Neurological Pupil Index as an Indicator of Irreversible Cerebral Edema: A Case Series

Michaela X. Cortes, Kathrina B. Siaron, Hend T. Nadim, Khalid M. Ahmed, Jia W. Romito

ABSTRACT

BACKGROUND: Assessing the pupillary light reflex is a core component of neurological assessments. Pupil size and reactivity can provide early warning about early neurological decline. Automated infrared pupillometry is noninvasive and easy to use and has greater reliability compared with manual assessments to obtain objective and consistent measurements of pupillary size and reactivity to light. **METHODS:** This is a case series of 3 patients who had poor baseline clinical neurological examinations. Because it would be more difficult to detect acute neurological deterioration, automated infrared pupillometry and the Neurological Pupil index (NPi) were used in addition to the clinical neurological examination. NPi values < 3.0 prompted further imaging. **RESULTS:** In each case, abnormal NPi values prompted emergent imaging that confirmed acute cerebral edema and resulted in a change in management and treatment plan. **CONCLUSION:** The automated infrared pupillometry is a noninvasive monitor that can provide additional objective data in patients with a poor baseline neurological examination in whom it may otherwise be difficult to detect neurological deterioration.

Keywords: herniation, neurocritical care, Neurological Pupil index, pupillary light reflex, pupillometry

Assessing the pupillary light reflex (PLR) is a core component of neurological assessments. Changes in pupil size and reactivity can provide early recognition of neurological decline and facilitate lifesaving interventions.[1–4] The standard of practice to evaluate PLR uses manual use of a penlight or similar light source; however, this method has low interrater reliability and intrarater consistency.[3] Automated infrared pupillometry (AIP) has greater reliability to obtain objective and accurate measurements of pupillary size and reactivity to light using the Neurological Pupil index (NPi).[1,5,6] Neurological Pupil index measurement between 3.0 and 5.0 is indicative of a normal pupil; patients admitted to a neurocritical care unit generally have NPi greater than 4.1.[7] NPi < 3.0 is considered abnormal, raising the concern for a neurological change. The following case series of 3 patients with baseline poor neurological examinations demonstrates the use of handheld AIP (NeurOptics NPi-200 Pupillometer) as an additional tool that provides information that can assist with early confirmatory diagnostic evaluation and progression of appropriate management.

Questions or comments about this article may be directed to Jia W. Romito, MD, at Jia.Romito@UTSouthwestern.edu. J.W.R. is an Assistant Professor, Departments of Anesthesiology & Pain Management, Neurosurgery, and Neurology, University of Texas Southwestern Medical Center, Dallas, TX.

Michaela X. Cortes, BSN RN, Department of Neurology, University of Texas Southwestern, Dallas, TX.

Kathrina B. Siaron, BSN RN, Department of Neurology, University of Texas Southwestern, Dallas, TX.

Hend T. Nadim, MBA, Department of Neurology, University of Texas Southwestern, Dallas, TX.

Khalid M. Ahmed, MBBS, Department of Neurology, University of Texas Southwestern, Dallas, TX.

Financial support was provided to the institution study procedures for the END PANIC Registry Study from NeurOptics Inc. The individual authors for this study did not directly receive financial support.

The authors declare no conflicts of interest.

DOI: 10.1097/JNN.0000000000000584

Methods

This is a retrospective case series of 3 patients admitted to the neurocritical care unit who presented with acute ischemic stroke and progressed to herniation. At this quaternary care center, AIP is routinely used for the PLR component of the serial neurological examinations. The institutional review board approved this retrospective analysis under the overarching Establishing Normative Data for Pupillometer Assessments in Neuroscience Intensive Care Registry.[8]

Patient 1

A 27-year-old woman with a recent history of lithotripsy and right ureter stent placement transferred to a quaternary care center with sagittal sinus thrombosis. Admission neurological examination was pertinent for bilateral pupillary NPi of > 3.0, lack of

