

Large Antecubital Vein Versus Small Vein on Dorsum of Hand for Propofol Injection Pain: A Comparative Study

Muhammad Arif¹, Aftab Imtiaz², Fareya Usmani³, Syed Hamid Ali⁴, Asim Masroor Rashid⁵, Atif Iqbal⁶

Abstract

Objective: To determine the mean difference in pain scores between large antecubital vein compared to small vein on hand dorsum for propofol injection pain in patients undergoing general anaesthesia surgery.

Methods: A randomized control trial was conducted at Department of Anaesthesiology, Abbasi Shaheed Hospital, Karachi from May 2018 to November 2018. All patients aged 18-60 years of either gender undergoing scheduled elective surgery under general anaesthesia having ASA status I or II were consecutively enrolled. Group A was offered propofol through antecubital vein and group B was given injection propofol through small vein on the dorsum of the hand. The 2% lidocaine 1 ml admixture in 1% propofol 19 ml was administered to patients through large antecubital vein and small dorsal vein at hand. Anaesthesia induction was carried out as routine and as per procedure. All patients were explained the use of VAS (Visual Analogue Scale) and were asked to report the intensity of the pain immediately after the injection propofol.

Results: Of 120 patients, the overall mean age and BMI of the patients was 40.92 ± 10.03 years and 27.11 ± 5.05 kg/m² respectively. An insignificantly higher mean difference of age ($p= 0.052$) and body mass index (BMI) ($p= 0.901$) were observed in small vein group as compared to the antecubital group. There were 64 (53.3%) males and 56 (46.7%) females. There were 43 (35.80%) smokers, 52 (43.3%) hypertension (HTN), and 29 (24.2%) diabetes mellitus patients. The mean difference of pain was significantly lower in antecubital vein group as compared to the small vein group, i.e. 2.48 ± 0.77 vs 5.67 ± 0.75 respectively ($p<0.001$).

Conclusion: A significant difference in mean pain scores was observed between large antecubital vein versus small vein on hand dorsum for propofol injection pain among patients undergoing surgery for general anaesthesia. We recommend using larger veins for propofol bolus while inducing general anaesthesia patients.

Keywords: Veins, pain, propofol, injections

IRB: Approved by Research Evaluation Unit, College of Physicians and Surgeons Pakistan. Ref No. CPSP/REU/ANS-2016-174-1667. Dated: 3rd May 2018.

Citation: Arif M, Imtiaz I, Usmani F, Ali SM, Rashid AM, Iqbal A. Large Antecubital Vein Versus Small Vein on Dorsum of Hand for Propofol Injection Pain: A Comparative Study (online). *Annals ASH KMDC* 2020;25:

(ASH & KMDC 25(2):104;2020)

Introduction

For general anaesthesia induction and sedation, propofol is a drug of choice mainly due to its rapid onset, limited time of action and simple titration. It has little hemodynamic improvement if

doses are given gradually and are measured¹. Hypersensitivity reaction with propofol is very rare and the incidence of pain recorded on propofol injection is 26-70 percent². Because propofol is used widely in clinical settings the injection discomfort cannot be ignored. Unfortunately, in reducing the pain absolutely, none of the treatment was considered successful. In many hospital settings propofol's everyday uses warrant its painless use. The mechanisms proposed for pain are local mediator release and/or the immediate painful effect of propofol on nerve endings³.

^{1,2,4,5}Department of Anaesthesia, Abbasi Shaheed Hospital

³Department of Surgery, Sir Syed College of Medical Sciences

⁶Department of Anaesthesia, Patel Hospital

Correspondence: Dr. Muhammad Arif
Department of Anaesthesia, Abbasi Shaheed Hospital
Email: m_arif80@hotmail.com

Date of Submission: 22nd April 2020

Date of Acceptance: 27th August 2020

Propofol was considered superior to other steps, such as shift in propofol temperature, intravenous catheter or injection speed, via a large antecubital vein⁴.

