Effect of topical or peribulbar analgesia on the incidence of oculocardiac reflex, postoperative pain and postoperative nausea and vomiting following vitreoretinal surgery under surgical pleth index-guided general anaesthesia.

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Abstract

**Background:** Despite of the risk of postoperative intolerable pain perception (PIPP), vitreoretinal surgery (VRS) requires general anaesthesia (GA) in selected patients. Intraoperative use of opioid analgesics (OA) during GA carries the risk of postoperative nausea and vomiting (PONV). The surgical pleth index (SPI) optimises the intraoperative titration of OA. Regional anaesthesia techniques are combined with GA to minimize the intraoperative use of OA. We evaluated the benefit of preventive analgesia techniques combined with GA using SPI-guided fentanyl (FNT) administration on the incidence of PONV, oculocardiac reflex (OCR) and PIPP in patients undergoing VRS.

**Methods:** One hundred and five patients undergoing VRS were randomly allocated to receive either GA with SPI-guided fentanyl (FNT) administration alone (GA group) or with preventive topical 2% proparacaine (topical anaesthesia (TA) group) or preoperative peribulbar block (PBB) using 0.5% bupivacaine with 2% lidocaine (PBB group). Fifteen patients were excluded due to problems with postoperative SPI measurement.

**Results:** Preventive PBB resulted in intraoperative reduction in FNT requirement, with no influence on perioperative outcomes. Intraoperative SPI-guided FNT administration during GA resulted in OCR in 7.78%, PONV in 10% and PIPP in 13.5% of patients undergoing VRS. Intraoperative SPI-guided FNT administration blunted the perioperative effect of preventive PBB and TA in terms of the presence of PONV, OCR and PIPP.

**Conclusions:** The utility of SPI-guided FNT administration during GA eliminated benefits of preventive analgesia with PBB and TA following VRS. We recommend using intraoperative SPI-guided FNT administration during GA to reduce the presence of OCR, PONV and PIPP following VRS.

**Trial registration:** The trial was approved and registered by The Ethical Committee of Medical University of Silesia on 29th of September 2015, as well as the project was
Background

Vitreoretinal procedures (VRS or Pars Plana Vitrectomy - PPV) are most commonly performed under regional anaesthesia (RA) [1, 2, 3, 4]. General anaesthesia (GA) is resorted to in elderly patients, who may not be able to co-operate for prolonged procedures [5, 6, 7, 8]. GA provides excellent intraoperative immobilisation during VRS; however, the intraoperative use of opioid analgesics (OA) during GA has been identified as an independent risk factor for the occurrence of postoperative nausea and vomiting (PONV) [9]. Therefore, these agents should be best avoided if possible [9]. However, they are often necessary if there are signs of insufficient intraoperative analgesia, such as hypertension or tachycardia, which may lead to cardiac and cerebrovascular events [10]. OA dosing during GA is currently determined by observation of haemodynamic parameters combined with the clinical judgement of the anaesthesiologist. However, insufficient intraoperative analgesia may not necessarily lead to tachycardia and hypertension as volatile anaesthetic agents tend to blunt the haemodynamic response to nociceptive stimulation [11]. The absence of a haemodynamic response may be more common in diabetes patients or in older patients with sick sinus syndrome, and may lead to postoperative intolerable pain perception (PIPP) [12].

In order to rationalize the administration of OA, intraoperative monitoring of analgesia using the analgesia-nociception index, surgical pleth index and pupillometry is gaining increasing popularity. The surgical pleth index (SPI) has recently been introduced to
titrate OA dosing during GA [13, 14]. SPI reflects a nociception-anti-nociception balance and there is increasing evidence that SPI-guided analgesia provides better titration of OA dose compared to the observation of haemodynamic response to intraoperative painful stimuli [15]. SPI has been shown to be a better measure of nociception/anti-nociception balance compared to heart rate and blood pressure variations [16, 17]. In addition, the change in SPI value after a bolus of FNT enables monitoring and titration of intraoperative dosing [18]. Rational titration of rescue doses of OA using SPI guidance appeared to reduce the cumulative dose of narcotic analgesics during GA [19]. SPI variations in response to painful stimuli have been shown to depend on the serum opioid concentration [20]. The utility of intraoperative FNT titration guided by monitoring of analgesia has also been shown to decrease postoperative pain perception compared to a standard practice [21].

