Section A-Research paper

A observational study on Comparative evaluation of visual analogue scale and pupillary diameter for post-operative pain

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ABSTRACT

Background: Visual analogue scales (VAS) and verbal rating scales (VRS) are widely used to assess pain. Pupillary dilatation has been successfully used to measure pain in quantitative terms.

Aims: The present study was conducted to study the correlation between VAS and pupillary diameter in the evaluation of postoperative pain.

Materials and methods: This observational study was carried out on 60 patients 18–65 years of age, scheduled for lower abdominal surgical procedures under general anaesthesia. Postoperative pain assessment was done using the VAS at 6 h, 12 h, 18 h and 24 hrs. In addition, the pupillary diameter of both eyes was measured simultaneously.

Results: Mean pupillary diameter values measured at baseline, 6 h, 12 h, 18 h, and 24 h postoperatively in two eyes, the difference was not statistically significant at any of the time points ($P > 0.05$), thus showing that the pattern of change in pupillary diameter was similar in both eyes. The mean change in pupillary diameter from baseline In both eyes was significant statistically at all the time points ($P < 0.05$). For VAS scores 0–2, 3–5, and 6–8, the mean change in pupillary diameter measured was 0.20 ± 0.3, 0.50 ± 0.53 and 0.42 ± 0.73 mm, respectively, thus showing a significant incremental trend ($P < 0.001$).

Conclusions: Change in pupillary diameter correlated well with the pain scores (VAS) and thus pupillary diameter can be chosen as an objective measurement of postoperative pain severity.

Keywords: pupillary diameter values, postoperative pain, numerical rating scale

INTRODUCTION

In a patient who is awake in the post-anaesthesia care unit (PACU), the presence of pain can be assessed using a 0–100 visual analogue scale (VAS), a 1–5 verbal rating scale (VRS), or a 0–10 numerical rating scale (NRS), although the standard method is still a topic of debate.[1,2] Analgesia or tolerable pain is usually defined as a VAS score of ≤30 mm or an NRS score of ≤3 and a VAS score of ≥70 mm or a NRS score of ≥7 should be considered indicative of severe pain.[3] However, some patient groups are at special risk for inadequate pain control and require additional analgesic considerations, including paediatric and geriatric patients, critically ill or cognitively impaired patients, or other patients who may have difficulty communicating.[4] Therefore, the objective assessment of postoperative analgesia would be valuable in the PACU setting to help optimize acute pain management.

Over the years, pupillary dilatation has been recognised as a reflex response to nociception mediated via autonomic innervation of the iris muscles. Consequently, it has been successfully used to measure pain in quantitative terms. It has been recently shown that pupillometer was an objective method to assess postoperative analgesia, with pupillary dilation reflex significantly correlated with VRS in PACU, helping titrating morphine in the immediate postoperative period.[5] With the availability of portable infra-red pupillometry devices, pupil size and pupillary reflexes can be easily measured. In addition, variation in pupillary diameter has been shown as an effective tool for postoperative pain assessment. The objective of this study was to find the correlation between VAS and pupillary diameter in the evaluation of postoperative pain.

MATERIALS AND METHODS

It is observational study done in 60 patients scheduled to undergo lower abdominal surgical procedures under general anaesthesia. After obtaining ethical approval from the Institutional Ethics Committee, this study was carried out in a tertiary care institute on 60 patients over 4 months from December 2022 to march 2023

The sample size was calculated based on a previous study showing a correlation of 0.42 between pupillary diameter and pain scores.[6]

The sample size projections were made at 99% confidence levels (α error 0.01) and 90% power (β error 0.10). The following formula was used for the calculation of sample size:[8]

$$n = [(Z_\alpha + Z_\beta)/C]^2 + 3$$

where C=0.4*

After adding for a contingency of 5%, the projected sample size was 60.

Inclusion criteria: Patients aged 18–65 years, scheduled to undergo lower abdominal surgical procedures under general anaesthesia.

Exclusion criteria: Iris, cornea or retina-related diseases, psychiatric disorders and inability to understand VAS.

Written informed consent was obtained from all the patients. Before the procedure, all the patients were explained the 10-point VAS score. Patients were asked to indicate their pain intensity by marking on a 0 to 10 cm long horizontal line labelled ’no pain’ at one end and ’worst possible pain’ at the other end. The pupillary diameter of both eyes was taken using a handheld portable infrared dynamic pupillometer before the procedure.