Propofol lidocaine admixture, ketamine pretreatment, antidepressants, anti-inflammatory anti-steroids, magnesium sulfate, ondansetron, ramosetron, and many of the medications were extensively studied. Pharmacological treatments were tested on different drugs with pretreatment of lidocaine with venous occlusion⁵⁻⁶.

The rationale of the study is that the data is scarce on this topic locally and anesthetists are using different modalities to alleviate the pain on propofol injections. Therefore, the present study is designed to assess the effectiveness of different sites of injection and the better of the two was used in subsequent patients in future.

Patients and Methods

This randomized controlled trial was conducted from May 2018 to November 2018 at Department of Anaesthesiology, Abbasi Shaheed Hospital, Karachi. The Abbasi Shaheed Hospital is among Pakistan's most prestigious hospitals. Located in one of the most populous neighborhoods in Karachi, it is also the third largest public sector hospital that comes under the umbrella of the City Government of Karachi. It has the strength of 850 beds and a total of 18 operation theatres for various departments.

Ethically all the patients were made clear about the purpose, procedure, risk, and benefits of the study and confidentiality was ensured. Signed informed consent was also obtained from all study participants after explaining the pros and cons of the study.

All patients age 18 to 60 years of either gender having ASA physical status I & II underwent scheduled elective surgery under general anesthesia were included. Non-probability consecutive sampling technique was applied. Whereas those who were obese, history of lidocaine / propofol allergy,

taking some analgesics, and pregnant women were excluded.

Open Epi sample size calculator was used for the purpose of sample size estimation. In previously published study VAS score of patients in antecubital vein group was 2.63 ± 1.80 while VAS score of patients in small vein on dorsum of hand was 5.95 ± 2.79 . In addition, significance level was taken as 01% and power of the test as 90%. The required sample size came out to be 150 however in order to generalize our results on population we took the sample of 120 (60 per group).

Pain scores were assessed using visual analogue scale of 0-10. Visual analogue score was used immediately after propofol injection to assess the pain score.

Post informed consents patients were randomly divided into two groups through sealed opaque envelop method. Envelop distribution was performed with the help of randomized number list which will generate by applying formulation method in Microsoft Excel 2016. Group A was offered propofol through antecubital vein and group B was given injection propofol through small vein on the dorsum of the hand. A 20-gauge intravenous catheter was inserted in respective veins by anesthesia staff having more than one-year experience. The use of visual analog scale was demonstrated to all the patients. Pain level was noted after the propofol injection was administered. The 2 percent lidocaine 1 ml admixture in 1 percent propofol 19 ml was administered to patients through large antecubital vein and small dorsal vein at hand. Anesthesia induction was carried on as routine as per procedure. Data like age, gender, place of residence, ASA status, and pain intensity was noted.

Statistical analysis was performed using SPSS version 22. Age, height, weight, body mass index, family income and pain score were computed as mean \pm standard deviation while gender, educational status, residential status, ASA status, smoking status, HTN, DM, were computed as frequencies and percentages. Two groups were compared with re-

spect to pain score using independent t-test. Significance level was set at 0.05.

Results

Of 120 patients, the overall mean age of the patients was 40.92 ± 10.03 years. The mean age was insignificantly higher in small vein group as compared to the antecubital group (p= 0.052). The mean weight of the patients was 60.10 ± 5.13 kg. The mean weight was insignificantly higher in antecubital group as compared to the small vein group (p=0.887). The mean height of the patients was 1.54 ± 0.06m. The mean height was insignificantly higher in antecubital group as compared to the small vein group (p=0.845). The mean BMI of the patients was 27.11 ± 5.05 kg/m². The mean BMI was insignificantly higher in small vein group as compared to the antecubital group (p=0.901).

There were 64 (53.3%) males and 56 (46.7%) females. There were 20 (16.7%) patients with <15,000 rupees monthly family income, 60 (50%) had in between 15,000 to 30,000 rupees monthly family income and 40 (33.3%) patients with >30,000 rupees monthly family income. ASA status I was observed in 57 (47.5%) patients whereas ASA status II in 63 (52.5%) patients. There were 43 (35.80%) smokers, 52 (43.3%) HTN, and 29 (24.2%) diabetic patients. Educational status of majority of the patients was intermediate or less (n=63, 53%), followed by graduate or more (n=43, 35.8%) whereas secondary or less in 14 (11.7%) patients. Residential status of 46 (38.3%) patients was rural while 74 (61.7%) patients had urban residential status.

