

Propofol injection pain during sedation for colonoscopy: the role of venous catheterization site

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Abstract

Background: The use of propofol has seen its greatest growth in the operating room and diagnostic centers. Pain associated with propofol injection is a common clinical issue. There have been many attempts to reduce pain, however, complete inhibition has not been achieved.

Methods: Data was collected from patients sedated with propofol in the Endoscopy room at San Juan de Dios Hospital. The data obtained included the McCrerrick pain on propofol injection scale, demographic variables, caliber and location of venous catheters, as well as concomitant medications. The data was recorded by the treating anesthesiologist and reviewed by the researcher.

Results: 58% of patients did not experience pain on propofol injection; 24,8% experienced mild pain, 12,8% moderate pain, and 1,7% severe pain. Statistically, the group of patients that received propofol through a venous catheter in the antecubital fossa, experienced less pain than those with a venous catheter placed in the hand, wrist, or anterior forearm. ($p=0,006$).

Conclusion: The best way to reduce pain on propofol injection is to place the venous catheter in the antecubital fossa.

Keywords: Pain, propofol, sedation, colonoscopy.

Received Date: April 19th, 2012

Accepted Date: October 25th, 2012

Sedation can be defined as the pharmacologically depression of the state of consciousness.¹ The majority of endoscopic procedures occurred with a moderate level of sedation.² It's goal is to relieved anxiety and discomfort, and to provided amnesia while preserving the cardiopulmonary function.³

In recent years, sedation with propofol has increased significantly for gastrointestinal endoscopy.⁴ Several studies had established the propofol is superior to traditional sedation systems, because its offers a rapid onset and a short recovery time, with an excellent satisfaction level for the patient and the endoscopist.⁵ Propofol is especially appropriate for the outpatient setting, since it markedly decreases the need for vigilance after the procedure.⁴

Propofol injection pain is a common clinical problem, presented in 28-90% of patients.^{6,7} Moderate to intense pain has been reported in 32-67% of patients that received a bolus of standard dose.⁸

Propofol is directly irritating on venous intima,⁹ also, it activates the kinin-kallikrein system, resulting in bradykinin production (a potent endogenous algesic) and provoked pain.¹⁰

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With the decrease of postoperative adverse events, the patient satisfaction is assuming great importance. Pain, and particularly pain caused by anesthetic, is a major important cause of dissatisfaction for the patient, which is particularly true during sedation for colonoscopy; therefore, it is necessary to have studies designed to identify factors associated with the onset of pain. In Costa Rica, there are no published studies on the matter and therefore, a research protocol was developed to document the factors associated with the onset of pain and propofol injection in sedation for colonoscopy, in order to obtain results that could be used for the benefit of future patients undergoing sedation with propofol.

This study evaluated the factors associated with the onset of pain during the administration of propofol, and compared the relative efficacy of different analgesic techniques to prevent pain caused by injecting propofol.

Materials and methodology

After the Bioethics Local Committee's (Comité Local de Bioética (CLOBI)) approval, an observational analytical cohort study was made. The outpatient population admitted to the Endoscopy Room of San Juan de Dios Hospital was analyzed, during the period between December 1st, 2008 and January 30th, 2009; to which were administered sedation with propofol for a colonoscopy procedure. This sample has a level of confidence of 95%, design effect of 1.0 and preciseness of 88%.

Variables taken into account were: age, genre, weight, co-administered medications, gauge and location of the employed venous catheter and the verbal or corporal manifestation of pain during propofol injection, according to MacCirrriek Scale.¹¹

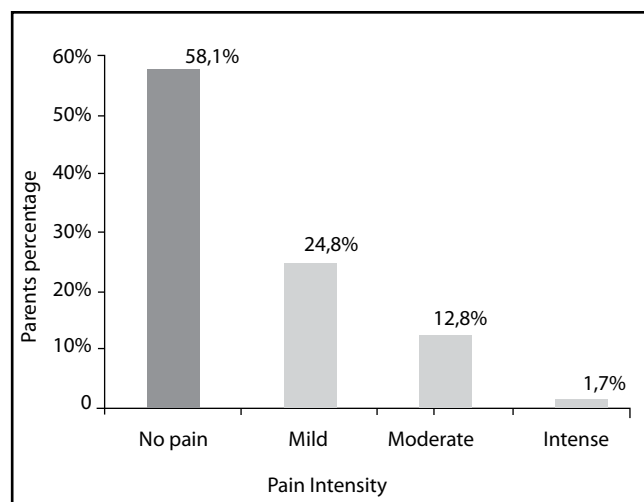


Figure 1. Percentage distribution of patients, according to pain intensity with propofol injection. San Juan de Dios Hospital. December 2008 - January 2009. Source: Data collection sheet

The study included all outpatients with ASA physical status 1 and 2, capable of giving informed consent. Pregnant women, patients with neurological diseases and those expose to sedatives and painkillers 24 hours prior were excluded.

