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Abnormal Downward Gaze and Cold Caloric Examination Due to Propofol: A Case Study

Thuy-Anh Vu
Virginia Commonwealth University, TVu@mcvh-vcu.edu

Alia O'Meara
Virginia Commonwealth University

Jean Teasley
Virginia Commonwealth University

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Thuy-Anh Vu, MD – Department of Child Neurology, Virginia Commonwealth University

Alia O'Meara, MD – Department of Pediatric Critical Care, Virginia Commonwealth University

Jean Teasley, MD – Department of Child Neurology, Virginia Commonwealth University

Correspondence: Dr. Thuy-Anh Vu, Resident, Virginia Commonwealth University, PO Box 980211, 1001 East Marshall St, Richmond, VA 23298-0211, USA; TVu@mcvh-vcu.edu; Tel: +1 804-828-0442; Fax: +1 804-828-6690

Abstract

BACKGROUND: Adolescent patient with isolated abnormal downward gaze and oculovestibular (cold caloric) testing during propofol administration prompting concern of brainstem injury. PATIENT: An otherwise healthy 16 year old female presented after an intentional hanging. Brainstem reflexes were normal except that both eyes were in tonic downgaze on initial examination. Propofol was suspended for 30 minutes to evaluate level of responsiveness with eyes normalizing to midposition from tonic downgaze. With reinitiation of propofol, the eyes returned to the former position. C-collar stabilization prohibited oculocephalic (doll's eyes) evaluation, and with cold caloric testing, eye movements were as follows: right sided cold water instillation resulted in right eye exodeviation to the right with minimal medial movement of the left eye to the right. Upon left sided instillation, the left eye deviated downward with minimal medial deviation of the right eye. Patient was weaned to extubation within 48 hours of admission, and off sedatives normal ocular motility returned. CONCLUSION: This patient manifested abnormal ocular motility and cold caloric exam with single-agent propofol exposure. The remainder of the cranial nerve exam was normal, and in the context of a normal brain and cervical spine MRI, the clinical picture was inconsistent with brainstem injury leading us to suspect propofol effect. This was supported by the return of normal ocular motility once propofol was discontinued. Consider pharmacologic disturbance of ocular motility and cold caloric testing in the absence of other brainstem dysfunction when concomitant propofol is administered.

Keywords: caloric tests; propofol; eye movement, neurological exam

Introduction

Brain stem examination is important in patients with decreased level of consciousness, whether pathologic or pharmacologically induced. Inability to comply with a routine neurologic exam often leads clinicians to rely on brain stem reflex testing as a surrogate for the extent and severity of brain injury. This is particularly valuable as brain stem imaging with head CT, often the only practical acute imaging modality, is inadequate. Findings may guide treatment in the acute setting, such as initiating intracranial pressure (ICP) protocols including hypothermia or invasive ICP monitoring, which have associated risks. Brain stem examination is also a cornerstone of brain death criteria.

In our case we were concerned for medication induced abnormal brain stem reflexes and a literature search did not return any specific case reports of brain stem reflex abnormality associated with single agent propofol. Publications addressed depressed metabolism in different brain regions including the brain stem in rats[1] and also in cortex, thalamus, and reticular formation in cats[2]. A human fMRI study demonstrated altered thalamic and pontine activity, but again, not related to specific function demonstrable on clinical exam[3].

More commonly encountered adverse effects of propofol include over-sedation, respiratory depression or apnea which can lead to hypoxemia, hemodynamic instability, nausea and vomiting[4]. Additionally it is known that propofol may cause movement disorders and also act as a treatment for them[5]. In a case report it was reported that dexmedetomidine was an effective treatment for propofol induced dyskinesia[6].

Case Presentation

This patient was a 16 year old otherwise healthy and developmentally normal female who presented after an intentional hanging from a second story window of unknown duration at the time of admission. At the time of discovery she had pulses and a Glascow coma score (GCS) of 4 for which she was intubated. When initially evaluated in the ICU during propofol interruption she was combative and moved all four extremities spontaneously, attempting to sit up and roll over and inconsistently squeezed hands to command, following no other commands. Pupils were predominantly in tonic downgaze with occasional return to midline. With radiographic tracheal and cervical spine abnormalities of uncertain significance pending surgical consultation, she was re-sedated with single agent propofol for safety. Additionally, given injury mechanism, there was an unclear hypoxic-ischemic duration and she was subsequently placed on a cooling blanket to maintain normothermia when she reached a temperature of 38.8 Celsius. Neurology was consulted for neurological evaluation and prognosis given unknown strangulation time and possibility of hypoxic-ischemic insult.

