Original Article

Comparison of Dexmedetomidine with Fentanyl for Sedation, Pain and Hemodynamic Control during Central Line Insertion in Intensive Care Unit under Conscious Sedation

M Santhisree[1], P Krishna Prasad[2], B Sowbhagya Lakshmi[3], N Krishnaveni[4]

[1]Assistant Professor, Department of Anesthesiology, Rangaraya Medical College, Kakinada, Andhra Pradesh, India, [2]Associate Professor, Department of Anesthesiology, Rangaraya Medical College, Kakinada, Andhra Pradesh, India, [3]Head & Professor, Department of Anesthesiology, Rangaraya Medical College, Kakinada, Andhra Pradesh, India, [4]Post-graduate, Department of Anesthesiology, Rangaraya Medical College, Kakinada, Andhra Pradesh, India

Abstract

Introduction: Aim of this study was to compare the efficacy of dexmedetomidine with fentanyl along with local field infiltration in controlling pain and discomfort associated with central venous catheter (CVC) insertion and procedural sedation.

Materials and Methods: A prospective, randomized, double-blind, trial of 50 patients scheduled for planned CVC insertion was undertaken. Patients were randomly assigned into two groups of 25 each, to receive either dexmedetomidine (1 μg/kg) or fentanyl (1 μg/kg) along with local anesthetic (LA) field infiltration. Pain, discomfort and sedation score were measured at 5 time points.

Results: The median pain scores were higher for fentanyl group at LA injection (5 [4-6]), which was significantly attenuated in the dexmedetomidine group (3 [3-5]; $P = 0.015$). The procedure related discomfort scores in the immediate post-procedural period was statistically significant in dexmedetomidine (4 [4-5]) group compared to fentanyl (5 [4-6]); $P = 0.008$. Dexmedetomidine provides intense sedation when compared to fentanyl during the procedure.

Conclusion: Pre-procedural bolus dexmedetomidine infusion provides adequate analgesia, sedation and patient comfort for CVC insertion along with LA field block.

Keywords: Analgesia, Central venous catheter, Dexmedetomidine, Fentanyl, Procedural pain

INTRODUCTION

Cannulation of a large central vein is a routine procedure in Intensive Care Unit (ICU) performed for monitoring the central venous pressure (CVP) and a number of additional therapeutic interventions.[1] For central line insertion, patient is required to stay in trendelenburg position and perfectly still. This causes considerable discomfort in a conscious patient. Steps such as anchoring of the catheter to the skin by suturing are also painful.[2] The field infiltration with local anesthetics (LAs) itself may be associated with significant pain.[3] Health care providers often underestimate the amount of pain that patient experiences regardless of cognitive impairment.[4] Combination of LA field block with sedation for procedural pain has several advantages. Sedatives can augment LA field block by acting as an anxiolytic and providing skeletal muscle relaxation, and amnesia. Fentanyl is a strong agonist at the μ-opioid receptors. It has a rapid onset and short duration of action.[5] Dexmedetomidine, is an α 2 adrenoreceptor agonist. It has sedative, sympatholytic, analgesic and anxiolytic actions. It does not produce significant respiratory depression.[6-9] Since, there are no studies comparing fentanyl with dexmedetomidine for procedural sedation, we have undertaken this study.

Access this article online

Website: www.ijss-sn.com

Corresponding Author:
Dr. M Santhisree, D.No. 13-2-2, D1 Apt., Sai Krishna Towers, Latchiraju Street, Kakinada - 533 002, Andhra Pradesh, India.
Phone: +91-7702322194. E-mail: santhisreemulam@gmail.com

- The objective of our study is to compare fentanyl with dexmedetomidine for sedation, pain and hemodynamic control during central venous catheter (CVC) insertion under conscious sedation.

MATERIALS AND METHODS

This study was conducted at GGH, Kakinada. This was a prospective randomized double blinded study conducted during April 2013-March 2014. 50 consenting patients of age 18-65 years, requiring central venous access via right internal jugular vein were enrolled in the study. After obtaining hospital ethics committee permission, they were divided into two groups using a computer generated randomization table.

Group F: Fentanyl 1 μ/kg intravenous (IV) was given.