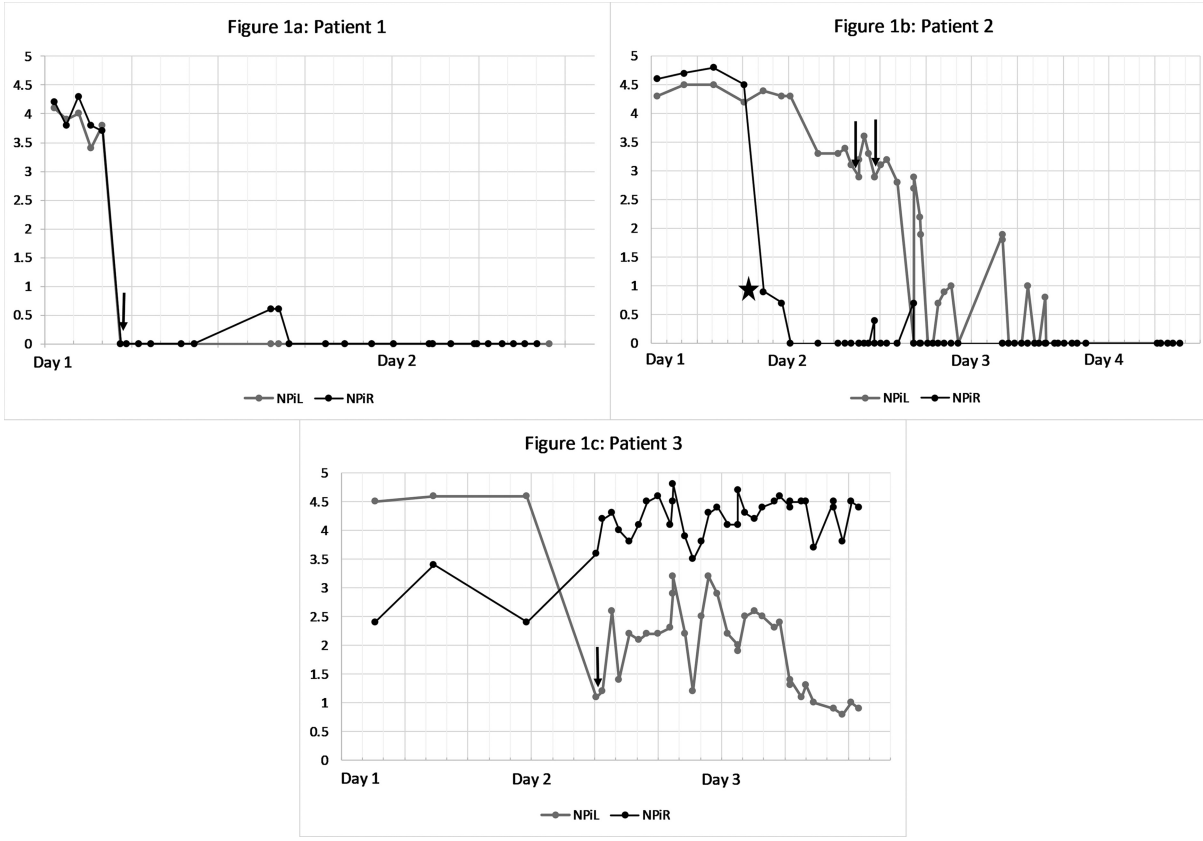
cough/gag reflex, and no motor response to noxious stimuli. Despite systemic anticoagulation with intravenous heparin infusion, attempted mechanical thrombectomy, and direct endovascular thrombolytic therapy with intrasinus alteplase, her clinical examination continued to remain poor. When bilateral PLR acutely deteriorated to NPi of 0, emergent head computed tomography (CT) was notable for transtentorial herniation (Fig 1A). The family declined further procedural or surgical intervention. Maximal medical management was continued; however, the patient progressed to brain death soon thereafter.

