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Original Contribution

Pupil diameter during postanesthetic recovery is not influenced by postoperative pain, but by the intraoperative opioid treatment☆,☆☆

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Abstract

Study Objective: To investigate whether pupil diameter (PD) measured during scotopic conditions is influenced by pain in conscious patients in the early postoperative period.

Design: Prospective, observational, cohort study.

Setting: Single-center, postanesthesia care unit (PACU).

Patients: Patients scheduled for a surgery during general anesthesia.

Interventions: Baseline PD was measured the day before surgery. Patients were observed on admission to the PACU, immediately after extubation, during the different steps of analgesic intervention (demand, relief, plus intermediate measures when relevant), and either at discharge or 3 hours after admission.

Measurements: PD, pain (numerical rating scale), and alertness (Observer's Assessment of Alertness/Sedation scale).

Main Results: Of 103 patients enrolled, 80 required analgesia in the PACU and completed follow-up. Pain intensity evolved in line with expectations (temporary increase then relief), and alertness increased with time. PD increased from low mean values at admission to the PACU (40% of baseline) to a plateau throughout the

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rest of the study period (80% of baseline) and was not related to pain intensity. Multivariate analyses suggested that the factors influencing PD (or its value related to baseline) were time since extubation and the type of opioid (remifentanil, sufentanil, or sufentanil at high doses) administered during surgery.
Conclusions: Because of a residual effect of intraoperative opioids and a level of nociceptive stimulation lower than in surgical conditions, PD is not significantly influenced by early postoperative pain or pain relief.

1. Introduction

The current pharmacological options to counteract nociception are the intraoperative administration of intravenous opioids, followed by postoperative analgesic regimens, guided by pain assessment tools based mostly on the patient's subjective sensation [1]. However, during surgery receiving general anesthesia, the challenge is to provide sufficient analgesia to avoid central sensitization of pain, without excessive amount of opioids and the resultant hyperalgesia [2,3].

The measurement of scotopic (ie, under low light) pupil diameter (PD) appears as an interesting approach to estimate nociception and analgesia in unconscious patients. Indeed, although nociceptive stimulation increases PD in an intensity-dependent manner [4], opioids induce a dosedependent constriction (miosis) [5]. Pupil dilation induced by a transient nociceptive stimulus, also known as the pupil dilation reflex (PDR), is regularly used in experimental research protocols [5-8], whereas infrared pupillometers dedicated to the practice of anesthesia are now available on the European market [9,10]. To build a mathematical model able to predict excessive nociception during surgery, the relationship between pain and PD was studied in conscious patients. The available data in conscious subjects had been obtained only with mild nociceptive stimulation [4,11,12]. Feeling that such conditions were far from the clinical context, the immediate postoperative period was studied. Two similar observational studies failed to find a significant relation between early postoperative pain and PD [13,14].

2. Materials and methods

Ethical approval for this study was provided by the *Comité de Protection des Personnes Sud-Est I*, Saint-Etienne, France (Chairperson Prof Ph. Rusch) on October 18, 2010. Patients were included if aged 18-90 years and scheduled for surgery requiring general anesthesia and opioids in the early postoperative period. Exclusion criteria were emergency surgery, regional anesthesia, planned intensive care unit admission, incapacity to understand the protocol and sign consent, ocular disease, or any abnormality that would interfere with pupillometry. Patients gave signed consent the evening before surgery. Pupillometry was performed by the same examiner for each patient, using an infrared-based Neurolight pupillometer (Idmed, Marseille, France). Scotopic conditions were obtained with the device's light-tight occlusive silicone collar between the camera and the edges of the orbit and with the examiner shielding the contralateral eye tightly with a hand. After application, the patient was asked to keep the eye open, and PD was noted after stable values were obtained (30 seconds in general). The baseline preoperative measurement of PD was undertaken the evening before surgery. To check any abnormality of the pupils, both eyes were controlled, and the PD was also measured under photopic conditions (ie, elicitation of photomotor reflex by a 320-lx flashlight applied during 1 second). All further measurements were undertaken on the right pupil or on the left in case of abnormality of the right eye.

No measurement was performed during surgery. The time point for the end of intraoperative analgesia was the time of discontinuation of the infusion when remifentanil was the sole opioid or the 20th minute after either the last bolus or the discontinuation of the infusion, otherwise. The protocol for anesthesia and analgesia and the decisions for other care in the postanesthesia care unit (PACU) were left to the choice of the practitioner in charge of the patient, but the morphine titration protocol was standardized. Patients were transferred after surgery to PACU, intubated, and ventilated. Tracheal extubation was performed on recovery from anesthesia and effective spontaneous ventilation. On extubation, vital signs were monitored every 30 minutes until discharge. Systematic analgesia included (except if contraindicated) intravenous (IV) paracetamol (1 g/6 hours) and could be supplemented with ketoprofen (50-100 mg/8 hours) or nefopam (20 mg/6 hours), depending on the medical history. All nurses were trained in pain assessment and able to perform morphine titration. After return of full consciousness, patients were questioned about the presence of pain and were shown a 0-10 visually enlarged laminated numerical rating scale [15]. When pain score was over 3/10, IV morphine was titrated every 5 minutes by 3-mg increments (2 mg in patients weighing < 60 kg or older than 85 years), and pain was assessed every 5 minutes until score was < 3. If the patient was asleep after extubation and did not answer when asked to quote pain, no further attempt was made at arousal, and the pain score was scored as 0. When the patient was conscious and claimed to feel strong pain but not able to quote pain on a visual scale, due to his/her perception of emergency to receive analgesics, 10 was scored. Titration was stopped in case of bradypnea, hypoxemia, or excessive sedation. In some cases, the opiate administered for titration was not morphine, but either oxycodone or tramadol, by bolus of 2-3 mg