Attempts have been made to reduce the dose of intraoperative OA with different techniques of preventive analgesia for VRS. Reduction in the intravenous dose of OA administered intraoperatively with a combination of GA and regional techniques, including preoperative peribulbar block (PBB) [22, 23, 24, 25, 26], retrobulbar block (RBB) [27, 28], subtendon block [29, 30] and topical anaesthesia (TA) [31] have been proven to provide adequate analgesia postoperatively [28], with reduced incidence of OCR [32] and PONV [23, 26], despite potential side effects [3].

To the best of our knowledge, so far, no study has been carried out to investigate the effect of preventive regional analgesia techniques in combination with GA with SPI-guided FNT administration on perioperative outcomes in patients undergoing VRS.

We aimed to assess the effect of SPI-guided intraoperative titration of FNT dose on the cumulative dose of FNT, haemodynamic stability, incidence of OCR, efficacy of postoperative analgesia assessed by SPI and NRS values and incidence of PONV in patients
undergoing VRS under GA alone or in combination with different techniques of preventive regional analgesia.

Methods

Patients who were scheduled for elective primary VRS via the pars plana approach, in the Department of Ophthalmology of 5th St. Barbara Regional Hospital in Sosnowiec, Poland, and met the inclusion criteria were requested to participate in the study. One hundred and five belonging to American Society of Anaesthesiologists (ASA) physical status I–III were enrolled after obtaining written informed consent.

Randomization was performed by opening sealed envelopes in compliance with the Helsinki Declaration, ethical approval for this study (KNW/0022/KB1/101/15) was provided by the Ethical Committee of Medical University of Silesia on 29th of September 2015 (Chairman: Prof. Maria Trusz-Gluza, MD PhD). The project was registered in the Clinical Trial Registry (SilesianMUKOAiT2, NCT02973581). Study data can be accessed in The Department of Anaesthesiology and Intensive Care of St Barbara 5th Regional Hospital in Sosnowiec.

Exclusion criteria were: pregnancy, drug or alcohol abuse, history of neurological disease or a neurosurgical operation that would impair entropy electroencephalography (EEG) monitoring, history of pulmonary disease, anticipated difficult laryngeal mask airway (LMA) placement, acute or chronic pain and cardiac arrhythmia in electrocardiography (ECG) that might impair SPI monitoring.

Patients were randomly allocated into three groups.

Group GA: Patients received general anaesthesia alone.
Group TA: Patients received preventive topical analgesia by triple instillation of 2% proparacaine 15 minutes before induction of GA.
Group PBB: Patients received peribulbar block using a mixture of 3.5 ml each of 2% lignocaine and 0.5% Bupivacaine using the Hamilton’s technique, 1 min before induction of GA [52]

On the day of surgery, all patients were premedicated with midazolam (dormicum) 3.75–
7.5 mg prior to induction of anaesthesia according to body weight and age [33]. Prior to commencement of surgery, patients were preoxygenated for 5 minutes with 100% oxygen and 10 ml/kg per body weight of Ringer’s lactate solution was infused intravenously. Anaesthesia was induced intravenously with fentanyl 1 mcg/kg body weight and etomidate (Etomidate Lipuro, Braun, Germany) 0.2–0.3 mg/kg of body weight intravenously. After loss of consciousness, rocuronium was administered in a standard intravenous dose of 0.6 mg/kg rocuronium (Esmeron, Fresenius, Poland) for neuromuscular blockade followed by placement of an LMA. The exhaled carbon dioxide concentration (EtCO$_2$) level was maintained at 35–37 mmHg after LMA placement and prior to commencement of surgery; the sevoflurane concentration was maintained at a level around 35–45 on State Entropy. Throughout anaesthesia induction and surgery, standard monitoring was carried out with close attention paid to vital parameters including non-invasive arterial pressure (NIBP), heart rate (HR), standard electrocardiography (ECG) lead II, pulse oximetry (SaO$_2$), fraction of inspired oxygen in the gas mixture (FiO$_2$), fraction of inspired sevoflurane (FiAA), fraction of expired sevoflurane (FeAA), EtCO$_2$ and minimal alveolar concentration of sevoflurane (MAC). The depth of anaesthesia was monitored with entropy EEG (State and Response Entropy). Intraoperative analgesia was guided by Surgical Pleth Index (SPI), and neuromuscular blockade was monitored (Carescape B650, GE, Finland).

