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1

Pupillary Pain Index Changes After a Standardized Bolus of Alfentanil Under Sevoflurane Anesthesia: First Evaluation of a New Pupillometric Index to Assess the Level of Analgesia During General Anesthesia.

Sabourdin N, Diarra C, Wolk R, Piat V, Louvet N, Constant I.

Abstract

BACKGROUND:
The pupillary pain index (PPI) is a novel pupillometric index, designed to assess intraoperative analgesia. It is based on the evaluation of the pupillary response to electrical stimuli of increasing intensity. It ranges from 1 (low level of pupillary reactivity, high level of analgesia) to 10 (high level of pupillary reactivity, low level of analgesia). In this first evaluation of the PPI, our objective was to investigate the PPI changes after a bolus of 10 µg·kg of alfentanil in children under sevoflurane general anesthesia.

METHODS:
After ethics committee approval and informed consent, 20 healthy children (9 ± 5 years) undergoing elective surgery under general anesthesia were included in this prospective, open, registered pilot study (NCT02646592). Anesthetic induction was standardized with sevoflurane 6% and propofol 1 mg·kg. After tracheal intubation, sevoflurane concentration was maintained at 2% for 10 minutes. A first PPI measurement was performed (PPI-1), and a bolus of 10 µg·kg was administered. Two minutes after this bolus, a second PPI measurement was performed (PPI-2). Heart rate, blood pressure, and bispectral index were recorded before and after each PPI measurement. Resting pupillary diameter was recorded before each PPI measurement. PPI scores before and after the bolus of alfentanil were compared using a Wilcoxon signed rank test.

RESULTS:
PPI scores decreased after administration of a bolus of alfentanil (median difference: -3 [95% confidence interval, -4 to -2]). The median (quartiles) of PPI-1 (baseline, before alfentanil) was 6 (4, 7), and the median (quartiles) of PPI-2 (after alfentanil) was 2 (2, 3) ($P < .001$). No difference was found in resting pupillary diameter before PPI-1 and PPI-2 (2.2 ± 0.2 and 2.2 ± 0.3 mm, respectively; $P = .86$). There were no significant changes in heart rate or blood pressure after PPI measurements ($P = .46$ and .49, respectively). Bispectral index was slightly increased after PPI measurements ($P = .01$; mean bispectral index increase <5%). No withdrawal movements occurred during PPI measurements.

CONCLUSIONS:
There was a significant decrease in PPI after alfentanil administration. The results of this pilot study suggest that PPI score decreases when the level of analgesia increases. PPI measurement was not associated with a clinical or hemodynamic nociceptive response. This new index might provide useful information to individually adapt opioid administration before nociceptive stimuli under general anesthesia.

https://www.ncbi.nlm.nih.gov/pubmed/30198934

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2

Using Pupillary Pain Index to Assess Nociception in Sedated Critically Ill Patients.

Vinclair M, Schilte C, Roudaud F, Lavolaine J, Francony G, Bouzat P, Bosson JL, Payen JF.

Abstract

BACKGROUND:
Pupillary reflex dilation is a reliable indicator of response to noxious stimulation. In a proof of concept study, we investigated the performance of pupillary pain index, a new score derived from pupillary reflex dilation measurements, to predict nociceptive response to endotracheal suctioning in sedated critically ill patients.

METHODS:
Twenty brain-injured and 20 non-brain-injured patients were studied within 48 hours of admission (T1) in the intensive care unit and at 48-72 hours later (T2). Video-based pupillometer was used to determine pupillary reflex dilation during tetanic stimulation. The tetanic stimulation (100 Hz) was applied to the skin area innervated by the ulnar nerve and was stepwise increased from 10 to 60 mA until pupil size had increased by 13% compared to baseline. The maximum intensity value allowed the determination of a pupillary pain index score ranging from 1 (no nociception) to 9 (high nociception). The Behavioral Pain Scale response to endotracheal suctioning was measured thereafter.

RESULTS:
Behavioral Pain Scale responses to endotracheal suctioning and pupillary pain index scores were positively correlated at T1 and T2 (both $P < .01$). After adjustments for repeated measurements and group of patients, the area under the receiver operating characteristic curve of pupillary pain index to predict Behavioral Pain Scale response to endotracheal suctioning was of 0.862 (95% CI, 0.714-0.954). In the combined set of patients, a pupillary pain index score of ≤4 could predict no nociceptive response to endotracheal suctioning with a sensitivity of 88% (95% CI, 68%-97%) and a specificity of 79% (95% CI, 66%-88%). By contrast with endotracheal suctioning, tetanic stimulation had no effect on intracranial pressure in the brain-injured group.