The attending anesthesiologist daily assigned to the Endoscopy Room performed sedation without the researcher's intervention. Since it is an observational study, no action was made to interfere with the sedation technique.

The data was processed in a SPSS version 13 statistical package, and Excel to create the graphics. All frequencies were distributed for all variables.

A comparison between groups was made, according to the level of pain reported (no pain, mild, moderate or intense pain). The results were put on a Chi-square (χ^2) test, under a null hypothesis of independence.

The average for quantitative variables (age, channelization attempts and doses/weight) was compare between the levels of pain reported; the results were analyzed through ANOVA. The correlation between the pain manifested in the I.V. route and the intensity of the pain from the propofol injection was analyzed, through Spearman's rank correlation coefficient. In all the analysis, it was considered significant when $p < 0.05$ (Figure 1).

Results

We worked with all the patients admitted in the Endoscopy Room that met the inclusion criteria in the period studied, a total of 117; it was found that 58.1% of patients did not have pain with propofol injection. Among those who did present pain, the majority (24.8%) was mild, 12.8% was moderate and 1.7% was intense (Table 1).

The most common site for venous catheterization was the antecubital fassa (34.5%), and less used were the back of the hand, the forearm and the wrist. A significant statistical difference was found ($p = 0.006$), since pain on the antecubital fossa was of lower intensity to propofol injection respect the other groups.

Discussion

Since there is no national statistics, or data that could be use for comparison, it was decided to use the numbers reported on international literature.

Table 1. Patient distribution, according to venous catheterization site. San Juan de Dios Hospital. December 2008 - January 2009

Pain to propofol	Catheterization site				
	Forearm	Back of the hand	Antecubital fossa	Wrist	Total
No pain	17	13	32	5	67
Mild	9	9	7	4	29
Moderate	3	8	0	4	15
Intense	0	1	0	1	2
Total	29	31	39	14	113

Source: Data collection sheet

Of a total of studied patients, 58.1% didn't have pain with propofol injection, on 2.6% the data was not recollected, because the data collection sheet was illegible or incomplete; which means that about 40% of patients did have some degree of pain with propofol injection, quantify on McCrerrick scale. Comparing this information with the one reported worldwide, the numbers found were similar.

Namely, multiple studies agreed that pain with propofol injection is a common adverse effect of this anesthetic and even, that is of high incidence. However, the exact percentage varies immensely among diverse related studies. For example, Stark et al study establish that up to 30% of patients presented pain when administered propofol intravenously.¹² Nathason *et al* establish the incidence of pain of discomfort with propofol injection in 45-75% of cases.¹³

Meanwhile, previous studies have reported that pain incidence goes from 40 to 86% in Cheong et al article,¹⁴ up to frequencies between 28-90% according to Agarwal et al.¹⁵ This is consistent with the current study, placing the incidence of pain with propofol injection in a 42% in our area, which is consistent with what Doenicke et al say, who argue that using propofol for anesthesia, without a previous dose of fentanyl or lidocaine, 30 to 70% of patients reported pain on the injection site. Similarly, the percentage found in our area is within the range indicated by Tan and Onsiang, who place the pain in 5 to 48% of cases.¹⁶

No differences were found in terms of demographic characteristics, which is consistent with the literature, in relation to pain onset.¹⁷ The incidence and intensity of propofol injection pain was similar in different age groups, genre, ASA physical states and weight.

When comparing different intravenous catheter gauges used to obtain vascular access, it was noted that there were no differences between groups. In the current study, the attending anesthesiologist was not limited to a choice of

venous catheter gauge, which provided an opportunity to compare sizes. Consistent with the current study, Picard and Tramer's meta-analysis, found no evidence of a relation between the size of the catheter or the injection rate, with the probability of pain with propofol administration.¹⁸

Considering that many studies have limited to one site of venous catheterization, in this study the door was left open for the attending anesthesiologist, with the purpose of using this variable for the review and the statistical analysis. A significant statistical difference was found between groups ($p=0.006$).