**Stage 1**

On admission to the operating theatre, the sensor of the entropy EEG (State and Response entropy) was placed on the patient’s forehead, the pulse oximeter (SPI) on the finger contralateral to venous access, NIBP cuff on the right arm, and standard ECG leads on the patient’s back according to manufacturer’s suggestions, and the baseline values were recorded.
PBB was performed by the same ophthalmologist (M. K-B) with over 6 years’ experience with the procedure, having performed at least 400 PBBs a year. Sensory block was confirmed based on the abolition of the corneal reflex.

Stage 2

SPI values were noted starting form 5 minutes after laryngeal mask placement to the beginning of sterilization of the orbit to calculate the mean SPI value and to allow calibration of the SPI sensor.

Stage 3—intraoperative

SPI score was monitored on-line and recorded at 1-minute intervals. When SPI value reached ΔSPI >15 points above the mean SPI value from stage 2, a rescue dose of 1 mcg/kg of FNT was administered intravenously every 5 minutes until the SPI value decreased to the mean SPI value of stage 2. The procedure time of VRS was taken as the duration from speculum insertion to removal.

We assumed that initial dose of FNT 1 mcg/kg would produce sufficient analgesia for insertion of the speculum. In addition, Gruenewald et al. [13] proposed a ΔSPI >10 or an absolute SPI value >50 as a predictor of inadequate analgesia. In other studies, an absolute value of ΔSPI >50 alone was an indication for a rescue analgesia [3]. In our study, we used protocol of ΔSPI >15, compared to the mean value of stage 2 lasting at least one minute as an indication for rescue analgesia. We used this threshold to avoid possible hazardous overdosing of FNT as a result of potential miscalculation of SPI score due to its variations.

Vitrectomies were performed by the same ophthalmic surgeon (A. L-B) with over 10 years of experience in VRS, having performed over 400
vitreoretinal procedures per year.

The incidence of intraoperative OCR was recorded, which is typically identified by a rapid decrease in heart rate by 20% from the baseline during ocular manipulations. If OCR occurred, the surgeon was asked to stop surgical stimulation; intravenous atropine, 0.5 mg was administered in case of persisting bradycardia.

Stage 4—postoperative

In the recovery room, patient monitoring was continued with SPI, heart rate (HR), systolic arterial pressure (SAP), mean arterial pressure (MAP), diastolic arterial pressure (DAP) and SaO₂ by the anaesthesiology team blinded to group allocation. Along with postoperative haemodynamic parameters, the level of sedation and the presence of adverse effects such as nausea, vomiting (PONV), and allergic reactions were monitored for each patient. These observations were made at the time of pain assessment for the first 24 hours postoperatively. In case of PONV, ondansetron (Ondansetron Accord, Accord Healthcare Limited, UK), 4 mg was administered intravenously. Optylite solution, 5 ml/kg was infused in case of MAP <65 mm Hg. Oxygen was administered at the rate of 3 l/min though a nasal cannula. Patients were asked to assess their perception of pain intensity using the Numeric Pain Rating Scale (NRS) ranging from 0 (no pain) to 10 (maximum pain) every 10 minutes. In the case of an NRS >3, a standard dose of non-steroid anti-inflammatory drug was administered according to contemporary guidelines of acute pain treatment issued by Polish Society of Anaesthesiologists [12]. SPI was monitored online and mean SPI values were recorded at 1-minute intervals (trends in a software provided by manufacturer). NRS and SPI values were recorded for severe (NRS 7-10), moderate (NRS 4-6) and mild pain (NRS 0-3) perception intervals. Patients were observed and monitored in the recovery room for at least 30 minutes until transfer to the Department of Ophthalmology.