The mean difference of pain was significantly lower in antecubital vein group as compared to the small vein group, i.e. 2.48 ± 0.77 vs 5.67 ± 0.75 respectively (p-value <0.001). (Table 2)

A significant mean difference of pain scores and groups when stratified according to age, gender, educational status, monthly income, residential status, smoking, HTN, and DM of the patients. (Table 3)

Discussion

This study was conducted with the aim to find out a mean difference in pain scores between large antecubital vein compared to small vein on hand dorsum for propofol injection pain in patients undergoing general anaesthesia surgery. For this purpose, all patients age 18-60 years of either gender undergoing scheduled elective surgery under general anaesthesia having ASA status I or II were consecutively enrolled.

The pain during injection cannot be dismissed as propofol is frequently used in healthcare settings². Pain mechanisms are the release and/or the immediate painful effect of propofol on nerve endings by local mediators⁴⁻⁵.

Table 1. Demographic characteristics of the patients (n=120)

	Total	Antecubital Vein	Small Vein	p-value	95% CI
Age years	40.92±10.03	39.15±10.09	42.71±9.74	0.052	-7.13 to 0.34
Weight kg	60.10±5.13	60.16±5.17	60.03±5.11	0.887	-1.72 to 1.99
Height m	1.54±0.06	1.54±0.06	1.53±0.03	0.845	-0.02 to 0.03
BMI kg/m ²	27.11±5.05	27.04±5.07	27.16±5.01	0.901	-1.95 to 1.72

Table 2. Mean difference of pain with respect to group (n=120)

Group	Mean ± SD	p-value	95% CI
Antecubital Vein	2.48 ± 0.77	<0.001	-3.45 to -2.91
Small Vein	5.67 ± 0.75		

Table 3. Comparison of mean pain difference to group and general characteristics (n=120)

Variables	Group	Mean±SD	p-value	95% CI
Male	Antecubital Vein	2.63±0.84	<0.001	-3.09 to -2.34
	Small Vein	5.34±0.62		
Female	Antecubital Vein	2.28±0.12	<0.001	-4.06 to -3.31
	Small Vein	5.96±0.75		
Smokers	Antecubital Vein	2.67±0.76	<0.001	-3.31 to -2.40
	Small Vein	5.53±0.69		
Non-smokers	Antecubital Vein	2.36±0.76	<0.001	-3.72 to -3.03
	Small Vein	5.73±0.78		
	Small Vein	5.59±0.79		

Independent t-test applied, p-value <0.05 considered significant

In the current study, the mean difference of pain was significantly lower in antecubital vein group as compared to the small vein group, i.e. 2.48 ± 0.77 vs. 5.67 ± 0.75 , respectively. Similar findings were observed in previous studies as well. In a study conducted by Narejo et al, it was reported that severity of pain was considerably lower in antecubital vein than that of small vein on dorsum of hand⁷. Similar findings were reported in a meta-analysis by Jalota et al⁸.

Since these theories of propofol mediated pain, different researchers have postulated various approaches for alleviating this issue. Propofol injection through large antecubital vein was considered a better option than other non-pharmaceutical procedures, such as changes in propofol temperature, a large intravenous catheter and speed of injection⁹.

Different drug pharmacologic treatments, lidocaine pretreatment with venous occlusion have been tested¹⁰. Admixture of propofol-lidocaine¹¹⁻¹², Ketamine pretreatment¹³, antidepressants¹⁴, magnesium sulfide¹⁵, ondansetron^{15,16}, ramosetron, and many other medications have been thoroughly studied¹⁷. In 20% vs 71% of patients, the efficacy of large antecubital vein and small vein in the dorsal hand were evaluated to severe pain, which means that 80% and 29%, respectively, for large antecubital vein and smaller vein were successful¹⁸.