When injecting propofol to the back of the hand, pain was present in 18 of 31 patients, for an incidence of 58%; on the wrist veins the pain incidence was present in 9 of 14 patients, corresponding to 64% of cases. This is perfectly consistent with what was stipulated in Dubey and Kumar article, who say that propofol injection pain is still a problem, when presenting in 32-67% of patients to whom, propofol injection was give through small veins of the hand.¹⁸

On contrast, propofol injection pain at the antecubital fossa was documented in only 7 of 39 patients neither of them referred moderate or intense pain. Thus, it coincides with what was reported by Iyilikci et al, who cite that one method to reduce propofol injection pain is to administered it into an antecubital large vein.¹⁹ Even Ohmizo et al referred that the use of a larger vein is one of the most effective methods to prevent this pain.²⁰ An article by Doenicke et al, established that with the injection on proximal large veins, the probability of a painful reaction was of 0-30%.²¹

Patients data were tabulated according to the incidence and level of pain with propofol injection, which were compared in relation to the administered dose of propofol, considering, of course, the weight of the patient and therefore, it was ordered according to dose by weight, through the following ranges: less than 1 mg/kg, 1 to 2mg/kg, and from

Table 2. Patient distribution, according to pain when injecting propofol and co-administrated drugs. San Juan de Dios Hospital. December 2008 - January 2009

Pain with Propofol	Fármacos coadministrados					
	Fentanyl	Fentanyl + midazolam	Lidocaine	Lidocaine + midazolam	Midazolam	None
No pain	12	2	7	4	8	35
Mild	4	10	1	1	2	11
Moderate	5	2	1	0	1	6
Intense	1	0	0	0	0	1
Total	22	14	9	5	11	53

Source: Data collection sheet

2 to 3 mg/kg for sedation. No relationship was found between the various infused doses of propofol and the degree of pain presented by patients.

In relation to the studied medication used prior to propofol injection, precisely to reduce pain associated with it, the literature is plenty. Although many strategies has been described to relief propofol injection pain, the complete inhibition has not been achieved.²² The most common method in clinical practice is mixing 10 to 40mg of lidocaine into a syringe with propofol prior to injection.¹⁶ However, lidocaine administration prior to the injection of propofol and the lidocaine mixture directly with propofol, are less effective than intravenous application with a tourniquet, emulating a Bier blockage.¹⁸

Fujii and Shiga study demonstrated that 40mg of lidocaine in young patients and 20mg for older ones were enough to minimize the pain associated with propofol.²³ Since lidocaine is absorbed by oil droplets, a mixture of lidocaine and propofol must be used quickly so the anesthetic effect is present in the vein.²¹ In the research, nine patients received lidocaine alone concomitantly with propofol, doses ranging from 10 to 80mg. In addition 5 patients received lidocaine and midazolam, prior to propofol. None of them presented moderate or intense pain to propofol injection, however despite the strong correlation, this finding did not reach statistical significance ($p=0.06$).

The use of opioids – especially those of short action like alfentanil or fentanyl – and derivatives has been described to prevent effectively the pain of propofol injection.²⁴ With the use of fentanyl, it is determined that it is required to administrate in 3 or 4 patients to prevent propofol injection pain ($NNT=3-4$).¹⁸

Pang *et al* and Mok *et al*, has demonstrated that 40mg of meperidine is equally effective as 60mg of lidocaine to reduce pain associated to propofol.^{25,26} This is similar to an

Egyptian study, which documented equal efficacy of premedicating with 0.5mg/kg of Meperidine as with 1mg/kg of lidocaine.²² This phenomenon can be attributed to meperidine's anesthetic effect, that could be related to an structure similarity to cocaine and tetracaine.²⁷ Also, butorfanol (an opioid agonist-antagonist) had demonstrated to reduce propofol injection pain as well. Two milligrams were equivalent to 40mg of lidocaine to attenuate this adverse effect, according to Agarwal *et al*.¹⁵

The only opioid used was fentanyl. This was applied alone or with midazolam in 36 patients, without documenting a significant pain reduction when injecting propofol. Interestingly, none of the attending anesthesiologists combined fentanyl with lidocaine, during the research period.

According to the collected data during the observation period of the study, there are no benefits in the prior administration of lidocaine, fentanyl or midazolam to reduce the incidence or the intensity of pain with propofol injection. Nor pain reduction with the combination of these drugs. Therefore, there is no significant statistical difference between studies patient groups, according to co-administered drugs, and the level of pain with propofol in sedation for colonoscopy on the Endoscopy Room at San Juan de Dios Hospital ($p=0,062$). (Table 2).

In conclusión, 40% of patients presented pain with propofol injection. 25% presented a mild pain; 13% presented moderate pain, and only 2% presented intense pain when administering propofol. There was not a significant statistical reduction on pain with propofol injection when using lidocaine or fentanyl concomitantly. A significant pain reduction was significant when placing the venous catheter on the antecubital fossa, but the used gauge of the venous catheter was not affected.

Thanks: We thank Mayra Cartín, Costa Rica University stateswoman, for the support of the statistical analysis.

We thank Dr. Franklin Dawkins Arce, anesthesiologist and epidemiologist from Calderón Guardia Hospital, for his contributions in the final preparation of this manuscript.

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