Patient 2

A 67-year-old woman with a history of chronic hypertension, type II diabetes, and previous stroke presented with acute right middle cerebral artery occlusion with a National Institutes of Health Stroke Scale score of 24 and an Alberta Stroke Program Early CT Score (ASPECTS) of 2 to 3, who received administration of intravenous alteplase. By hospital day 2, the patient had clinical neurological decline due to cerebral edema with 10 mm of midline shift requiring right-sided decompressive hemicraniectomy. Postoperatively, the patient had AIP notable for right pupil NPi of 0 and left pupil NPi > 3.0, and she had persistently poor serial clinical neurological examinations. Left pupil NPi progressed to < 3.0 and prompted emergent imaging (Fig 1B). Head CT was notable for increased right-sided cerebral edema and a worsened midline shift. Maximal medical management was initiated; however, after further discussion with the family, the care was transitioned to a focus on comfort.

> Pupillometry reduces the time needed to complete the PLR evaluation.

FIGURE 1 **A, Patient 1. The arrow indicates NPi immediately before emergent imaging. B, Patient 2. The star indicates surgical intervention, and the arrow indicates NPi immediately before emergent imaging. C, Patient 3. The arrow indicates NPi immediately before emergent imaging. NPi, Neurological Pupil index; NPiL, left NPi; NPiR, right NPi.**



Patient 3

A 79-year-old woman with a history of atrial fibrillation without chronic anticoagulation presented with right-sided hemiplegia and global aphasia. Imaging was notable for left internal carotid artery occlusion, ischemic core volume of 151 mL, and diffusion-perfusion mismatch ratio of 1.5. Because of the delayed hospital presentation, she did not receive intravenous alteplase or endovascular intervention. Serial neurological examinations were performed. The left pupil deteriorated to NPi of 1.1 with the right pupil NPi of 3.6 (Fig 1C). Subsequent emergent head CT was notable for increased cerebral edema in the left anterior cerebral artery/middle cerebral artery territory with 13 mm of midline shift. Maximal medical therapy with osmotic therapy was initiated. After discussion with the family, surgical decompression was not pursued because of the patient's age and comorbidities. Further discussions regarding the goals of care resulted in a transition to comfort care only.

Discussion

The serial clinical neurological examinations by the bedside nurse are vital for early detection of clinical decline in patients with neurological deficits. The neurological assessments include evaluations of a patient's level of consciousness, orientation, PLR, visual fields, language, and strength. Neurological examinations are tailored to each patient with consideration of his/her neurological conditions. In the neurocritical care unit at this quaternary care center, neurological assessments are evaluated hourly by the bedside nurse for these critically ill patients. To maintain consistency, the nurse conducts the neurological examination approximately at the same time every hour. At each shift change, a neurological assessment is also performed together by the incoming and outgoing nurses as part of the handoff process. Each aspect of a patient's examination may have minor fluctuations due to time of day and patient fatigue, and there can also be variation of the examination between examiners. It is time consuming for the bedside nurse to evaluate and then reevaluate to confirm whether a neurological change is reproducible and/or within an accepted fluctuation for a patient. Patients with severe neurological deficits are especially more difficult to elicit neurological changes outside accepted variation.

AIP eliminates uncertainty in 1 aspect of the neurological assessment by providing objective data to trend, similar to blood pressure readings, telemetry, and pulse oximetry. For each nursing neurological assessment, AIP reduces the time needed to complete the PLR evaluation, and this can add up to time savings for the bedside nurse to complete other necessary tasks. By providing a more consistent and reliable way to assess PLR, AIP improves intrarater and interrater consistency and may indicate PLR trends that the human eye cannot spot. It can provide critical information in patients who have limited neurological examinations, such as those who are paralyzed and sedated, because nurses will be able to use the AIP to objectively assess the pupillary response to light. If the NPi is < 3.0 or the nurse notices a significant drop in the value compared with the previous assessment, the nurse should inform the provider immediately for further evaluation of the neurological examination change.

The pupillometer machine itself is capable of showing trend data through graphs of NPi and pupillary sizes, as well as video clip playbacks of recordings made from each pupillary evaluation. The objective data from pupillometer evaluation can be input into nursing flow sheets to trend in the electronic medical record. These data can be used to compare the time of each AIP data point and medication administration, imaging, and surgical events. This allows a more cohesive clinical course of a patient's gradual neurological decline or improvement.