Propofol reduces cerebral blood flow, intracranial pressure, and cerebral metabolic rate while maintaining dynamic and static self-regulation¹⁹ and vascular responsiveness to CO₂²⁰. Such beneficial effects on cerebral physiology make propofol an almost perfect hypnotic for anesthesia during neurosurgery. There is conflicting evidence of propofol's neuroprotective effects during ischaemia-reperfusion injury²¹. However, its function has been developed in multimodal neuroprotection²².

Propofol has both pro- and anticonvulsive activity. On one side, during or shortly after the start or end of propofol anaesthesia, a number of reports of convulsions and exciting events such as myoclonus

and tremor have been reported²³. Such events could be the product of the subcortical region's preferential depression. On the other hand, the function of propofol has been well known as an effective treatment of epileptic status^{24,25}.

Some investigators suggest that the lipid solvent for propofol activates the plasma kallikrein-kinin system and produces bradykinin, which in turn causes local vein vasodilation and hyper-permeability. This modification of the peripheral vein may increase the contact between the aqueous phase propofol and free nerve endings of the vessel resulting in pain²⁶. Others investigators believe that propofol as a member of phenol group can have direct irritant effect on local vein by stimulating nociceptors and free nerve endings giving rise to an immediate sensation of pain^{27,28}. Based on these assumptions of propofol induced pain pathway, different investigators postulated different interventions to alleviate this problem. The injection of propofol through large antecubital vein was considered as a superior method than any other non-pharmacological measures like changing the temperature of propofol, large intravenous catheter and speed of injection⁸.

Among the all above interventions, propofol-lidocaine admixture is well known to be the best simple method⁷. Lidocaine is a local anesthetic. It reduces the pain by two possible mechanisms, direct effect of local anesthetic on vascular smooth muscle and modifying the pH of propofol. As lidocaine is a weak base solution when it dissolves with lipid it decreases the pH of the mixture. Thus, more propofol in lipid phase cause less pain on injection²⁹. Injection of propofol through large vein is another effective way in reducing pain. The vein diameter, flow rate, and endothelial structure might account for the reduction in pain. The injection of propofol through a large antecubital vein, minimize the extent to which a high concentration of propofol comes into contact with the sensitive endothelial wall. Furthermore, propofol will move faster from the injection site when more blood will be available to dissipate the bolus. Additionally, the composition of

nociceptors along the endothelial wall might differ between the smaller veins of the hand and the larger antecubital veins. A meta-analysis showed that among the non-pharmacological and pharmacological interventions for the most effective method was the use of large antecubital vein followed by pretreatment with lidocaine combined with venous occlusion⁸.

Propofol is a popular drug used for induction of anesthesia and sedation in intensive care, emergency room and for endoscopic procedures. Propofol injection pain was ranked seventh among the most important thirty-three low-morbidity clinical anesthesia problems²⁸. Unfortunately; despite its popularity pain on its injection is still unresolved issue because exact mechanism of this pain is not clear so far. This limitation in understanding the cause of propofol injection pain necessitates many investigators to address the issue.

Thus, use of large antecubital vein for propofol injection is associated with significantly less pain when compared with smaller veins at back of the hand. It is recommended larger veins for propofol bolus could be use while inducing general anesthesia patients.

The finding of the study could be highlighted in the light of limitation the study failed to analyze data on certain important variables like clinical and laboratory characteristics. Despite of these limitations, this study has reported current finding from a large public sector hospital of metropolitan city Karachi. Further studies are recommended on larger sample size to preclude the finding of this study.

Conclusion

A significant difference in mean pain scores was observed between large antecubital vein versus small vein on hand dorsum for propofol injection pain among patients undergoing surgery for general anaesthesia. We recommend using larger veins for propofol bolus while inducing general anaesthesia patients.

