

Dilation of the Pupil in Human Subjects after Intravenous Thiopental

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A better understanding of pupillary responses under anesthesia might be of use to the anesthesiologist. With the exception of the meiotic response to morphine, the pupillary changes seen following administration of the drugs used by the anesthesiologist have not been thoroughly studied. Some inhalation anesthetics produce meiotic and nonreactive pupils;¹ however, the mechanism is unknown.

A survey of the literature has failed to uncover any investigations on the course of pupillary changes after bolus injections of sodium thiopental in humans. In the cat, thiopental has been shown to produce a marked dilation of the pupil followed by eventual constriction.²

The present investigation was designed to measure the response of the pupil during the first few minutes following bolus injections of thiopental in human subjects. Of primary interest was the question whether thiopental produces a dilation in humans, such as is seen in cats, and under what conditions.

METHODS

The project was approved by the Institutional Review Committee of the French Hospital-Medical Center. Healthy ASA I patients of either sex scheduled for elective surgery were chosen. Four groups of patients were selected on a sequential basis. Group I patients were unpremedicated and were given a standard 4 mg/kg dose of thiopental. Group II patients were unpremedicated and given 6 mg/kg thiopental. The effects of narcotic premedication were studied by measuring the responses of Group III and Group IV patients. Group III patients were given meperidine, 50-75 mg, promethazine, 12.5-25 mg,

and atropine, 0.4 mg, intramuscular (im), 1 hr before induction with 4 mg/kg thiopental. Group IV patients were given fentanyl, 0.075 mg, intravenous, 5-8 min before induction with 4 mg/kg thiopental. Because age can have an effect upon the diameter of the pupil,³ the mean age of each group was matched within 3 years (table 1). Patients with cataracts, Adie's syndrome, glaucoma, previous cataract surgery, blindness, or a history of drug abuse (alcoholism, amphetamines, or heroin) were excluded from the study.

Preoperative pupillograms were taken with the Skyoldvik[®] pupillometer⁴ and handwritten into the anesthetic record. The Skyoldvik[®] pupillometer allows quick measurement of the diameter of the pupil and grading of the light reflex. The precision of this pupillometer is dependent upon the diameter of the pupil. Changes of 0.3 mm on diameters below 3.2 mm, 0.4 mm on diameters between 3.2-4 mm, and 0.5 mm on diameters between 4 and 5 mm can be detected.

An intravenous solution of 5 per cent dextrose and 0.45 per cent NaCl was started on all patients. After baseline pupillary measurements had been made, sodium thiopental, 2.5 per cent, was injected as a bolus (15 s) while the patient was breathing room air. Pupil size and reactivity were determined at 0.5, 1, 2, and 3 min after injection. Time was measured starting from the completion of the injection. Upon loss of consciousness a mask was lightly placed upon the patient's face and oxygen was administered through a semi-closed circle absorber. Irregular breathing, with apneic periods lasting up to 10 s, occurred in all patients and was overcome by intermittent gentle positive pressure on the breathing bag. No attempt was made to control breathing, and the patients were allowed to breathe spontaneously once a rhythmic pattern ensued. Patients who struggled to maintain an airway or those that required an oral or nasal airway were eliminated from the study. Stimulation of the patient was kept to a minimum. The circulating nurse was not permitted to prep or position the patient or to insert catheters until the completion of the study. The study was terminated if the patient showed signs of awakening (opening eyes, moving extremities, resisting retraction of eyelid) or at the end of 3 min.