Group D: Dexmedetomidine 1 μ/kg IV given.

The study drug was prepared according to the dosage, and the total volume was made to 10 ml in both the groups. An anesthetist, who was unaware of the study drug injected the drug just before the start of the procedure. Anatomical landmark of the targeted jugular vein was marked, and the skin over it was infiltrated with 5 ml of 2% lignocaine. This injection was given slowly over 15 s including suture sites. CVP cannulation was done with 7 French, tripe lumen catheter into right internal jugular vein using central approach.

Following parameters were recorded at 5 time points:
1. Discomfort
2. Pain
3. Sedation
4. Cardiovascular and respiratory events
5. Peripheral oxygen saturation.

Time 1: Baseline before infusion of study drugs (T1);

Time 2: After LA injection (LAI) (T2);

Time 3: Immediately, after the procedure, patient was asked to report the peak pain experienced during the procedure (T3);

Time 4: 10 min after the procedure is completed (T10) and

Time 5: 1 h after completion of the procedure (T60).

Discomfort was measured using an 11-point verbal numeric rating discomfort scale (VNRDS) from 0 to 10 (0: None, 10: Extreme discomfort); pain was measured by a verbal numeric rating pain scale (VNRPS) from 0 to 10 (0: No pain, 10: The worst pain imaginable).[9] Both the scales were explained to each patient while counseling the patient about the procedure. Sedation was measured by Ramsay sedation scale.

Respiratory events were taken as oxygen saturation by pulse oximetry (SpO_2) <92%, respiratory rate (RR) <8 breaths/min. If there is a decrease in SpO_2 to <92% for >30 s, it was treated sequentially with verbal stimulation, head tilt, chin lift, Guedel's airway and bag mask assisted ventilation. If there is a decrease in RR <8 breaths/min, then it was treated sequentially with verbal stimulation, mild prodding, and nasopharyngeal stimulation.

Cardiovascular events were taken as a single episode of variation in heart rate (HR) and systolic blood pressure (SBP) by >20% from patient baseline. If repeated or recurrent SBP <90 mmHg, it was treated with boluses of IV ephedrine 6 mg. Repeated or persistent (>30 s) decrease in HR was treated with IV atropine 0.6 mg and repeated as necessary.

The main outcomes of this study were measurement of pain and discomfort at five predefined time points. The additional outcomes were sedation score and occurrence of predefined adverse cardiovascular and respiratory events. For an alpha error of 0.05 and beta error of 0.20, a total of 25 patients were required in each group.

Statistical Analyses

Statistical analyses were performed using Graphpad software. (Graph pad prism 6.0 automated version held by California corporation) Data are expressed as means (standard deviation), or numbers (*n*). Before applying a particular statistical test, approximate normality of the distribution was assessed by Shapiro–Wilk test. For comparison of demography, baseline hemodynamic and respiratory data, unpaired Student's *t*-test (two-tailed) was employed. To compare gender distribution, and adverse effects in the groups, Chi-square and Fisher's exact tests were employed. To analyze pain, discomfort and sedation score Mann–Whitney test was used. $P < 0.05$ is considered as significant.

RESULTS

50 patients were recruited, with all completing the study. Both groups were comparable with respect to demographics, baseline respiratory, cardiovascular parameters, level of consciousness and indications for CVC insertion (Table 1).

Comparison between groups revealed that fentanyl group had worst pain scores at LAI, than dexmedetomidine group (fentanyl 5 [4-6] vs. dexmedetomidine 3 [3-5]; $P = 0.015$), which is statistically significant. When compared with fentanyl group, dexmedetomidine appeared to have more

analgesic effect, i.e., reduction in pain intensity to CVC insertion at all steps. However, no significant difference was observed in scores between the two groups 60 min after the procedure. The median pain score in fentanyl and dexmedetomidine groups are shown in Table 2.

Discomfort scores were significantly lower in dexmedetomidine group compared with fentanyl group at each step of the procedure (T2-T10) after LAI (T2, dexmedetomidine, (2 [1-2] vs. fentanyl, 2 [2-3]; $P = 0.02$), (T3, dexmedetomidine, 4 [4-5] vs. fentanyl, 5 [4-6]; $P = 0.008$), T10, (dexmedetomidine, 3 [3-5] vs. fentanyl, 4 [4-5]; $P = 0.02$) and these values are statistically significant. No significant difference exists at T60 with respect to discomfort ($P = 0.7$) (Table 3).