In a previous study, manual pupillary examination combined with Glasgow Coma Scale (GCS) scores provided useful prognostic information. This study found patients who were admitted with a GCS score of 3 and had fixed and dilated pupils did not have a reasonable chance of survival whereas patients with an admission GCS score of 4 and reactive pupils had a 33% survival rate.[4] A previous case series of 3 patients reported the median time for detection of abnormal NPi occurred 7.4 hours before clinical transtentorial herniation. It found normal intracranial pressure during 10 of the 12 herniation events in these 3 patients.[9] Another study found that the NPi did not improve after osmotic therapy administration for cerebral edema, hypothesizing that the underlying mechanism for the cerebral edema was due to changes in global pressure.[10]

In this case series, we presented 3 patients who had poor baseline neurological examinations with anticipated difficultly in clinical recognition of neurological deterioration. The AIP became a vital tool for providing objective data to proceed with further diagnostic evaluation. In each patient, acute change of NPi < 3.0 prompted notification of the provider and completion of emergent imaging within 30 minutes of the NPi change. Each imaging result was notable for significant cerebral edema. Our first and second patients did not have reversal of pupillary response after osmotic therapy administration. In the third patient, the NPi value improved after osmotic therapy administration, and this may be due to the lateralized cerebral edema from the ischemic stroke.

In all 3 patients, the early detection with the AIP effectively guided early additional evaluation and maximal medical management. Surgical options and goals of care were also able to be assessed before implementation of invasive interventions that were not in line with the patients' and family's wishes. There were no significant barriers that were noted in the medical management after AIP detection of pupillary change in this setting of a neurocritical care unit in a quaternary care center.

Given that AIP is a noninvasive and portable tool, there is a large potential benefit with minimal risk in increasing its use in patients at risk of neurological deterioration. More studies are needed to bring pupillometry to a standard of practice.

References

1. Zafar SF, Suarez JI. Automated pupillometer for monitoring the critically ill patient: a critical appraisal. *J Crit Care*. 2014;29(4):599–603.
2. Aoun SG, Welch B, Cortes M. Objective pupillometry as an adjunct to prediction and assessment for oculomotor nerve injury and recovery: potential for practical applications. *World Neurosurg*. 2019;121:e475–e480.
3. Kerr RG, Bacon AM, Baker LL, et al. Underestimation of pupil size by critical care and neurosurgical nurses. *Am J Crit Care*. 2016;25(3):213–219.
4. Lieberman JD, Pasquale MD, Garcia R, Cipolle MD, Mark Li P, Wasser TE. Use of admission Glasgow Coma Score, pupil size, and pupil reactivity to determine outcome for trauma patients. *J Trauma*. 2003;55(3):437–443.
5. Zhao W, Stutzman S, DaiWai O, Saju C, Wilson M, Aiyagari V. Inter-device reliability of the NPi-100 pupillometer. *J Clin Neurosci*. 2016;33:79–82.
6. Yan S, Tu Z, Lu W, et al. Clinical utility of an automated pupillometer for assessing and monitoring recipients of liver transplantation. *Liver Transpl*. 2009;15(12):1718–1727.
7. Lussier BL, Stutzman SE, Atem F, et al. Distributions and reference ranges for automated pupillometer values in neurocritical care patients. *J Neurosci Nurs*. 2019;51(6):335–340.
8. Olson DM, Stutzman SE, Atem F, et al. Establishing normative data for pupillometer assessment in neuroscience intensive care: the "END-PANIC" registry. *J Neurosci Nurs*. 2017;49(4):251–254.
9. Papangelou A, Zink EK, Chang W-TW, et al. Automated pupillometry and detection of clinical transtentorial brain herniation: a case series. *Mil Med*. 2018;183(1–2):e113–e121.
10. Ong C, Hutch M, Barra M, Kim A, Zafar S, Smirnakis S. Effects of osmotic therapy on pupil reactivity: quantification using pupillometry in critically ill neurologic patients. *Neurocrit Care*. 2019;30(2):307–315.