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Review Article

A REVIEW OF VARIOUS MODALITIES FOR PREVENTION OF PAIN ON PROPOFOL INJECTION

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A B S T R A C T

Propofol is chemically 2,6 diisopropyl phenol, an alkylphenol. All phenols have a propensity to cause irritation of skin and mucous membrane; and propofol is no exception. Pain after propofol injection can be immediate as well as delayed. The immediate pain is due to irritation of endothelium lining of the peripheral vein whereas delayed pain is due to release of various mediators such as kininogen from kinin cascade. Various methods have been proposed to decrease the pain on propofol injection such as selection of large calibre vein, fast injection speed, diluting it prior to administration and preadministration of various drugs such as lignocaine, antiemetics, ketamine etc. No single drug or measure is completely effective in alleviating PPI. Hence, it is advisable to have at least two or more measures in combination to effectively prevent the pain on propofol injection.

INTRODUCTION

Propofol is chemically 2,6 diisopropyl phenol, an alkylphenol. All phenols have a propensity to cause irritation of skin and mucous membrane; and propofol is no exception. Pain on propofol injection (PPI) is also described as angialgia which implies that pain is due to vascular involvement.[1] Medical literature is full of various methods to check the pain on propofol injection. The aim of this review was to study various methods available for preventing or decreasing PPI.

Mechanism

Pain after propofol injection can be immediate as well as delayed after 10-20 seconds.[2] The immediate pain is due to irritation of endothelium lining of the peripheral vein whereas delayed pain is due to release of various mediators such as kininogen from kinin cascade.[3] At the molecular level, non selective ligand gated cation channels such as transient receptor potential ankyrin 1 (TRPA1) and transient receptor potential vanilloid 1 (TRPV1) are the main mediators responsible for propofol induced pain and release of neuropeptides.[4]

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METHODS

Various methods have been proposed to decrease the pain on propofol injection. These methods can be broadly divided into: (a) modification of patient/doctor factors, (b) modification in propofol formulation, and (c) pre administration of various drugs.

Modification of patient/doctor factors

(i) Selection of large calibre vein- when drug is injected into large calibre vein (antecubital vein), most of the drug is injected in midstream and there is lesser contact of propofol with the endothelial lining, leading to less pain.[5]

(ii) Speed of injection- many studies indicate that slow injection causes more pain than the fast injection since slow injection may increase the concentration and duration of exposure of propofol to the vein wall.[6,7,8]

Modification in propofol formulation

(i) Increasing lipid content- PPI can be diminished by increasing the lipid content of propofol as it decreases the concentration of propofol in the aqueous phase. The propofol emulsion constitutes of two phases: outer aqueous phase and inner lipid phase. It is the aqueous phase which causes pain on coming in contact with the venous endothelial lining.[3]

(ii) Cooling- Injecting propofol at low temperature decreases the pain significantly probably, by decreasing the speed of kinin cascade. Terada *et al*, in their study found that topicalcooling decreased the incidence of pain from 39% to 17%.[9]

(iii) Warming- Fletcher *et al*, in their study found that warming propofol to 37°C decreased the incidence of pain from 59% to 22%.[10]

(iv) Diluting- decreasing the cocentration of propofol from 1% to 0.5% is also found to decrease incidence of PPI significantly.[11,12]

Preadministration of various drugs

(i) Lignocaine- IV lignocaine, in dose of 0.5mg/kg with a rubber tourniquet tied in the forearm, given 30-120 seconds prior to propofol has been shown to decrease the incidence of PPI.[13] Some authors recommend occlusion time of 60 sec for lignocaine action to decrease pain.[14] In a randomised controlled trial performed by Massad *et al*, no difference was found when varying duration of venous occlusion (15, 30 or 60 seconds) was applied during lignocaine injection.[15]

(ii) Antiemetics- 10mg metoclopramide given prior to propofol injection reduces the propofol pain.[16] Granisetron 2mg IV along with venous occlusion for 1 minute effectively decreases the pain on propofol injection.[17]

(iii) Ketamine- ketamine in dose of 0.1mg/kg IV given over 15 seconds, just before propofol decreased the incidence of PPI.[18,19] Wang *et al* in their study found that ketamine in the dose of 0.3mg/kg was effective in decreasing the pain.[20] Saadawy *et al*, in their study, recommended pretreatment with ketamine 0.4mg/kg along with venous occlusion to prevent propofol injection pain.[21]

(iv) Opioids- Fentanyl 150 mcg along with venous occlusion for 1 minute effectively decreases the PPI.[22] Alfentanil 1 mg IV bolus, given 15 seconds before propofol decreases the pain on propofol injection.[23]

(v) Nitrous oxide- pretreatment with inhaled nitrous oxide 67% also decreases the incidence of PPI.[24,25] Kim *et al* in their study found nitrous oxide with or without lignocaine to be superior to lignocaine alone.[24]

(vi) Sevoflurane- pretreatment with sevoflurane also alleviates the pain of propofol injection. In one RCT, it was found that using 3% sevoflurane at the time of preoxygenation for 1 minute along with lignocaine-tourniquet completely prevented the pain upon propofol injection, whereas sevoflurane alone provided analgesia similar to that provided by lignocaine premixed with propofol.[26]

(vii) Sodium Bicarbonate- alkalinizing lignocaine with 1 ml of 8.4% sodium bicarbonate for pretreatment decreased the PPI significantly compared to lignocaine alone.[27]

(viii) NSAIDS- Diclofenac in dose of 15 mg and 25 mg decreases the severity of pain but has no significant effect on the incidence of PPI.[28] Pretreatment with ketorolac 10 mg IV along with venous occlusion for 120 seconds alleviates propofol pain.[29] Parecoxib in 40 mg dose with venous occlusion effectively reduces the severity and frequency of PPI.[30]

(ix) Hyoscine N-butylbromide (HnBB)- Pretreatment with 20 mg HnBB, 20 seconds prior to propofol significantly alleviates PPI.[31]

(x) Dexamethasone- 6 mg dexamethasone along with venous occlusion for 1 minute significantly rduces the incidence of pain, which is comparable to lignocaine 20 mg. However, when both are combined (lignocaine plus dexamethasone), they are more effective in alleviating PPI than alone.[32]

As none of the available techniques or drugs is fully effective in blocking PPI, it is advisable to have multimodal approach for alleviating PPI. Using two or more drugs or measures reduces the incidence of PPI to single digit as compared to PPI incidence of double digits when only single drug or measure is used.[33]

CONCLUSION

No single drug or measure is completely effective in alleviating PPI. Hence, it is advisable to have at least two or more measures in combination to effectively prevent the pain on propofol injection.

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