ORIGINAL ARTICLE

A Comparative Study of Dexamethasone vs Dexmedetomidine to Attenuate Propofol-induced Intravenous Pain

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Abstract

Pain experienced by the patient while the inducing dose being given in the peripheral vein is the most common drawback of this widely used agent. Seen to vary from mild to moderate pain and complained by 2/3rd of the patients around the globe. It is among one of the high-priority outcomes which need changes during general anesthesia. Propofol is supposed to directly irritate the venous tunica intima and release nitric oxide. Propofol itself in emulsion or microemulsion form or opioid adjuvants like fentanyl, alfentanyl, remifentanyl and tramadol are tried with good results. Other agents like ketamine, ketorolac, diclofenac, flurbiprofen and combination of clonidine–ephedrine are also tried but using a larger vein and using it with lignocaine seems to be the best and easiest so far. In this randomized study, we have observed that the pain alleviation was superior in dexmedetomidine (DX) group compared to dexamethasone (DM) group, however, the drop in heart rate was significantly more in DX group, but it was treated only with a single dose of atropine in four patients. Hence dexmedetomidine can be used to attenuate the propofol-induced intravenous pain.

Keywords: ASA grade 1, ASA grade 2, Dexamethasone, Dexmedetomidine, Propofol.

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Introduction

Pain experienced by the patient while the inducing dose being given in the peripheral vein is the most common drawback of this widely used agent.[1] Seen to vary from mild to moderate pain and complained by 2/3rd of the patients around the globe.[2,3] It is among one of the high-priority outcomes which need changes during general anesthesia.[4] Propofol is supposed to directly irritate the venous tunica intima and release nitric oxide.[4] Many interventions are tried and intravenous lignocaine being the most commonly use drug to alleviate pain as it is widely available during all procedures.[4] Physical means like cooling the site of injection, local spray of nitrous oxide and accessing the largest vessel available are some means tried.[5,6]

Propofol itself in emulsion or microemulsion form or opioid adjuvants like fentanyl, alfentanyl, remifentanyl and tramadol are tried with good results.[7] Other agents like ketamine, ketorolac, diclofenac, flurbiprofen and combination of clonidine–ephedrine are also tried but using a larger vein and using it with lignocaine seems to be the best and easiest so far.[8,9]

Other drugs tried with varying results are dexmedetomidine a newer α adrenergic agonist agent, 5-hydroxytryptamine-3 (5-HT3) antagonists such as ondansetron, granisetron, ramosetron and palonosetron.[10,11] Here we conducted a study with easily available drugs in the operation theater dexamethasone and dexmedetomidine in alleviating the pain while injecting the drug for induction.

Materials and Methods

This is a triple-blind study and 60 patients were randomly selected and randomized into two groups by using closed envelop method. Two drug interventions were tried to reduce the intravascular propofol induced pain, that is, dexamethasone (DM) and dexmedetomidine (DX). Group DM (dexamethasone) received 0.1 mg/kg of dexamethasone whereas group DX (dexmedetomidine) received 0.5 mcg/kg body weight of dexmedetomidine (Table 1).

All cases posted for surgeries under general anesthesia of ASA grade 1 and 2 aged between 18 and 65 years were included. Patients with major and uncontrolled comorbid illness, mentally unsound and those who were not able to understand the pain scale and apprehensive patients were excluded (Table 2).

The patients were informed about the procedure in their native language and the pain grading was explained in detail on the day before the surgery and informed written consent documented. On the day of the surgery OT (operation theater) technician 1 prepares the syringes with either DX 0.5 mcg/kg body weight in 5 mL syringe or DM 0.1 mg/kg body weight and reconstitute to 5 mL with saline as well as the technician 1 notes down the patient details and the drug details and hand over the drug to technician 2, who administers the drug. Pain was assessed by the anaesthesiologist 1 and graded based on the VAS score and objective score. The data was collected and given to anesthesiologist 2 who does the statistical analysis.

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Once the patient was shifted to the operation theater monitors were connected and the baseline vitals were noted and intravenous line was secured on the dorsum of the hand with 18 g cannula. Tourniquet was tied distal to the cannula in order to achieve venostasis. Patients were injected either DM or DX with the tourniquet in place. The tourniquet was released after five minutes and 25% of the calculated dose of the propofol was injected over 10 seconds. The pain was assessed both by subjective and objective methods.