CONCLUSIONS:
These results are a proof of concept. The nociceptive response to endotracheal suctioning could be accurately predicted using the determination of pupillary pain index score in sedated critically ill patients whether they have brain injury or not.

https://www.ncbi.nlm.nih.gov/pubmed/30998560

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3

Prediction of movement to surgical stimulation by the pupillary dilatation reflex amplitude evoked by a standardized noxious test.

Guglielminotti J, Grillot N, Paule M, Mentré F, Servin F, Montravers P, Longrois D.

Abstract

BACKGROUND:
Individual assessment of the amplitude of a physiologic reflex evoked by a standardized noxious test (SNT) before surgical stimulation has been suggested to predict movement upon the forthcoming surgical stimulation. This study aimed to compare the ability of pupillary dilatation reflex amplitude (PDRA) evoked by an SNT and estimated remifentanil effect-site concentration (Ce) to predict movement upon surgical stimulation.

METHODS:
Eighty female patients were anesthetized for vacuum aspiration with propofol (Ce 4 μg/ml) and remifentanil. Remifentanil Ce was randomized to 0, 1, 3, or 5 ng/ml. SNT was a 60-mA, 5-s, 100-Hz tetanus applied on median nerve before cervix dilatation. PDRA was calculated as the difference in pupillary diameter after and before SNT. Movement upon cervix dilatation was recorded by an independent observer. Ability of PDRA and estimated remifentanil Ce to discriminate movers from non-movers during cervix dilatation was measured as the area under the receiver operating characteristics curve.

RESULTS:
Twenty-one of the 76 patients analyzed moved during cervix dilatation. Mean PDRA (±1 SD) evoked by SNT was 2.0 ± 1.2 mm in movers and 0.6 ± 0.7 in non-movers ($P < 0.0001$). Remifentanil Ce was 0.2 ± 0.4 ng/ml in movers and 3.0 ± 1.7 in non-movers ($P < 0.0001$). Area under the receiver operating characteristics curve for PDRA was 0.90 (95% CI, 0.83 to 0.96) and for remifentanil Ce 0.94 (0.89 to 0.98), without any significant difference between the two areas.

CONCLUSIONS:
PDRA evoked by an SNT is as accurate as the estimated remifentanil Ce to predict movement upon cervix dilatation. PDRA could be valuable when estimated opioid Ce is not available or reliable.

Comment in
Pupillary Reflex Dilation to Predict Movement: A Step Forward Toward Real-time Individualized Intravenous Anesthetics. [Anesthesiology. 2015]
Limitations of the Pupillary Reflex: Do the Eyes Have It? [Anesthesiology. 2015]
In Reply. [Anesthesiology. 2015]

https://www.ncbi.nlm.nih.gov/pubmed/25730338

Anesthesiology. 2015 May;122(5):985-93. doi: 10.1097/ALN.0000000000000624.
PMID: 25730338 DOI: 10.1097/ALN.0000000000000624

4

Pupillometry-guided Intraoperative Remifentanil Administration versus Standard Practice Influences Opioid Use: A Randomized Study.

Sabourdin N, Barrois J, Louvet N, Rigouzzo A, Guye ML, Dadure C, Constant I.

Abstract

BACKGROUND:
Pupillometry has shown promising results for assessing nociception in anesthetized patients. However, its benefits in clinical practice are not demonstrated. The aim of this prospective randomized study was to evaluate the impact of intraoperative pupillometry monitoring on perioperative opioid consumption in major gynecologic surgery.

METHODS:
After receiving ethics committee approval and written consent of patients, American Society of Anesthesiologists status I to II women undergoing gynecologic surgery were included in this single-blinded, prospective, parallel-arm randomized study. General anesthesia was standardized with propofol-remifentanil target-controlled infusion. Patients were randomly assigned into two groups. In the pupillometry group, remifentanil administration was guided by pupillary diameter changes. In the standard group, remifentanil administration was left to the discretion of the anesthesiologist. The primary outcome was intraoperative remifentanil consumption.