References

1. Sahinovic MM, Struys MM, Absalom AR. Clinical pharmacokinetics and pharmacodynamics of propofol. *Clin Pharmacokinet* 2018;57:1539-1558. [doi:10.1007/s40262-018-0672-3]
2. Sim JY, Lee SH, Park DY, Jung JA, KIKH, Lee DH, et al. Pain on injection with micro emulsion propofol [Online]. *Br J Clin Pharmacol* 2009;67:316-325. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2675042/>. Accessed on: 19th August 2020. [doi: 10.1111/j.1365-2125.2008.03358.x]
3. Desousa KA. Pain on propofol injection: Causes and remedies. *Indian J Pharmacol* 2016;48:617-623. [doi:10.4103/0253-7613.194845]
4. Youn AM, Hsu TM. Heated carrier fluids in decreasing propofol injection pain: a randomized, controlled trial. *Korean J Anesthesiol* 2017;70:33-38. [doi:10.4097/kjae.2017.70.1.33.]
5. Bano F, Zafar S, Sabbar S, Aftab S, Haider S, Sultan ST. Intravenous Ketamine attenuates injection pain and arterial pressure changes during the induction of Anaesthesia with Propofol: a comparison with Lidocaine [Online]. *J Coll Physician Surg Pak* 2007; 17: 390-393. Available from <https://europepmc.org/article/med/17686348>. Accessed on 5th March 2020
6. Fujii Y, Itakura M. A comparison of pretreatment with Fentanyl and Lidocaine preceded by venous occlusion for reducing pain on injection of Propofol: a prospective, randomized, double blinded, placebo-controlled study in adult Japanese surgical patients. *Clin Ther* 2009;31:2107-2112.[doi:10.1016/j.clinthera.2009.10.012.]
7. Narejo AS, Khan MU, Aljaza TS, Sheraz M, Aqil M. Comparison of large antecubital vein versus small vein on dorsum of hand for the prevention of propofol injection pain [Online]. *Anaesthesia, Pain & Intensive Care* 2017;21:8-12. Available from <http://apicareonline.com/index.php/APIC/article/view/151>. Accessed on 31st March 2020.
8. Jalota L, Kalira V, George E, Shi YY, Hornuss C, Radke O, et al. Prevention of pain on injection of Propofol: Systemic review and meta-analysis. *BMJ* 2011;342:1110.. [doi: 10.1136/bmj.d1110.]
9. Madan HK, Singh R, Sodhi GS. Comparison of Intravenous Lignocaine, Tramadol and Keterolac for Attenuation of Propofol Injection Pain. *J Clin Diagn Res* 2016;10:UC05-UC8. [doi:10.7860/JCDR/2016/20444.8118]
10. Alipour M, Tabari M, Masoomeh A. Paracetamol, Ondansetron, Granisetron, Magnesium Sulfate and Lidocaine and Reduced Propofol Injection pain. *Iran Red Crescent Med J* 2014;16:e16086. [doi:10.5812/ircmj.16086]