Monitoring and data recording were ceased except for any occurrence of PONV, recorded
during the first 24 h postoperatively. Ondansetron, 4 mg was administered intravenously in case of PONV.

**Statistical analysis**

Statistical analysis were performed using MS Excel, STATISTICA 12, Stat Soft Poland and R package 3.1.2. Data are expressed as mean and standard deviation (X ± SD) or as median with interquartile range M (IQR). Normality of distribution analysed with the Shapiro-Wilk W test. The difference between means was tested for significance using ANOVA for multiple groups, and for skewed distributions their compatibility in groups was examined using the Kruskal-Wallis test by ranks. Additionally, post-hoc tests were carried out to confirm differences between groups. For nominal data, we used percentages and tested for equality of proportions with pairwise comparisons for proportions. Relationships between nominal variables were analysed by the $\chi^2$ test of independence. Statistical significance was set at the level $p < 0.05$ (NS: not statistically significant).

**Results**

Ninety patients were included in the final analysis; 15 were excluded because of temporary SPI artefacts due to postoperative arousal [34] or inability to assess pain perception using NRS. No statistically significant differences were noted in terms of anthropometric parameters of patients in the studied groups (Table 1).

**[Table 1]**

The duration of surgery was comparable between the studied groups ($p = 0.69$); all patients were potentially subjected to a similar degree of intraoperative nociceptive stimulation. The performance of preventive PBB resulted in a statistically significant reduction in intraoperative rescue OA with FNT ($p < 0.01$). There was no difference in Apfel scores between groups for prediction of possible PONV. Intraoperative fluid therapy was
also not different between groups; over hydration constitutes an independent risk of nausea and vomiting (Table 2).

**[Table 2]**

Among all patients, the highest mean pain score reported in the recovery room was $1.4 \pm 2$ by the NRS; 75 patients (83.2%) reported mild and 14 (15.7%) reported moderate pain. There was only one patient (1.1%) who experienced severe pain perception postoperatively. There was no statistically significant difference between groups in the incidence of mild ($p = 0.59$), moderate ($p = 0.92$) or severe ($p = 0.36$) postoperative pain.

The incidence of PIPP was also not statistically different ($p = 0.79$) (Table 3).

**[Table 3]**

Overall, PONV was observed in 9 patients (10%); the lowest incidence was in the PBB group compared to the TA and the GA groups (3.3% vs. 13.3% vs. 13.3%, respectively; $p = 0.38$). However, this was not statistically significant (Figure 1, Table 4).

**OCR** occurred in 7 patients (7.8%) overall; the incidence was comparable between groups (10% vs. 6.7% vs. 6.7%, respectively; $p = 0.99$). (Figure 1, Table 4).

**[Table 4]**

Additionally, we analysed the influence of preventive analgesia on intraoperative haemodynamic parameters. Before induction of GA (stage 1) and before VRS (stage 2) no statistically significant difference was found in haemodynamic parameters between groups. During VRS (stage 3) significantly lower mean values of SAP, MAP and DAP were observed in the PBB group compared to the GA and TA groups, although such differences seemed to bear little clinical significance. Analysis of postoperative parameters revealed
significantly higher mean SAP in TA group, which was also clinically irrelevant (Table 5).

[Table 5]
We also analysed the influence of preventive analgesia on haemodynamic stability. Between induction of GA and onset of VRS (stage 2) no statistically significant difference in maximal and minimal values of haemodynamic parameters was noted. During VRS (stage 3) significantly higher values of maximal SAP, MAP, DAP and HR were seen in the GA group, whereas the minimum values MAP and DAP were significantly lower in the PBB group postoperatively (stage 4); The minimum values of SAP were significantly higher in the TA group (Table 6).

[Table 6]
Maximum values of SAP, MAP and DAP were found to be lower in patients allocated to PBB group, as compared to the TA and GA groups.