In the objective method anesthesiologist assesses the pain by using the pain scale devised by Rochette and colleagues to evaluate the propofol induced pain. In the subjective method pain was assessed by using visual analogue score, where the pain score was marked from 1 to 10. One mark being no pain and 10 mark indicating the worst pain ever. The patients were given the scale to mark the severity of the pain after one minute. If the patients score was more than four in subjective method and more than two in objective pain assessment method, patients were injected 1.5 mg/kg loxicard and induced with remaining dose of the propofol. After assessment of the pain, patients were induced and vitals were recorded at 1, 2 and 3 minutes.

Results

The baseline characters of the patients are depicted in Table 1 and there was no significant differences in both the groups as well as the vitals were also not statistically significant. The vitals post injection of the propofol recorded at 1st, 2nd and 3rd minute are depicted in Table 2. We have observed that the heart rate had significantly decreased in DX group at 2nd and 3rd minute, however, only four patients in DX group had heart rate <50/minute, which was treated with 0.5 mg of atropine. There was no significant decrease in mean blood pressure in both the groups (Table 3).

The VAS pain score in the group DX was 3.83 with a standard deviation of 2.28 and the pain score in the DM was 4.53 with a standard deviation of 2.44 the *p* value being <0.0001 was statistically significant. Hence DX is more effective in pain alleviation compared to DM. The objective pain score in DX group was 1.00 with a standard deviation of 0.83 and the pain score in group DM was 1.5 with a standard deviation of 0.94. The *p* value is 0.0328, which is statistically significant. Hence the pain alleviation was better in DX group. The pain score was more in females in both the groups compared to the males (Table 4).

Discussion

In Indian anesthestic scenario as far as general anesthesia is concerned propofol is the most common intravenous inducing agent and the added advantage is its minimal side effects.[12-14] Two pathways of pain have been described to explain the pain during intravenous injections of propofol.[15] One explains the direct irritant effect of the drug and the other by stimulation of venous nociceptive receptors or free nerve endings involving myelinated Aδfibres.[14,15] The pain experienced immediately and the latent pain mediated by activation of kallikrein–kinin system have been targeted.[14,15] Kinin–kallikrein system activation release bradykinin leading to the vasodilatation and hyperpermeability thus exposing the free nerve endings to the propofol causing pain.[16] As mentioned earlier methods to reduce direct irritation like infusing propofol in emulsion or micro emulsion form, increasing the flow rate, cooling and diluting it.[17] Also aiming at inhibition of activation of kallikrein–kinin system by pretreating it with lignocaine, ephedrine, ondansetron, metoclopramide, thiopentone or ketamine are also tried.[17]

Dexmedetomidine a more selective alpha 2 agonist is being used as it has both sedative and analgesic effects systemically acts on the dorsal horn of the spinal cord, inhibiting the release of

Table 1: Demographic profile

Sl no.		*Dexamethasone group*	*Dexmedetomidine group*	*p value*
1	Age in years	66.13	65.87	0.8858
2	Wt in kgs	54.45	55.39	0.778
3	Ht in cm	153.41	155.21	0.2590
4	ASA1/2	25/5	23/7	0.768
5	Sex	19 males/11 females	20 males/10 females	0.866

Table 2: Baseline vitals

Sl no.		*Dexamethasone group*	*Dexmedetomidine group*	*p value*
1	Heart rate	72.55 ± 3.24	71.84 ± 4.33	0.420
2	Mean BP	80.08 ± 5.47	78.08 ± 4.92	0.11
3	SpO_2	97.97 ± 1.03	98.23 ± 1.25	0.3713

Table 3: Vitals at 1–3 minutes following 25% drug injection

Sl no.			*Dexamethasone group*	*Dexmedetomidine group*	*p Value*
1	Heart rate	1st min	71.67 ± 4.38	71 ± 3.47	0.5163
		2nd min	71.43 ± 4.13	61.87 ± 5.47	0.0001
		3rd min	69.77 ± 2.39	62.17 ± 4.97	0.001
2	Mean BP	1st min	75.23 ± 5.66	74.23 ± 6.75	0.756
		2nd min	74.04 ± 6.58	77.90 ± 4.9	0.4525
		3rd min	85.23 ± 6.14	82.23 ± 15.07	0.319

