeeded in the O-L test 30 minutes earlier than those in the 0.4 group. The difference of time is thought to be a dose-dependent effect. The subjects participated in this study were such young healthy volunteers that they could all recover their sense of equilibrium within 90 minutes. It is predicted to take 90 minutes or more to recover the sense of equilibrium when an elderly patient is sedated with DEX or a continuous infusion dose of DEX is more than 0.4 $\mu\text{g}/\text{kg}/\text{hr}$.

Additionally, MAP and HR in both groups still showed a significant decrease at 60 minutes after the end of the DEX infusion. This suggests that neither MAP nor HR recovers fully until at least 120 minutes pass post DEX infusion. From the viewpoint of the cardiovascular system, the decrease to within the normal range in MAP and HR can have some advantages which are helpful in patients with ischemic heart disease due to a decreasing myocardial oxygen demand.

Other Issues

This study evaluated various parameters of DEX infusion but no operative procedure was carried out. The utility of DEX remains to be seen in an oral/dental surgery model where there is increased stimulation of the surgical procedure despite good local anesthesia.

CONCLUSION

In comparison of sedation in the 0.2 group and in the 0.4 group, both groups have minimum influence on respiration and circulation, so that DEX infusion in the present study appears safe. Sedative level in the 0.4 group reached the optimal level earlier than that in the 0.2 group; however, sedative level in the 0.4 group tended to be higher than that in the 0.2 group at 25 and 30 minutes after the start of DEX infusion. No significant difference in amnesia was seen between

both groups to a mild pinprick. In comparison with the 0.2 group, DEX infusion in the 0.4 group may need to be discontinued earlier than that in the 0.2 group if earlier discharge is planned, particularly based on the O-L test used in this study. Lastly, sedation always includes a risk of an upper airway obstruction or unconsciousness, usually in a dose-dependent manner with a sedative agent. No airway obstruction was seen in our study; however, if a dentist confronts this situation during a dental procedure, the procedure will have to be discontinued and airway support provided until the situation improves.

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