Above mentioned differences (Table 5 and 6) and those associated with SE values do not seem to bear any clinical relevance (values of SE 45–60 reflect adequate depth of surgical anaesthesia; minimum values of SE in stage 3 were associated with temporary artefacts lasting up to 3 minutes, related to rocuronium administration, which has already been well established)

Discussion
VRS is commonly performed under different techniques of RA; PBB without sedation provides excellent postoperative analgesia depending on the anaesthetic technique and local anaesthetic solutions used [35, 36]. Nevertheless, in selected subgroups of patients, intolerable pain perception during surgery negatively influenced patient satisfaction from the surgery in some reports [35; 37]. Therefore, in some elderly patients who are unable to co-operate during VRS under RA,
those refuse to consent for RA alone, and those with contraindications to RA [22], GA is performed to ensure adequate immobilisation on the operating table for the comfort of the surgeon. This is in spite of an additional 20% cost incurred with GA compared to RA with monitored anaesthesia care (MAC) [38]. Because intraoperative use of OA during GA carries a risk of PONV [9], different RA techniques are added to GA to reduce intraoperative OA requirement, and reduce the incidence of PIPP.

**Surgical Pleth Index (SPI)**

Addition of RA to GA was reported to reduce the necessity of rescue OA administration, but did not eliminate it completely. Therefore, the aim of the current study was to assess the utility of SPI to guide OA administration in case of intraoperative afferent nociceptive stimulation due to incomplete effect of preventive RA.

Volatile anaesthetics administered during GA have been shown to blunt the haemodynamic response to nociceptive stimulation [11]. During surgical manipulation, patients receiving volatile anaesthetics may experience afferent nociceptive stimulation without change in haemodynamic parameters. The anaesthesiologist may not administer rescue OA in the absence of changes in blood pressure and heart rate; this may lead to PIPP due to central sensitization. Struys et al. [16] have shown that SPI values change in response to afferent nociceptive stimulation; SPI monitoring constitutes a better measure of nociception/anti-nociception balance than haemodynamic parameters including heart rate and blood pressure variations in optimising intraoperative OA titration [15]. SPI value is derived by finger plethysmography and displayed on the screen; hence, it is simple to use and does not require any preoperative preparation. Bergmann et al. [19] reported that SPI guidance during GA resulted in rational titration of rescue doses of OA and a reduction in the cumulative dose of OA administered during GA. Ledowski et al. [18] showed that the change in SPI value after a bolus of rescue FNT enabled monitoring of intraoperative
titration. Hence, SPI guidance of rescue OA administration also helps to monitor the effectiveness of rescue bolus doses of FNT. Based on these studies, we hypothesised that the use of SPI in conjunction with RA techniques could produce lead to improved perioperative outcomes with a lower incidence of OCR, haemodynamic instability, PIPP and PONV.

Upton et al. [21] utilized Anti-Nociception Index (ANI) guidance to administer FNT intraoperatively during GA with sevoflurane for lumbar discectomy and laminectomy. They observed that a more objective, ANI-guided intraoperative FNT administration resulted in decreased perception of pain intensity in the immediate postoperative period compared to a standard practice of FNT administration based on observation of haemodynamic fluctuations and anaesthesiologist’s judgement. On the contrary, Wennervirta et al. [17] showed that the addition of RA to GA was more efficient in providing perioperative analgesia than SPI-guided OA titration in patients who underwent GA combined with brachial plexus block (BPB).

Preventive regional analgesia

Different types of preventive regional analgesia techniques were utilised to ensure smooth postoperative recovery. Analgesia initiated before a nociceptive afferent surgical stimulation is considered to be more effective than analgesia commenced afterwards, as it suppresses the afferent nociceptive barrage perioperatively; this is the concept of preemptive analgesia [39]. The action of local anaesthetics (LAs) is a result of a reversible block of sodium channels that prevents the propagation of painful afferent nerve impulses from the cornea, conjunctiva and sclera [39].

Although addition of PBB to GA was reported to diminish the requirement for intraoperative rescue OA, techniques of RA are not free from potential complications. During the course of the current study, no adverse events were observed; nevertheless,
PBB was reported to result in transient vision impairment, which may be an unwelcome, distressing experience for patients postoperatively [40, 41], whereas TA may cause local allergic reactions. After PBB, systemic LA toxicity was reported to be likely to induce cardiac arrhythmias, an increase in mean arterial blood pressure and heart rate [3] or a severe decrease in systolic blood pressure [42]. Perioperative haemodynamic fluctuations constitute a subsequent risk factor of destabilization of atherosclerotic plaques that may result in life-threatening cardiac and cerebrovascular events [10]. Central retinal vein occlusion [43], brainstem anaesthesia [44], transient complete visual loss and a partial third nerve palsy [45], pulmonary oedema [46], ocular explosion [47] and generalized tonic-clonic seizures [48] have been reported following PBB due to LA toxicity.