Vital signs were heart rate of 97 beats per minute, blood pressure of 100/58, respiratory rate of 16 breaths per minute over mechanical ventilation rate of 10 breaths per minute, saturation of 100%, Temp 37.5Celsius. She was intubated on synchronized volume ventilation at 8 ml/kg, FiO2 0.40, PEEP 5, PS 6.

Vecuronium 5mg was given at 9:25 AM. Exam was at 11:00 AM on propofol 74mcg/kg/min infusion. Propofol was not stopped for this exam. Other medications at the time were isotonic saline drip, famotidine and the cooling blanket titrated for normothermia.

Exam showed an obtunded patient that responded to pain with withdrawal. Cranial nerve exam showed 2mm pupils reactive to light bilaterally. Corneal reflexes were intact bilaterally. At

rest patient's eyes were in tonic downgaze. With stimulation pupils returned to midline. Staff reported that when propofol was halted previously eyes returned to midline. C-collar precluded oculocephalic maneuver, but ice-cold caloric testing was done. With cold water instillation into the right ear the right eye exodeviated to the right with minimal movement of the left eye. Upon cold water instillation into the left ear, right eye had minimal medial movement with subtle downward left eye movement. Patient was clearly uncomfortable with caloric testing with purposeful upward arm movements and a gag response. Reflexes were initially hyperreactive in the bilateral lower extremities with downward plantar responses.

Head CT, c-spine CT-angiogram were normal and done prior to the neurology team's examination. C-spine CT was concerning for reverse lordosis at C4-C5 but no fractures. Subsequent MRI of head and c-spine were normal without abnormal signal or ligamentous injury. With a more complete assessment including the above neurologic exam and imaging, medications were titrated from single agent propofol to include fentanyl and haldol.

Given otherwise reassuring neurological exam and head imaging, and with resolved concerns for cervical injuries, the patient was weaned to extubation the next day. She had return of normal ocular motility after sedation was turned off for several hours (8 hours from fentanyl and propofol and 6 hours from haldol), along with other normal brain stem responses. The rest of her neurological exam was also normal except for some lethargy and slow responses. She was hoarse and ENT and speech therapy evaluation diagnosed para-tracheal emphysema and hypomobility of right true vocal cord.

Conclusion

Given abnormal tonic downgaze and abnormal cold caloric testing, initial concern was for brain stem injury. Localization for the tonic downgaze is usually ventral midbrain, in our patient's case potentially caused by increased intracranial pressure from anoxia-related cerebral edema given unknown time of hanging. The abnormal caloric testing would most likely localize to cranial nerve eight (vestibular nerve) injury. In the acute setting these findings were distressing, however with the remainder of the neurological exam normal in a sedated patient, particularly the brainstem reflexes, we questioned these findings and were less concerned for acute brain stem injury. We were further reassured with normal brain and cervical spine MRI. A literature review for abnormal eye movements specific to propofol did not return any reports. We elected to follow with serial exams until exam normalized and hypothesized the abnormal movements were due to pharmacologic effect of propofol.

In researching this case we sought to link propofol to the abnormal eye findings. Sedative-hyponotic drug overdose patients have been observed with several abnormal eye movements during cold caloric testing including: forced downward deviation of one or both eyes during cold caloric testing, and delayed or absent adduction of contralateral eye, which was not observed in non-drug-induced coma[7]. This finding was published as a case series in 1978 prior to propofol introduction, though given propofol's proficiency as a sedative, it could certainly be implicated as well. Similar to the barbiturates in that series, propofol also enhances gamma-aminobutyric acid (GABA) inhibitory action via $GABA_A$ receptors, although there may be additional neurotransmitters involved[8,9]. Further supporting pharmacological effect in our patient was a case report of barbiturate intoxication causing vertical upgaze palsy[10]. Suppressing the upgaze component with GABA involvement would explain our patient's downward gaze at rest with propofol.

This case also poignantly reviewed the performance of cold-caloric testing in a semi-conscious patient. If pupillary position had been midposition, and had the cervical collar not precluded “doll’s eyes” maneuver, we would likely not have performed caloric testing at that time. She was clearly uncomfortable and we apologized to her.

Another consideration in our case is cervical neck injury and vestibular effects. However, imaging and clinical exam did not otherwise support any cervical injury nor the vestibular effects usually associated with cervical injury[11].

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