Table 4: Scoring system for propofol injection pain

		Score
Motor events	1. No movements	0
	2. Slight hand withdrawal	1
	3. Marked withdrawal rubbing, trying to tear off the IV line	2
	4. General restlessness	3
Verbalization scale	5. No vocalization	0
	6. Purposeless moaning	1
	7. Explicit process	2
	8. Screams, cries	3
Total		0–6

substance P.[18] It also inhibit the kallikrein–kinin system signaling pathway.[18] Its action at the intimal level has been hypothesized as due to the alpha 1 and alpha 2 agonist action leading to release of prostaglandins.[1] Prostaglandins nullifies the vasoconstrictor effect of propofol thus reducing the pain.[1]

The other drug in the study is the widely used dexamethasone which decreases the production of nitric oxide which mediates the propofol induced pain at the venous intima.[10,19] It can control inflammation in response to multiple stimuli and reduce the vasoactive and chemical factors, the secretion of lipolytic and proteolytic enzymes.[10,19] They reduce the destruction of leukocytes in the affected areas and reduce the expression of antiinflammatory cytokines such as NOS-2 and COX-2.[10,19] They act on macrophages, monocytes, endothelial cells, basophils, fibroblasts and lymphocytes, and reduce formation of leukotrienes, cytokinins, including interleukins, and tumor necrosis factor-α and prostaglandins.[10,19]

Linage et al., in their study to reduce the propofol induced pain used different concentration of dexmedetomidine at different time interval.[10] They observed that dexmedetomidine at 1 mcg/kg body weight is more effective in pain reduction.[10] They found dexmedetomidine to be effective at 5 minutes before induction with no hemodynamic instability.[10] Shireen et al., compared dexamethasone with lignocaine pretreatment to reduce te propofol induced vascular pain and observed that dexamethasone is as effective as lignocaine in this regard.[20] Mitesh et al., observed that ondansetron 0.1 mg/kg, dexamethasone 0.1 mg/kg and lignocaine 0.5 mg/kg is better than cold propofol in alleviating propofol induced pain.[21] Huridrome et al., observed that pretreatment with dexmedetomidine 0.25 mcg/kg body with venous occlusion for minute is as effective as lignocaine in alleviating propofol induced vascular pain.[10] Similar study by Ahmed et al., reported reduction in propofol injection pain from 60 to 15% after granisetron pre-treatment.[10] Meta-analysis of 56 studies shows IV lignocaine (0.5 mg/kg) can reduce the pain up to 60% where 12 types of interventions were compared.[5]

Alipour et al., observed differences in pain caused by intravenous agent propofol in different groups.[1] They observed better pain relief in lignocaine and ramosetron group compared to ondansetron and magnesium sulfate group.[1] Sumalatha et al., pre-treatment with ramosetron was as effective as lignocaine and more effective than ondansetron in reducing the occurrence of propofol-induced pain.[1] Similar study by Swarika et al., reported ramosetron as an effective method of reducing the occurrence of propofol-induced pain and has the advantage of preventing post-operative nausea vomiting without the additional administration of other drugs.[1]

Conclusion

In this randomized study, we have observed that the pain alleviation was superior in DX group compared to DM group, however, the drop in heart rate was significantly more in DX group, but it was treated only a single dose of atropine in four patients. Hence dexmedetomidine can be used to attenuate the propofol induced intravenous pain.