Postoperative Intolerable Pain Perception (PIPP)

VRS may cause PIPP. In a study by Fekrat S et al. [49], 56% of patients complained of some eye pain after VRS, whereas 48% requested an analgesic within 5 hours after surgery, and 27% percent of patients required OA. Schönfeld CL et al. [25] found GA with PBB using 0.75% ropivacaine with 75 IU of hyaluronidase in a volume of 5 ml superior for the prevention of PIPP compared to a volume of 1 or 3 ml. Sixty percent of patients receiving 5 ml experienced no PIPP after one hour of VRS in this study. Ghali et al. [23] observed reduced PIPP in patients receiving PBB combined with GA compared to GA alone in patients undergoing VRS with scleral buckling. In the PBB group, 7% of patients reported acute postoperative pain perception defined as a score of >7 on the Visual Analogue Scale (VAS) compared to 30% of patients in GA group. Rescue doses of tramadol and total diclofenac consumption administered for moderate pain perception (VAS >4), was also significantly higher in the GA group compared to the group that had GA combined with PBB.

In our study, among 90 patients included in the final analysis, 14 patients (15.7%)
complained of moderate pain and one patient (1.1%) reported PIPP in the immediate postoperative period in the recovery room. Interestingly, performance of neither PBB nor TA resulted in a significant decrease in PIPP expressed by NRS values; PIPP was reported by four patients in PBB group (13.3%), six in TA group (20%) and five in the GA group (16.7%).

Jaichandran et al. [35] observed the efficacy of PBB, expressed as adequate globe akinesia, to be 20–60%, depending on the LA mixture used; hence, on average, half of PBBs may theoretically provide insufficient analgesia. This is because estimation of sensory block by abolition of the corneal reflex may not always imply that there is no sensory perception of surgical manipulations. Therefore, supplementation of PBB with intraoperative intravenous OA during GA under SPI guidance, may be necessary in case of partly or completely failed block [35, 37]. This may play a key role in the utility of SPI guidance for supplemental FNT administration. Introduction of ultrasound-guided, perineural stimulation-directed (dual guidance) interscalene BPB increased its efficacy from 41.46% with the perineural stimulation technique to 80.43% with the dual guidance technique [24]. Hopefully, similar to dual guidance BPB, ultrasound-guided PBB combined with GA in patients undergoing VRS may in the future [50], improve the efficacy of PBB by more precise needle placement and observation of LA deposition at the target destination. This may reduce the necessity of intraoperative rescue OA administration using SPI guidance, as in the current study the demand for rescue FNT was the lowest in the PBB group compared to other groups, although this was not statistically significant.

Overall, in our study, we did not observe marked improvement in perioperative outcomes in patients receiving preventive PBB or TA, compared to GA alone, although there was no statistically significant difference in the dose of intraoperative FNT administered.

In the current analysis, with the use of SPI-guided FNT administration during GA, afferent
nociceptive stimulus was reflected as an intraoperative delta SPI >15 compared to the baseline value. Inadequate RA detected by SPI monitoring resulted in more efficient suppression of central sensitisation. As a result, the use of preventive RA using either PBB or TA did not influence the incidence of PIPP; with a similar incidence in all three groups.

We believe that preventive RA, with the added risk of rare, but serious complications, seems no longer justified in combination with GA to reduce the incidence of PIPP after VRS.

A similar result was observed by Bayerl et al. [27] with preoperative RBB using bupivacaine 0.5% and mepivacaine 1% in combination with GA in patients undergoing VRS. They induced GA with fentanyl and propofol and maintained anaesthesia using propofol and remifentanil administered by observing haemodynamic parameters and anaesthesiologist judgement. They observed no advantage by combining RBB with GA as compared to GA alone with postoperative analgesia in the early postoperative period; however, in the GA group, cyclooxygenase inhibitors or non-steroidal anti-inflammatory drugs were infused before emergence, which may have influenced the incidence of PIPP.