Sedation scores for dexmedetomidine group were significantly less compared to fentanyl group at the insertion of LAI (T2) and immediately after the procedure (T3 and T10). For the rest of the steps, no significant differences were found between the groups (Table 4). At the end of study period (T60), all the patients were conscious and responding to verbally spoken words. No patient from any group was excluded from the study.

A significant number of patients from dexmedetomidine group had a fall in HR by >20% from baseline and bradycardia than fentanyl. Four patients in D group had a fall in HR >20% when compared to one patient in F group ($P = 0.01$). More number of patients in the dexmedetomidine group (3/25) had a fall in SBP >20% of baseline in contrast to fentanyl group (2/25). Seven cases in F group had a fall in SpO_2 <92% when compared to two patients in D group and required a sequential verbal stimulation to maintain oxygen saturation above 98%. However, the difference between total events did not reach statistical significance ($P = 0.16$) (Table 5).

Of four patients from dexmedetomidine group, who had HR below 20% of the baseline, 2 patients experienced bradycardia and treated with atropine (0.6 mg bolus IV). All 3 patients from dexmedetomidine group who had >20% fall in SBP below the baseline are treated with a single dose of IV ephedrine (6 mg) because of persistent low SBP below 90 mmHg.

Table 1: Demographic data

Study variable	*n*=25		*P* value
	Group F	Group D	
Age	44.9	43.7	0.75
Sex	M=13 F=12	M=11 F=14	0.77
Height	5.5	5.8	0.84
Weight	62.10	63.44	0.83
SpO_2	97.50	97.89	0.61
HR	87.30	80.11	0.27
RR	17.00	15.75	0.41
SBP	117	114	0.80
Indication for central line			
Venous access	15	12	0.24
TPN	10	13	

RR: Respiratory rate, SBP: Systolic blood pressure, HR: Heart rate

Table 2: Pain scores

Time	Group F	Group D	*P* value
T1	1 (1-2)	1 (1-2)	0.7
T2	5 (4-6)	3 (3-5)	0.015
T3	5 (4-5)	4 (3-5)	0.04
T1	3 (2-4)	2 (2-3)	0.04
T60	2 (1-2)	2 (1-2)	0.67

Table 3: Discomfort score using VNRDS

Time	Group F	Group D	*P* value
T1	1 (1-2)	1 (1-2)	0.7
T2	5 (4-6)	4 (4-5)	0.02
T3	5 (4-6)	3 (3-5)	0.008
T10	4 (3-5)	3 (3-5)	0.02
T60	2 (1-2)	2 (1-2)	0.7

VNRDS: Verbal numeric rating discomfort scale

DISCUSSION

Central line insertion is a routine procedure in ICU, usually, done under local anesthesia. Even though LA effectively reduces pain, there is a considerable amount of discomfort and anxiety associated with the procedure. Sedation effectively reduces this anxiety, and comforts the patient.

The reason for choosing the study is to compare fentanyl the most commonly used opioid with novel drug dexmedetomidine, which has the additional hypnotic, sedative, and anxiolytic properties with very low respiratory depression.[8,9]

Pain is an unpleasant sensory and emotional experience that arises from actual or potential tissue damage associated

Table 4: Sedation score

Time	Group F	Group D	*P* value
T1	5 (4-5)	5 (4-5)	0.7
T2	5 (4-5)	4 (3-4)	0.02
T3	4 (3-4)	3 (2-4)	0.03
T10	4 (3-4)	3 (3-4)	0.04
T60	5 (4-5)	5 (4-5)	0.7

Table 5: Adverse effects

Study variable	I	II	*P* value
Respiratory	7	2	0.16
Cardiovascular	3	7	0.28

with central line insertion.[10] The sensory and emotional component of pain were measured with VNRPS and VNRDS respectively.[11]

Literature search revealed two studies, describing pain and discomfort as two separate perceptions experienced by patients during central line insertion. Morrison *et al.* in their five-point numeric rating scale described CVC as a "moderately painful and severely uncomfortable procedure."[4] There are two studies comparing fentanyl with placebo[12] and dexmedetomidine with placebo[13] both asserting sedative and analgesic effects of this drugs, but there are no studies comparing the two drugs.

