

Original Article

Sevoflurane versus propofol sedation during periocular anesthetic injections in oculoplastic procedures: An open-label randomized comparison



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Abstract

Purpose: The purpose of the current investigation was to make an objective controlled comparison of pain tolerance, patient satisfaction and potential complications during the injection of local anesthesia in oculoplastic procedures under short-term sedation using inhalational versus parenteral sedatives.

Methods: This was an open-label, randomized clinical trial where patients were randomized to 3 groups. Group I: Sedation with intravenous propofol. Group II: Sedation with inhaled sevoflurane. Group 3: Control group receiving no sedation.

Results: A total of 396 patients were randomly assigned, and 375 were included in the final analysis. Study groups were similar in age, gender, and distribution of operative procedures performed. There was no statistically significant difference in the adjusted primary composite outcome measure between propofol and sevoflurane (pain scores and patient satisfaction). Significantly more patients in group I required restraining during periocular injections than group II or III ($p < 0.001$). Significantly more patients sneezed in group I than group II ($p < 0.001$) and none in the control group. Three patients in group II suffered severe excitation–disinhibition during emergence from sedation which was rapidly reversible, and 3 more suffered a severe bout of postoperative nausea and vomiting (PONV).

Conclusion: Sevoflurane and propofol during periocular anesthetic injections produce an equally favorable experience. Sevoflurane is introduced painlessly, and offers better patient control with less induction of the sneezing reflex which may provide a higher safety profile, however short-term aggression/disinhibition and PONV may be an issue in some patients.

Keywords: Propofol sedation, Sevoflurane, Periocular anesthesia, Peribulbar anesthesia, Ophthalmic anesthesia

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Introduction

To date the ideal preoperative sedative drug is still elusive. An ideal sedative should be introduced painlessly, should have a rapid onset of action, minimal side effects, and speedy recovery and should not lead to intraoperative behavioral disturbances.¹ The most commonly used

sedatives in oculoplastic procedures nowadays are propofol, midazolam, and alfentanil alone or in combination.^{2–8}

We hypothesized that volatile anesthetics might fulfill the criteria of the 'ideal sedative' in an oculoplastic setting, and to test our hypothesis we designed a 3-arm randomized study to compare sevoflurane versus propofol with no sedation as the control group. To the best of our knowledge,

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studies evaluating the use of inhalational anesthetics during periocular injections for ophthalmic or oculoplastic procedures have not been previously conducted.

Materials and methods

Participants

All consenting adult patients undergoing elective oculoplastic procedures during the period between September 2010 and May 2012 in 3 Ophthalmology centers were enrolled. After institutional review board certification, all patients were given a written informed consent. Exclusion criteria included patients under 18 years or older than 75, patients refusing to sign the consent, pregnancy, dementia, known psychiatric disorders, hepatic or pancreatic insufficiency, patients with a known history of habitual drug or alcohol abuse, patients who underwent any surgical procedure under local anesthesia in the past 3 years, patients with a known allergy, or sensitivity to volatile anesthetics or to propofol, and patients undergoing any bilateral procedures.

Study design

This was an open-label, multi-center, three-arm parallel group, randomized controlled study comparing 2 different methods of preoperative sedation during the injection of local anesthetics in oculoplastic procedures with a no-treatment (no sedation) concurrent control group as the third arm of the study. Randomization was carried out prior to starting the study with an online computer generated list.

Anesthesia technique

No preoperative medications or antiemetics were given to any patient. Inside the operating room (OR), patients were monitored with an electrocardiograph, non invasive arterial blood pressure and pulse oximetry. In groups I and III, an intravenous (IV) access line was placed in all patients followed in group I by an injection of an IV bolus of 0.5 mg/kg propofol premixed with lidocaine (2 mL, 2% lidocaine is mixed with each 20 mL syringe of propofol).

In group II the patient was asked to firmly hold the face mask herself under close observation from the attending anesthesiologist, breath heavily through the mouth and count till 10. The face mask was connected to a semi-closed anesthetic unit, with sevoflurane 8% mixed with oxygen at a fresh gas flow rate of 6 L/min. Inadequate sedation was managed by maintaining mask application until the desired effect is reached. In group II an IV access line was placed after abolishment of the lash reflex immediately before injection of the local anesthetic.

In arms I and II local anesthetic injections were given immediately after confirmation of abolishment of the eyelash reflex.