RESULTS:
Fifty-five patients were analyzed. Remifentanil consumption was markedly decreased in the pupillometry group (3.8 [3.4 to 4.8 μg · kg · h] vs. 7.9 μg · kg · h [6.5 to 9.0 μg · kg · h] in the standard group; difference = 4.2 μg · kg · h [95% CI, 3.0 to 5.3 μg · kg · h]; P < 0.001). Cumulative 0- to 12-h morphine consumption was reduced in the pupillometry group (two-way repeated measures ANOVA 0.3 ± 0.1 vs. 0.4 ± 0.2 mg/kg; P = 0.048). A telephone survey 3 months after surgery revealed that 15 of 29 patients in the standard group still experienced procedure-related pain versus 3 of 23 in the pupillometry group (chi-square P = 0.037). No adverse events associated with pupillometry were observed during the study.

CONCLUSIONS:
The use of pupillometry to guide intraoperative analgesia reduced intraoperative remifentanil consumption and postoperative morphine requirements. The possible consequences of decreasing intraoperative remifentanil in terms of chronic pain require further investigation.

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5

Pupillary Reflex for Evaluation of Thoracic Paravertebral Block: A Prospective Observational Feasibility Study

Duceau, Baptiste MD; Baubillier, Mélanie MD; Bouroche, Gaëlle MD; Albi-Feldzer, Aline MD; Jayr, Christian MD, PhD

Abstract

BACKGROUND:
Although thoracic paravertebral block (TPVB) is recommended in major breast surgery, there is no gold standard to assess the success of TPVB. Pupillary dilation reflex (PDR) is the variation of the pupillary diameter after a noxious stimulus. The objective was to evaluate the feasibility of recording the PDR to assess analgesia in an anesthetized thoracic dermatome after TPVB.

METHODS:
This prospective, observational, single-center study included 32 patients requiring breast surgery under general anesthesia and TPVB. TPVB was performed before surgery under ultrasound guidance with 20 mL of 0.75% ropivacaine. At the end of the surgery, remifentanil was stopped and the PDR was recorded after a 5-second tetanic stimulation (60 mA, 100 Hz) applied to the anterior chest wall. The PDR was defined as the maximal increase in pupil diameter after a standardized noxious stimulus, expressed as a percentage of the initial pupil diameter. The PDR was recorded twice in the same eye for each patient after a stimulus on both the TPVB and the control sides. Postoperative pain scores were recorded in a postanesthesia care unit. The primary outcome was the difference between the PDR on the TPVB and the control sides.

RESULTS:
The median (interquartile range) PDR was 9% (4%–13%) on the TPVB side and 41% (27%–66%) on the control side. There was a significant difference in the PDR between the TPVB and the control sides with a Hodges-Lehmann estimate of absolute difference of 37% points (95% confidence interval, 25–52, $P < .001$). Median postoperative pain scores (interquartile range) in the postanesthesia care unit were 1 (0–3) at rest and 1 (0–3) during mobilization, respectively. There was a linear correlation between maximal postoperative pain scores and the PDR on the TPVB side with a Pearson's correlation coefficient $r = 0.40$ (95% confidence interval, 0.06–0.66, $P = .02$). No correlation was found between the number of blocked dermatomes and maximal postoperative pain scores ($P = .06$) or between the number of blocked dermatomes and the PDR on the TPVB side ($P = .15$).

CONCLUSIONS:
This proof-of-concept trial suggests that the effect of TPVB could be monitored by measuring the PDR after anterior chest wall stimulation in the dermatome of interest.

https://journals.lww.com/anesthesia-analgesia/Abstract/2017/10000/Pupillary_Reflex_for_Evaluation_of_Thoracic.41.aspx

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Regional Anesthesia and Acute Pain Medicine: Original Clinical Research Report

6

Pain assessment by pupil dilation reflex in response to noxious stimulation in anaesthetized adults.

Wildemeersch D, Peeters N, Saldien V, Vercauteren M, Hans G.

Abstract

BACKGROUND:
In response to noxious stimulation, pupillary dilation reflex (PDR) occurs even in anaesthetized patients. The aim of the study was to evaluate the ability of pupillometry with an automated increasing stimulus intensity to monitor intraoperative opioid administration.

METHODS:
Thirty-four patients undergoing elective surgery were enrolled. Induction by propofol anaesthesia was increased progressively until the sedation depth criteria (SeD) were attained. Subsequently, a first dynamic pupil measurement was performed by applying standardized nociceptive stimulation (SNS). A second PDR evaluation was performed when remifentanil reached a target effect-site concentration. Automated infrared pupillometry was used to determine PDR during nociceptive stimulations generating a unique pupillary pain index (PPI). Vital signs were measured.