The main finding of this study is that the dexmedetomidine reduces pain and discomfort better than fentanyl, and this difference is statistically significant except at T60 where there is no significant difference. This can be explained by multidimensional model of procedural pain.[14] Dexmedetomidine acts as an analgesic by modulating both the sensory-discriminative component of the pain and also the motivational-affective and cognitive component of pain.

The sedation provided with dexmedetomidine is profound compared to fentanyl. Even though cardiovascular events are high in the dexmedetomidine group they are not statistically significant. Respiratory events are comparable in both the groups. No group showed serious adverse effects of the drugs that require abandonment of the procedure.

CONCLUSION

Dexmedetomidine provides less discomfort, better sedation, analgesia when compared with fentanyl for central line insertion under conscious sedation in ICU. However, the risk of adverse effects requires monitoring for a ready intervention.

REFERENCES

1. Lindaiau L, Gropper M. Millers anaesthesia. 7th ed., Section 8. Philadelphia: Elsevier; 2010.
2. Donati A, Damiani E, Adrario E, Romano R, Pelaia P. Pain and discomfort management during central venous catheter insertion. Indian J Crit Care Med 2014;18:417-8.
3. Morris RW, Whish DK. A controlled trial of pain on skin infiltration with local anaesthetics. Anaesth Intensive Care 1984;12:113-4.
4. Morrison RS, Ahronheim JC, Morrison GR, Darling E, Baskin SA, Morris J, *et al.* Pain and discomfort associated with common hospital procedures and experiences. J Pain Symptom Manage 1998;15:91-101.
5. Stoelting RK, Hillier SC. Opioid-agonists. Pharmacology & Physiology in Anaesthetic Practice. 4th ed., Ch. 3. Philadelphia: Lippincott Williams & Wilkins; 2006.
6. Puntillo K, Casella V, Reid M. Opioid and benzodiazepine tolerance and dependence: application of theory to critical care practice. Heart Lung 1997;26:317-24.
7. Arain SR, Ruehlow RM, Uhrich TD, Ebert TJ. The efficacy of dexmedetomidine versus morphine for postoperative analgesia after major inpatient surgery. Anesth Analg 2004;98:153-8.
8. Unlugenc H, Gunduz M, Guler T, Yagmur O, Isik G. The effect of pre-anaesthetic administration of intravenous dexmedetomidine on postoperative pain in patients receiving patient-controlled morphine. Eur J Anaesthesiol 2005;22:386-91.
9. Talke P, Richardson CA, Scheinin M, Fisher DM. Postoperative pharmacokinetics and sympatholytic effects of dexmedetomidine. Anesth Analg 1997;85:1136-42.
10. Katz J, Melzack R. Measurement of pain. Surg Clin North Am 1999;79:231-52.
11. Todd KH, Funk JP. The minimum clinically important difference in physician-assigned visual analog pain scores. Acad Emerg Med 1996;3:142-6.
12. Techanivate A, Dusitkasem S, Anuwattanavit C. Dexmedetomidine compare with fentanyl for postoperative analgesia in outpatient gynecologic laparoscopy: A randomized controlled trial. J Med Assoc Thai 2012;95:383-90.
13. Samantaray A, Rao MH. Effects of fentanyl on procedural pain and discomfort associated with central venous catheter insertion: A prospective, randomized, double-blind, placebo controlled trial. Indian J Crit Care Med 2014;18:421-6.
14. Samantaray A. Effects of dexmedetomidine on procedural pain and discomfort associated with central venous catheter insertion. Indian J Anaesth 2014;58:281-6.

How to cite this article: Santhisree M, Prasad PK, Lakshmi BS, Krishnaveni N. Comparison of Dexmedetomidine with Fentanyl for Sedation, Pain and Hemodynamic Control During Central Line Insertion in Intensive Care Unit under Conscious Sedation. Int J Sci Stud 2014;2(8):1-4.

Source of Support: Nil, **Conflict of Interest:** None declared.