Data collection

An independent observer not involved in the study collected data during the induction process and filled the questionnaire with the patients after the surgery in the outpatient recovery room. Inside the OR, vital data were monitored and

recorded by the anesthesiologist in charge, the level of sedation was noted by using a simplified sedation score devised by Epstein et al.⁹ Additional data included the degree of co-operation of the patient under sedation, presence or absence of sneezing, and his/her behavior during recovery.

In postoperative holding area, patients were asked to rate their pain between 1 and 10 with 0 being the least pain and 10 being severe intolerable pain. To assess the level of recall, patients were asked if they remembered any details while they were sedated, and whether they were satisfied with experience overall or not?

Statistical analysis

Statistical analysis was done with the SPSS software version 21 for Windows (IBM Corporation, New York, United States). Pairwise comparisons were carried out using the Student *t*-test for equality of means (equal variance not assumed) for continuous variables, and Fisher's exact test for categorical variables (age, type of procedure, percentage of sneezers, patient satisfaction, etc.). We integrated average pain scores and overall patient satisfaction as a composite outcome measure. We also set several secondary outcome measures for evaluation including sedation score, recovery behavioral scale, the level of cooperation during anesthetic injections, the rate of induction of the sneezing reflex, and finally patients' recollection of the events. *p* values were calculated as 2-tailed values. A *p* value less than 0.05 was considered statistically significant.

Results

A total of 396 patients were randomly assigned and 375 were included in the final analysis. There were 124 patients in group I, 128 in group II, and 123 in group III. [Table 1](#) summarizes the baseline data. Age, gender, the type of the procedure, and SpO₂ were homogeneously distributed and were not statistically different among the 3 groups.

No difference was noted between propofol and sevoflurane in pain scores (*p* 0.192), sedation scores (*p* 0.282), or recovery behavior scale (*p* 0.347). Although sevoflurane patients achieved a lower average recovery behavior scale, 3 patients from this group suffered a brief but severe bout of emergence delirium (ED) during recovery from sedation which was not expected and therefore not accounted for statistically. Two of them had severe hyperexcitability (laughter episode) while the third suffered hysterical crying. All 3 patients had no later recollection of these events.

When we evaluated the adjusted primary outcome measure, both sedation groups fared well (*p* 0.222) but each fared better than the control group (*p* < 0.001). Significantly more propofol patients were restrained during sedation than sevoflurane and even the control group (*p* < 0.001). There were significantly more sneezers in group I than in group II (*p* < 0.001), but the control group had no sneezers and performed better than the 2 study groups (*p* < 0.001).

In the outpatient recovery room, both treatment modalities impaired memory, but more patients in group I claimed remembering OR events, however this did not reach statistical significance (*p* 0.0986). Awareness and recall with propofol as well as sevoflurane sedation, and even with the

Table 1. Baseline data are expressed in means, standard deviation and percentages.

	Group I Propofol N, 124	Group II Sevoflurane N, 128	Group III No sedation N, 123
Age, mean (SD)	45.7(15.4)	43(17.2)	44.7(19.2)
Women, n (%)	74(59)	70(54)	71(57)
Minor procedures, n (%)	78(62)	77(60)	75(60)
SpO ₂	97.69(0.47)	97.75(0.42)	97.6(0.65)

use of propofol during total IV anesthesia has been reported before.^{10–12}

Slightly more patients in group I were satisfied with the sedation type than group II or the control group but this did not reach statistical significance except when group I was paired with the control group (p 0.0049). Three patients in group II suffered severe postoperative nausea and vomiting (PONV) in the recovery room.

Eight patients from group I voiced their discontent because of the pain associated with cannula placement. Four patients in group II were annoyed with the mask placed on their face, and one patient from group II recalled a repugnant smell from the mask. Five patients from the control group mentioned that the experience could have been better if they were 'asleep' during the injections. The main effects of treatment are summarized in [Tables 2 and 3](#).