Patients fasted adequately before the surgery. After wheeling the patient into the operation theatre, intravenous access was secured, and patients were connected to non-invasive monitors and baseline parameters including pulse rate, non-invasive blood pressure and oxygen saturation, electrocardiography and respiratory rate were recorded. Patients were pre-medicated with injection midazolam (1–2 mg) and injection fentanyl (1–2 μg/kg) intravenously (IV). Anaesthesia induction was performed with injection propofol (1–2 mg/kg) and injection Vecuronium(0.08 mg/kg) IV. After tracheal intubation, mechanical ventilation was initiated with a mixture of 50% oxygen and 50% air and the respiratory rate was adjusted to keep end-tidal carbon dioxide between 30 and 35 mmHg. Anaesthesia was maintained with isoflurane (1-minimum alveolar concentration) and intermittent bolus doses of Vecuronium(0.08 mg/kg) and fentanyl (0.5–1 μg/kg).

For postoperative analgesia, all patients were given injection paracetamol (1 gm) IV half-hour before the conclusion of surgery and 8 hourly in the postoperative period till 24 hours. Anti-cholinesterases were not administered in any patient. Neuromuscular monitoring was done in all patients, and extubation was done after spontaneous recovery from the neuromuscular block with a train-of-four ratio of >0.8. Patients were shifted to the recovery room, and time was noted. Total operative time (duration of surgery) was noted from the point of induction of anaesthesia till extubation after spontaneous recovery from neuromuscular block. Post-operatively, the assessment was done using the VAS at 6 h, 12 h, 18 h and 24 h intervals. The pupillary diameter of both eyes was measured simultaneously at all the above-mentioned time points.

The other eye was covered to prevent consensual reflex while pupillary diameter was taken. Injection tramadol was given as rescue analgesia, if required, and the dose and time of administration were noted.

Data were represented as mean ± standard deviation (SD) and analysed using SSPS software. Paired t-test was used for quantitative variables and analysis of variance (ANOVA) was used to compare independent variables. Pearson's correlation coefficient was calculated to assess the bivariate correlation between VAS and pupillary diameter. A *P* value less than 0.05 indicated a statistically significant association.

RESULTS

Table-1: Demographic details of study

Variables	**Mean + SD**
Age in years	45.31 ± 14.26
Duration of surgery	189.11 ± 52.3

All patients were extubated after spontaneous recovery from the neuromuscular block with a train-of-four ratio of >0.8.

Table-2: VAS Scores for pain at baseline and changes at intervals

VAS scores	**Mean** ± SD	**Change from baseline in Mean** ± SD	**P -value**
Baseline	0	-	-
6 hrs	4.6 ± 0.8	4.6 ± 0.8	<0.001
12 hrs	3.4 ± 0.8	3.4 ± 0.8	<0.001
18 hrs	2.1 ± 0.6	2.1 ± 0.6	<0.001
24 hrs	1.4 ± 0.4	1.4 ± 0.4	<0.001

Mean VAS scores at baseline, 6 h, 12 h, 18 h and 24 h postoperative intervals were 0, 4.6 ± 0.8, 3.4 ± 0.8, 2.1 ± 0.6and 1.4 ± 0.4, respectively. Compared to the baseline, at all the time intervals, the mean change was statistically significant ($P < 0.001$)