Haemodynamic stability

Haemodynamic instability during GA constitutes a serious risk factor of the development of cardiac and cerebrovascular events [10]. During VRS (stage 3) significantly lower mean values of SAP, MAP and DAP were observed in PBB group compared to GA and TA group, whereas maximum values of SAP, MAP and DAP were observed to be lower in patients allocated to PBB group. Although such differences seem to bear little clinical significance (on average, not more than 10 mmHg and 10 beats/min), and no complications were observed, PBB combined with GA with SPI-guided FNT administration resulted in the most stable conduct of GA. Nevertheless, the use of SPI-guided intraoperative analgesia with
FNT in all groups could have resulted in stable haemodynamics during VRS, with a tendency for the most stable heart rate and blood pressure in the PBB group.

**PONV**

Every episode of PONV leads to a rapid increase in intraocular pressure, which may even lead to wound dehiscence; besides, it impairs patient satisfaction in the recovery period. In recent literature, the incidence of PONV after intraocular surgery is 18–56% [51, 52]. According to Nitahara et al. [53], who analysed risk factors of PONV after VRS, the overall incidence of nausea and vomiting was 15% and 23% respectively. Fekrat et al. [49] reported PONV in 16% of patients, most likely occurring in those receiving OA. Shende et al. [8] observed the incidence of PONV in 12 out of 30 patients receiving GA with PBB for retinal detachment surgery. In many previous reports, preventive analgesia techniques were utilised to reduce intraoperative OA administration which reduced the rate of PONV. Ghali et al. [23] observed PONV in 10 out of 30 patients receiving GA only (33%) and in 3 patients out of 30 (10%) in whom additional PBB was performed. In all abovementioned studies, intraoperative FNT administration was performed based on observation of haemodynamic fluctuations and the anaesthesiologist’s judgement. In our study, only 9 patients out of 90 (9%) developed of PONV. The incidence of PONV was lowest in the PBB group compared to the TA and GA groups [1/30 (3.3%) vs. 4/30 (13.3%) vs. 4/30 (13.3%), respectively; p = 0.38], although this was not statistically significant. We believe that appropriate administration of intraoperative rescue FNT under SPI guidance probably prevented an excessive dose which resulted in a lower incidence of PONV compared to abovementioned data from literature.

**OCR**

Oculocardiac reflex is a trigeminal-vagal reflex triggered by intraoperative pressure on the
eyeball, traction of extra-ocular muscles and is defined as rapid decrease in heart rate by over 20% [54] that may lead to serious cardiac arrhythmias with haemodynamic instability (bradycardia, ectopic beats, nodal rhythm, ventricular fibrillation or asystole) and therefore constitutes an intraoperative complication of a great concern.

Ghali et al. [23] observed OCR in 8 out of 30 patients (27%) receiving GA alone and in 2 patients out of 30 (7%) in whom additional PBB was performed. Shende et al. [8] compared patients undergoing elective retinal detachment repair under GA alone and in combination with PBB and observed an incidence of OCR in 9 patients out of 30 in PBB group (30%) and in 21 out of 30 patients in GA-only group (70%). Contrary to literature data, in our study the use of SPI-guided FNT administration resulted in OCR 7 out of 90 patients included in the final analysis (7.78%). The incidence of OCR was observed to be similar in all groups [PBB: 2/30 (6.7%) vs. TA: 2/30 (6.7%) vs. GA: 3/30 (10%); p = 0.38].

In our view, adequate administration of intraoperative rescue OA using SPI-guided FNT administration probably led to stable intraoperative analgesia and therefore resulted in a low incidence of PONV compared to abovementioned data from literature. SPI-guided FNT administration during GA reduced afferent nociceptive stimulation evoked by intraoperative muscle traction, which could have also prevented central hyperexcitability [55], thus reducing the incidence of OCR.