RESULTS:
After opioid administration, anaesthetized patients required a higher stimulation intensity (57.43 mA vs 32.29 mA, P < .0005). Pupil variation in response to the nociceptive stimulations was significantly reduced after opioid administration (8 mm vs 28 mm, P < .0005). The PPI score decreased after analgesic treatment (8 vs 2, P < .0005), corresponding to a 30% decrease. The elicitation of PDR by nociceptive stimulation was performed without changes in vital signs before (HR 76 vs 74/min, P = .09; SBP 123 vs 113 mm Hg, P = .001) and after opioid administration (HR 63 vs 62/min, P = .4; SBP 98.66 vs 93.77 mm Hg, P = .032).

CONCLUSIONS:
During propofol anaesthesia, pupillometry with the possibility of low-intensity standardized noxious stimulation via PPI protocol can be used for PDR assessment in response to remifentanil administration.

KEYWORDS:
analgesia; assessment; monitoring; reflex

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7

Pupillary reflex measurement predicts insufficient analgesia before endotracheal suctioning in critically ill patients.

Paulus J, Roquilly A, Beloeil H, Théraud J, Asehnoune K, Lejus C.

Abstract

INTRODUCTION:
This study aimed to evaluate the pupillary dilatation reflex (PDR) during a tetanic stimulation to predict insufficient analgesia before nociceptive stimulation in the intensive care unit (ICU).

METHODS:
In this prospective non-interventional study in a surgical ICU of a university hospital, PDR was assessed during tetanic stimulation (of 10, 20 or 40 mA) immediately before 40 endotracheal suctionings in 34 deeply sedated patients. An insufficient analgesia during endotracheal suction was defined by an increase of ≥1 point on the Behavioral Pain Scale (BPS).

RESULTS:
A total of 27 (68%) patients had insufficient analgesia. PDR with 10 mA, 20 mA and 40 mA stimulation was higher in patients with insufficient analgesia ($P < 0.01$). The threshold values of the pupil diameter variation during a 10, 20 and 40 mA tetanic stimulation to predict insufficient analgesia during an endotracheal suctioning were 1, 5 and 13% respectively. The areas (95% confidence interval) under the receiver operating curve were 0.70 (0.54 to 0.85), 0.78 (0.61 to 0.91) and 0.85 (0.721 to 0.954) with 10, 20 and 40 mA tetanic stimulations respectively. A sensitivity analysis using the Richmond Agitation Sedation Scale (RASS) confirmed the results. The 40 mA stimulation was poorly tolerated.

CONCLUSIONS:
In deeply sedated mechanically ventilated patients, a pupil diameter variation ≥5% during a 20 mA tetanic stimulation was highly predictable of insufficient analgesia during endotracheal suction. A 40 mA tetanic stimulation is painful and should not be used.

Comment in
The value of pupillary dilation in pre-emptive analgesia: is there more to this than meets the eye? [Crit Care. 2013]

https://www.ncbi.nlm.nih.gov/pubmed/23883683

Crit Care. 2013 Jul 24;17(4):R161. doi: 10.1186/cc12840.
PMID: 23883683 PMCID: PMC4056098 DOI: 10.1186/cc12840

8

Pupillometry pain index decreases intraoperative sufentanyl administration in cardiac surgery: a prospective randomized study

V. Berthoud, M. Nguyen, A. Appriou, O. Ellouze, M. Radhouani, T. Constandache, S. Grosjean, B. Durand, I. Gounot, P.-A. Bahr, A. Martin, N. Nowobilski, B. Bouhemad & P.-G. Guinot

Abstract

Pupillometry has proven effective for the monitoring of intraoperative analgesia in non-cardiac surgery. We performed a prospective randomized study to evaluate the impact of an analgesia-guided pupillometry algorithm on the consumption of sufentanyl during cardiac surgery. Fifty patients were included prior to surgery. General anesthesia was standardized with propofol and target-controlled infusions of sufentanyl. The standard group consisted of sufentanyl target infusion left to the discretion of the anesthesiologist. The intervention group consisted of sufentanyl target infusion based on the pupillary pain index. The primary outcome was the total intraoperative sufentanyl dose. The total dose of sufentanyl was lower in the intervention group than in the control group and (55.8 µg [39.7–95.2] vs 83.9 µg [64.1–107.0], p = 0.04). During the postoperative course, the cumulative doses of morphine (mg) were not significantly different between groups (23 mg [15–53] vs 24 mg [17–46]; p = 0.95). We found no significant differences in chronic pain at 3 months between the 2 groups (0 (0%) vs 2 (9.5%) p = 0.49). Overall, the algorithm based on the pupillometry pain index decreased the dose of sufentanyl infused during cardiac surgery.

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