References

1. Sumalatha GB, Dodawad RR, Pandarpurkar S, et al. A comparative study of attenuation of propofol-induced pain by lignocaine, ondansetron, and ramosetron. Indian J Anaesth 2016;60:25–29. DOI: 10.4103/0019-5049.174810
2. Huang C-L, Wang Y-P, Cheng Y-J, et al. The effect of carrier intravenous fluid speed on the injection pain of propofol. Anesth Analg 1995;81(5):1087–1088. DOI: 10.1097/00000539-199511000-00033
3. Gehan G, Karoubi P, Quinet F, et al. Optimal dose of lignocaine for preventing pain on injection of propofol. Br J Anaesth 1991;66(3): 324–326. DOI: 10.1093/bja/66.3.324
4. Macario A, Weinger M, Truong P, et al. Which clinical anesthesia outcomes are both common and important to avoid? The perspective of a panel of expert anesthesiologists. Anesth Analg 1999;88(5):1085–1091. DOI: 10.1097/00000539-199905000-00023
5. Picard P, Tramèr MR, Prevention of pain on injection with propofol: a quantitative systematic review. Anesth Analg 2000;90(4):963–969. DOI: 10.1097/00000539-200004000-00035
6. Jalota L, Kalira V, George E, et al. Prevention of pain on injection of propofol: systematic review and meta-analysis. BMJ 2011;342:d1110. DOI: 10.1136/bmj.d1110
7. Wang H, Cork R, Rao A. Development of a new generation of propofol. Curr Opin Anaesthesiol 2007;20(4):311–315. DOI: 10.1097/ACO.0b013e3281667777
8. King SY, Davis FM, Wells JE, et al. Lidocaine for the prevention of pain due to injection of propofol. Anesth Analg 1992;74:246–249. DOI: 10.1213/00000539-199202000-00013
9. Vijayant GA, Tej KK, Avtar S, et al. Analgesic effect of lignocaine, tramadol, ketorolac, and ketoprofen in ameliorating propofol inducedpain. J Anesthesiol Clin Pharmacol 2005;21:389–393. DOI: 10.18410/jebmh/2019/146
10. He L, Xu JM, He T, et al. Dexmedetomidine pretreatment alleviates propofol injection pain. Ups J Med Sci 2014;119:338–342. DOI: 10.3109/03009734.2014.941049
11. Ambesh SP, Dubey PK, Sinha PK. Ondansetron pretreatment to alleviate pain on propofol injection: a randomized, controlled, double blinded study. Anesth Analg 1999;89:197–199. DOI: 10.1097/00000539-199907000-00035
12. Ayoglu H, Altunkaya H, Ozer Y, et al. Does dexmedetomidine reduce the injection pain due to propofol and rocuronium? Eur J Anaesthesiol 2007;24:541–545. DOI: 10.1017/S0265021506002250
13. Turan A, Memis D, Kaya G, et al. The prevention of pain from injection of propofol by dexmedetomidine and comparison with lidocaine. Can J Anaesth 2005;52:548–549. DOI: 10.1007/BF03016541
14. Koo SW, Cho SJ, Kim YK, et al. Small-dose ketamine reduces the pain of propofol injection. Anesth Analg 2006;103:1444–1447. DOI: 10.1213/01.ane.0000243334.83816.53
15. Scott RP, Sunders DA, Norman J. Propofol: Clinical strategies for preventing the pain on injection. Anaesthesia. 1988;43:492–494. DOI: 10.1111/j.1365-2044.1988.tb06641.x
16. Lee JW, Park HJ, Choi J, et al. Comparison of ramosetron's and ondansetron's preventive anti–emetic effects in highly susceptible patients undergoing abdominal hysterectomy. Korean J Anesthesiol 2011;61:488–492. DOI: 10.4097/kjae.2011.61.6.488

17. Mc Crirrick A, Hunter S. Pain on injection of propofol: the effect of injectate temperature. Anaesthesia 1990;45:443–444. DOI: 10.1111/j.1365-2044.1990.tb14329.x
18. Erdivanli B, Altun M, Sezen OK, et al. Anti-nociceptive, analgesic and pathohistological effects of intrathecal dexmedetomidine and bupivacaine in rats. Rev Bras Anestesiol 2013;63:183–187. DOI: 10.1016/j.bjane.2012.02.006
19. Kwak HJ, Min SK, Kim JS, et al. Prevention of propofol-induced pain in children: combination of alfentanil and lidocaine vs alfentanil or lidocaine alone. Br J Anaesth 2009;103:410–412. DOI: 10.1093/bja/aep163
20. Ahmad S, De Oliveira GS Jr, Fitzgerald PC, et al. The effect of intravenous dexamethasone and lidocaine on propofol-induced vascular pain: a randomized double-blinded placebo-controlled trial. Pain Research and Treatment 2013;2013: Hindawi Publishing Corporation (article ID: 734531). DOI: 10.1155/2013/734531
21. Patel M, Patel N, Vachchrajani P. A comparative study of attenuation of propofol induced pain by lignocaine, ondansetron, dexamethasone and cold propofol per se. Int J Sci Res 2018;8:2319-7064. DOI: 10.21275/ART201837