Limitations

There are several limitations to the current study. First, PIPP is a subjective phenomenon, which is difficult to quantify [56]. Our study did not include a control group without SPI guidance; such studies have already been conducted and the findings are well established. Moreover, the use of GA alone without any supplemental medication to
prevent PIPP may raise ethical concerns. We did not analyse the rate of PIPP after discharge from recovery room to the wards; this was because our study involved monitoring NRS as well as SPI values in stage 4. Patient arousal, including change in position and cough, markedly interferes with SPI monitoring [34], making such a comparison difficult to interpret. Finally, it was impossible to verify the akinesic effect of PBB after induction of GA, as we only aimed to produce a sensory block.

Conclusions

In conclusion, the current study shows that addition of PBB or TA to GA, despite a statistically significant reduction in the dose of intraoperative FNT, resulted in no benefit in perioperative outcomes. Contrary to numerous studies reporting the efficacy of preventive analgesia with PBB or TA, in patients undergoing VRS under GA, we conclude that rational intraoperative, SPI-guided FNT administration enabled titration of optimal analgesia and resulted in a low incidence of OCR and PONV. Suppression of central sensitization resulted in a similarly low incidence of PIPP in all the studied groups. Therefore, we suggest that the risk of potential perioperative complications due to PBB, mainly due to systemic toxicity and vision impairment, overweighs its potential benefits when FNT is administered intraoperatively under SPI guidance.

Abbreviations

ANI - anti-nociception index
BPB - brachial plexus block
DAP - diastolic arterial pressure
ECG - electrocardiography
EEG - electroencephalography
EtCO2 - exhaled carbon dioxide concentration
FiAA - fraction of inspired sevoflurane
FeAA - fraction of inspired sevoflurane
FiO2 - fraction of inspired oxygen in the gas mixture
FNT - fentanyl
GA - general anaesthesia
HR—heart rate
LAs - local anaesthetics
LMA - laryngeal mask airway
MAC - minimal alveolar concentration
MAP - mean arterial pressure
NIBP - non-invasive arterial pressure
NRS - numeric pain rating scale
OA - opioid analgesics
OCR - oculocardiac reflex
PBB - preoperative peribulbar block
PIPP - postoperative intolerable pain perception
PONV - postoperative nausea and vomiting
PPV—pars plana vitrectomy
RA - regional anaesthesia
RBB - retrobulbar block
SaO2 - pulse oximetry
SAP - systolic arterial pressure
SPI - surgical pleth index
TA—topical anaesthesia
VAS - visual analogue scale
VRS - vitreoretinal surgery
Declarations

Ethics approval and consent to participate
Ethical approval for this study (KNW/0022/KB1/101/15) was provided by the Ethical Committee of Medical University of Silesia on 29th of September 2015 (Chairman: Prof. Maria Trusz-Gluza, MD PhD). All subjects have signed written consent form before the study. The project was registered in the Clinical Trial Registry (SilesianMUKOAiiT2, NCT02973581).

Consent for publication
Not Applicable.

Availability of data and material
The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Competing interests
The authors declare that they have no competing interests.

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Authors’ contributions
MJS - main researcher, responsible for project of the study, anaesthesiologist collecting and analysing the data, contribution—30%, AP - anaesthesiologist collecting and analysing the data, contribution—11%, ALB - ophthalmologist, vitreoretinal surgeon performing vitrectomies and collecting the data, contribution—10%, IS - anaesthesiologist collecting
the data, contribution—6%, MBP - anaesthesiologist collecting the data, contribution—6%,
MKB - ophthalmologist, responsible for peribulbar anaesthesia, contribution—6%, EN -
specialist on epidemiology and statistics responsible for data analysis, contribution -6%,
DD ophthalmologist, responsible for peribulbar anaesthesia, responsible for manuscript
final preparation, contribution—15%, LK—head of anaesthesiologists’ team, responsible for
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Tables

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Figures

Figure 1

Incidence of postoperative nausea and vomiting (PONV) and oculocardiac reflex (OCR).

Supplementary Files

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Table_1 BMC.docx
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Table_6 BMC.docx
Table_5 BMC.docx
Table_4 BMC.docx
Table_2 BMC.docx