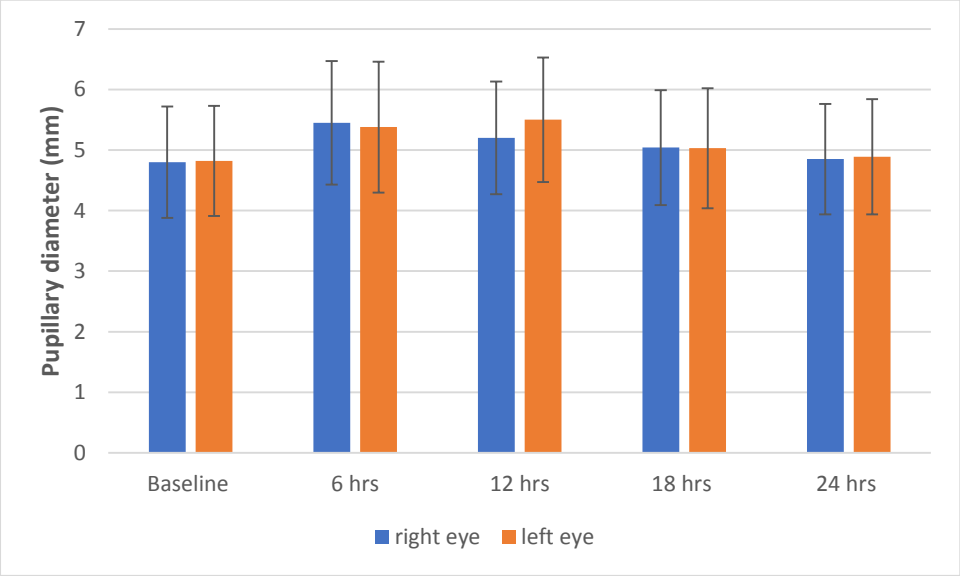
Table-3: Comparison of pupillary diameter (mm) between two eyes at baseline and changes at intervals

Pupillary diameter (mm)	**Right eye Mean** ± SD	**Left eye Mean** ± SD	**P -value**
Baseline	4.80 ± 0.92	4.82 ± 0.91	0.698
6 hrs	5.45 ± 1.02	5.38 ± 1.08	0.420
12 hrs	5.25 ± 0.93	5.25 ± 1.03	0.984
18 hrs	5.04 ± 0.95	5.03 ± 0.99	0.682
24 hrs	4.85 ± 0.91	4.89 ± 0.95	0.612

Mean pupillary diameter values measured at baseline, 6 h, 12 h, 18 h, and 24 h postoperatively were 4.80 ± 0.92, 5.45 ± 1.02, 5.25 ± 0.93, 5.04 ± 0.95 and 4.85 ± 0.91 mm in the right eye and 4.82 ± 0.91, 5.38 ± 1.08, 5.25 ± 1.03, 5.03 ± 0.99 and 4.89 ± 0.95 mm

respectively in the left eye. On comparing the two eyes, the difference was not statistically significant at any of the time points ($P > 0.05$), thus showing that the pattern of change in pupillary diameter was similar in both eyes

Figure-1:Pupillary diameter at baseline and different follow-up points in the right eye and left eye



The mean change in pupillary diameter from baseline was 0.65, 0.45, 0.24 and 0.05 mm in the right eye and 0.56, 0.43, 0.21and 0.07 mm respectively in the left eye at 6 h, 12 h, 18 h and 24 h. In both eyes, the change from baseline was significant statistically at all the time points ($P < 0.05$)

Table-4: Correlation of change in VAS scores and change in average pupillary diameter

VAS score category	**Change in pupillary diameter**		**P value**
	Mean	SD	
0-2	0.20	0.3	<0.001
3-5	0.50	0.53	
6-8	0.42	0.73	
>8	-	-	

For VAS scores 0–2, 3–5, and 6–8, the mean change in pupillary diameter measured was 0.20 ± 0.3, 0.50 ± 0.53 and 0.42 ± 0.73 mm, respectively, thus showing a significant incremental trend ($P < 0.001$).

On bivariate correlation, a near mild positive significant correlation was found between the mean change of VAS score and change in pupillary diameter (r = 0.3; $P < 0.001$).

DISCUSSION

Pupillometry has been postulated as analternative to ANI for the assessment of postoperative pain and assesses the pupillary dilation response to a stimulus in the operative site.3 4 However, this approach is difficult to perform in younger paediatric patients, who will barely tolerate pupillometry performance and will not bear any further manipulation of the surgical wound. For this reason, we decided to use an approach similar to that of Bosselli and colleagues[7] but with the pupillary pain index (PPI). The PPI consists in measuring the changes in pupillary dilation in response to a continuously increasing electric stimulus discharge until 13% of pupillary variation is reached. The measurement of PPI immediately before extubation after anaesthesia was significantly associated with the observational pain intensity measurement upon arrival in the postanaesthesia care unit. The measurement of PPI under these circumstances can be predictive for immediate postoperative pain in a simple and effective way to assist physicians in optimizing acute pain management