Discussion

Intravenous medications have been the mainstay of sedation to alleviate patients' anxiety during periocular anesthetic injections. Drugs like propofol, ketamine, alfentanil and

midazolam have been used alone or in combination,^{2–6} with propofol usually claiming the lion's share.^{3,6} Despite the popularity of propofol, questions have always been raised about its potential safety particularly the risk of sneezing which could theoretically lead to catastrophic ocular complications.^{3–6} Interestingly, despite extensive discussion in the general medical literature,^{13–22} the pros and cons of IV sedation using propofol versus inhaled sedation have never been studied in the ophthalmic literature. Sevoflurane, one of the relatively newer inhalational anesthetics is a sweet-smelling, nonflammable, highly fluorinated anesthetic providing fast induction, potent hypnosis and speedy recovery with lower accumulation in the tissues and minimal irritation of the mucous membranes,^{23–25} and therefore our hypothesis was that it might fulfill the criteria for the ideal sedative, however, as evidenced by our adjusted primary composite outcome measure neither sedative confers any statistical advantage over the other. A closer look at the secondary outcome measures will tell a different story. Two powerful trends where sevoflurane proved to be superior to propofol is better control (lesser patient movements) during anesthetic injections and less sneezing.

Table 2. Primary and secondary outcome measures. Data are expressed in means, standard deviation and percentages.

	Group I Propofol N, 124	Group II Sevoflurane N, 128	Group III No sedation control N, 123
Pain score [#] , mean (SD)	0.148(0.57)	0.073(0.26)	2.36(2.37)
Sedation score, mean (SD)	4.1(0.882)	3.98(0.891)	–
Cooperative scale, mean (SD)	1.7(0.7)	1.21(0.48)	1.27(0.63)
Recovery behavior scale, mean (SD)	1.31(0.53)	1.24(0.61)	–
Sneezers, n (%)	33(26)	3(2.3)	0(0)
Patient remembers, n (%)	7(8)	2(1.5)	110(89)
Satisfied patients, n (%) [*]	117(94)	114(92.6)	102(82)
Adjusted primary composite index, mean (SD)	0.940(0.314)	0.944(0.226)	0.824(0.1167)

[#] Measurements are made with the VAS or the numerical score depending on patients' education level.

^{*} Percentage of satisfied patients is calculated here as a categorical value, but was converted into integers when we adjusted to calculate the primary composite measure.

Table 3. Pairwise comparisons of baseline data, intraoperative and postoperative sedation profiles for propofol, sevoflurane and the control group expressed in p values.

	Group I, II p value	Group I, III p value	Group II, III p value
Age	0.18513	0.63717	0.46422
Women	0.4469	0.79	0.7028
Minor procedures	0.6985	0.4367	0.7940
SpO ₂	0.647	0.637	0.906
Pain score	0.192	$p < 0.001$	$p < 0.001$
Sedation score	0.282	–	–
Cooperative scale	$p < 0.001$	$p < 0.001$	0.385
Recovery behavior scale	0.34711	–	–
Sneezers	$p < 0.001$	$p < 0.001$	$p < 0.001$
Patient remembers	0.0986	$p < 0.001$	$p < 0.001$
Satisfied patients	0.1715	0.0049	0.2022
Adjusted primary composite index	0.222	$p < 0.001$	$p < 0.001$

Patient movement under propofol sedation with or without globe perforation has been documented before and is significantly reduced with the addition of remifentanyl.^{7,26}

The rate of sneezing in the propofol group was 26% which is comparable to previous studies related to propofol use where the rate of sneezing varied from as high as 43.6%⁵ to as low as 5%.³ To our surprise, 3 patients from the sevoflurane group suffered a vigorous sneezing episode. This finding is unusual as it has never been reported before and neither the manufacturer nor the FDA list sneezing as one of the potential side effects of sevoflurane, and it lends credence to the notion that drugs other than propofol may also induce sneezing.⁵

Sevoflurane is associated with some unique problems of its own which were not accounted for in our statistical analysis. Three patients suffered a severe episode of emergence delirium (ED) after recovering from the effect of sevoflurane. Fortunately the episodes were short ranging from 2 to 3 min and patients had no memory of the event thereafter. ED which is also referred to as emergence agitation is a well-known side effect of sevoflurane when used as a general anesthetic particularly in the pediatric population but has rarely been reported in adults receiving anesthetic doses of the drug.²⁷ To the best of our knowledge, this is the first time ED has ever been documented in adults receiving a sedative dose of sevoflurane.

In conclusion both agents provide comparable results regarding the depth of sedation, pain control and overall satisfaction, but sevoflurane could deliver a better safety profile as a short-term sedative for patients receiving periocular anesthetics without the need for a prior IV access line and with minimal and partly preventable side effects which only occurred after and not during the administration of anesthetic injections.

Conflict of interest

The authors declared that there is no conflict of interest.

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