11. Rahimzadeh P, Faiz SH, Nikoobakht N, Ghodrati MR. Which one is more efficient on Propofol 2% injection pain? Magnesium sulfate or ondansetron: A randomized clinical trial. *Adv Biomed Res* 2015; 4: 56. [doi:10.4103/2277-9175.151593]
12. Taloh Y, Singh NR, Borang M, Sinam P, Pyngrope JF. Low dose ketamine pretreatment for alleviation of propofol injection pain-A study [Online]. *Indian Journal of Clinical Anaesthesia* 2018; 5:170-174. Available from: <https://www.ipinnovative.com/journals/IJCA/article-details/6660/volume/178/issue/529>. Accessed on: 19th August 2020. [doi: 10.18231/2394-4994.2018.0031]
13. Thompson KA, Goodale DB. The recent development of propofol (DIPRIVAN) [Online]. *Intensive Care Med* 2000;26 Suppl 4:S400-S404. Available from: <https://link.springer.com/article/10.1007/PL00003783>. Accessed on: 19th August 2020. [doi:10.1007/pl00003783]
14. Schuttler J, Schwilden H, editors. *Modern anesthetics (handbook of experimental pharmacology)*, vol. 182. Heidelberg: Springer; 2008. Available from <https://www.springer.com/gp/book/9783540728139> Accessed on: 5th March 2020
15. Baker MT, Naguib M. Propofol: the challenges of formulation. *Anesthesiology* 2005;103:860-876. [doi:10.1097/0000542-200510000-00026]
16. Mohammadi SS, Khosravi M, Shoeibi G. Comparing Intravenous Lidocaine, Ondansetron and Their Combination on Reducing Pain of Injection of Propofol [Online]. *Archives of Anesthesiology and Critical Care* 2016; 2: 154-156. Available from <http://aacc.tums.ac.ir/index.php/aacc/article/view/37>. Accessed on: 5th March 2020.
17. Sumalatha GB, Dodawad RR, Pandarpurkar S, Jajee PR. 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]
18. Strebel S, Lam AM, Matta B, Mayberg TS, Aaslid R, Newell DW. Dynamic and static cerebral autoregulation during isoflurane, desflurane, and propofol anaesthesia. *Anesthesiology* 1995;83:66-76. [doi:10.1097/0000542-199507000-00008]
19. Vimala S, Arulvelan A, Vilanilam GC. Comparison of the Effects of Propofol and Sevoflurane Induced Burst Suppression on Cerebral Blood Flow and Oxygenation: A Prospective, Randomised, Double-Blinded Study. *World Neurosurg* 2019;S1878-8750:33043-8. [doi:10.1016/j.wneu.2019.12.015]
20. Kotani Y, Nakajima Y, Hasegawa T, Satoh M, Nagase H, Shimazawa M, et al. Propofol exerts greater neuroprotection with disodium edetate than without it. *J Cereb Blood Flow Metab* 2008;28:354-366. [doi:10.1038/sj.jcbfm.9600532]
21. Fan W, Zhu X, Wu L, Wu Z, Li D, Huang F, et al. Propofol: an anesthetic possessing neuroprotective effects. *Eur Rev Med Pharmacol Sci* 2015;19:1520-1529.
22. Krishna HM. Neuroprotection under Anesthesia. *Yearbook of Anesthesiology*-8. 2019; 31: 79. Available from: http://www.jaypeebrothers.com/pgDetails.aspx?book_id=9789352706037 Accessed on: 5th March 2020
23. Fernando SM, Fitzpatrick T, Hurdle H, Anand A, Skinner CR, Boyd KU, et al. Recurrent non-epileptiform seizure-like phenomena secondary to propofol administration. *Can J Anaesth* 2017;64:783-785. [doi:10.1007/s12630-017-0869-1]
24. Prabhakar H, Kalaivani M. Propofol versus thio-pental sodium for the treatment of refractory status epilepticus. *Cochrane Database Syst Rev* 2017; 2: CD009202. [doi: 10.1002/14651858.CD009202.pub4]
25. Prisco L, Ganau M, Aurangzeb S, Moswela O, Hallett C, Raby S, et al. A pragmatic approach to intravenous anaesthetics and electroencephalographic endpoints for the treatment of refractory and super-refractory status epilepticus in critical care. *Seizure* 2020;75:153-164. [doi:10.1016/j.seizure.2019.09.011]
26. Nakane M, Iwama H. A potential mechanism of propofol-induced pain on injection based on studies using nafamostat mesilate. *Br J Anaesth* 1999;83:397-404. [doi: 10.1093/bja/83.3.397.]
27. Ambesh SP, Dubey PK, Sinha PK. Ondansetron pretreatment to alleviate pain on propofol injection: A randomized, controlled, double-blinded study. *Anesth Analg* 1999;89:197-9. [doi: 10.1097/0000539-199907000-00035.]
28. Wang W, Wu L, Zhang C and Sun L. Is propofol injection pain really important to patients? *BMC Anesthesiol* 2017;17:24. [doi: 10.1186/s12871-017-0321-7.]
29. Amir MS. Prevention of propofol injection pain, using lidocaine in a large volume does it make a difference? A prospective randomized controlled double blinded study [Online]. *Egyptian Journal of Anaesthesia* 2013;29:291-294. Available from: <https://www.tandfonline.com/doi/full/10.1016/j.egja.2013.04.003>. Accessed on: 19th August 2020. [doi: 10.1016/j.egja.2013.04.003]