Monitoring analgesia is a new and very challenging concept and developing tools for the prediction of immediate postoperative pain may have an important impact in clinical practice. Indeed, it as been shown in a recent study that severe pain still occurs in 20–40% of patients, including patients undergoing so-called minor surgical procedures (appendectomy, tonsillectomy, etc.).[8] In this perspective, the use of analgesia monitors such as the ANI or PPI may provide useful information to physicians to optimize the management of immediate postoperative pain. It is postulated that ANI or PPI values immediately before extubation may be highly predictive of acute pain within the following minutes, thus the administration of a prophylactic dose of opioid may provide a reduction in pain scores at arrival in the post-anaesthetic care unit. This, however, remains to be demonstrated in prospective studies. For us, use of the ANI presents an advantage over the PPI since it allows for continuous analgesia monitoring directly from the patient monitor, whereas the PPI requires measuring the changes in pupil dilation in response to increasing electric stimulations. Moreover, in cephalic procedures such as ear– nose–throat surgery, the use of a device placed over the face is not possible. Nevertheless, the authors should be commended for performing this study in young children in an effort to optimize postoperative analgesia. Prospective studies comparing various monitors such as the ANI and PPI are urgently needed in both adults and children to determine the clinical benefit of analgesia monitoring in routine practice for acute postoperative pain management.

Compared to the present study, where the correlation between VAS pain scores and pupillary diameter was made at different pre-determined postoperative intervals, various previous studies have avoided frequent measurements of pupillary diameter and focused only on targeted scores. Aissou *et al*.[9] targeted a score of more than one on a verbal rating scale for the measurement of size without fixing a particular time for evaluation of pain as done in the present study. Charier *et al*.[10] on the other hand, did not specify the time of pain measurement and targeted a VAS pain score >4 as a clinical event at which pupillary measurement was made. A similar criterion for pain detection was used by Kantor *et al*.[11] who targeted a numerical rating scale (NRS) score >4 for such evaluation. We conducted our assessments at

different pre-fixed time points, thus measuring the pattern of VAS and pupillary diameter changes at different time points.

In present study Compared to baseline, mean values of average pupillary diameter at all the time points were significantly higher, thus showing a similar trend as observed for VAS scores, reflecting that pupillary diameter goes hand-in-hand with perceptional changes of pain as illustrated by VAS scores. Charier *et al*.[10] found a strong correlation between the VAS score and the variation coefficient of pupillary diameter (PD). We observed a mild positive and significant correlation in pupillary diameter changes and VAS scores in the present study. The PD increases in response to painful stimulation in proportion to the intensity of the nociceptive stimulus. This variation of PD has been proposed to evaluate pain in patients under general anaesthesia.

In cumulative assessment, we found a change in average pupillary diameter to be better correlated with VAS pain scores at different time intervals. Guglielminotti *et al.*,[12] in their study, found a significant correlation between NRS pain scores and pupillary diameter; they found a derived parameter, pupillary light reflex amplitude, to be more strongly associated with pain scores.

However, despite having a physiological basis and thus being more objective in terms of measurement, pupillary diameter changes do not always reflect only pain. It is, in fact, a reflex response to any stimulus that is strong enough to increase the level of arousal. Its usefulness is thus limited to assessment in well-controlled environments only where such confounders' role is minimal.[13]

The absence of a strong correlation of pupillary diameter change or absolute pupillary diameter with VAS scores for pain in the present study also shows that although the pupillary diameter is affected by painful stimuli, this relationship is multifaceted and not linear. Sabourdin *et al*.[14] compared pupillometry-guided intraoperative remifentanil administration compared to standard practice and found that pupillometry was able to reduce intraoperative remifentanil consumption and postoperative morphine requirements.
Nevertheless, the authors should be commended for performing this study in an effort to optimize postoperative analgesia. Prospective studies comparing various monitors such as the ANI and PPI are urgently needed in adults to determine the clinical benefit of analgesia monitoring in routine practice for acute postoperative pain management.

CONCLUSION

Change in pupillary diameter correlated with pain scores. Pupillary diameter showed a tendency to enlarge with increasing pain, thus validating that it could be chosen as an objective measurement of pain severity.

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