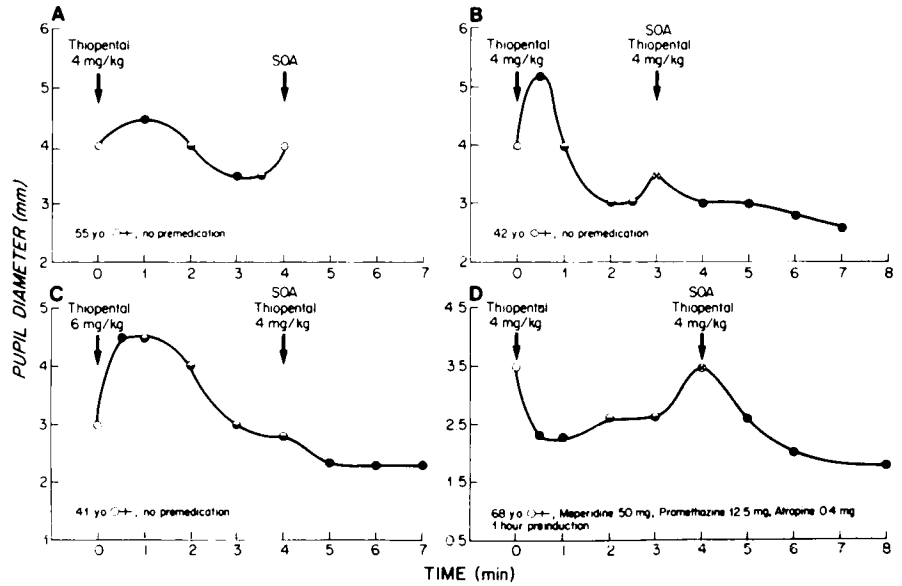
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FIG. 1. Pupillograms of four patients following thiopental. Pupil light reflex: ○ Brisk, ● Sluggish, ● Absent, ⊗ Patient resisting lid retraction. Doses and times as indicated. SOA: signs of awakening; y.o.: year old; 0+: female. Note that the ordinate begins at 2 mm in A and B, at 1 mm in C, and 0.5 mm in D.



None of the patients were allowed to awaken and orient themselves to their surroundings. Six patients were given additional thiopental when signs of awakening appeared, and the pupillary activity in these patients was followed for longer periods of time.

Statistical comparisons with the control group (Group I) were made using the Student *t* test for unpaired data; $P < 0.05$ was considered as a significant difference between the groups.

RESULTS

The typical pupillary responses of the Group I (control) patients are shown in figures 1A and 1B. The light reflex was depressed soon after injection but recovered as the subject showed signs of awakening. Three separate phases could be identified based upon the diameter of the pupil. An initial dilation gave way to a constriction, and when the patient showed signs of awakening, the pupil dilated again to the preinduction diameter (fig. 1A). Of the 15 patients studied in Group I, 14 of them showed an initial dilation. Only one patient was atypical in that no initial dilation was seen, with the pupil entering the phase of constriction immediately following the injection. The Group I pupillary measurements were averaged at each time interval, and the aggregated response can be seen as one of the curves in figure 2.

The typical response of Group II patients was similar to that of Group I patients. Again, 14 of the 15 patients showed an initial dilation. The average response is shown in figure 2 and can be compared

to the average Group I response. The per cent increase at 30 s was significantly greater than the Group I patients. The difference between the two groups at 3 min suggests that the initial dilation phase is of longer duration.

Four of the unpremedicated patients (Groups I and II) showed signs of awakening following the initial dilation just as the pupil was returning to the preinduction diameter. This pattern was atypical in that no constriction phase preceded the signs of awakening (fig. 1C). All other unpremedicated patients who developed signs of awakening did so only after a phase of constriction.

Three of the unpremedicated patients (Groups I and II) were given additional bolus injections of thiopental when the first signs of awakening appeared. These patients had all shown dilation of the pupil to the first injection, but it was noted that this second injection produced only constriction of the pupil. Two such pupillograms are shown in figure 1B and figure 1C. To observe this absence of dilation following a second injection, it was necessary to adhere strictly to the protocol because it was noted on other patients that unwanted sensory stimulation dilated the pupil following this second injection.

Premedication decreased the preinduction diameter (table 1) and altered the pupillary response to thiopental significantly. Of the 15 patients in Group III, only 4 showed an initial dilation; the remaining 11 patients were all similar in showing a gradual constriction which then returned to the preinduction diameter as the signs of awakening appeared. The

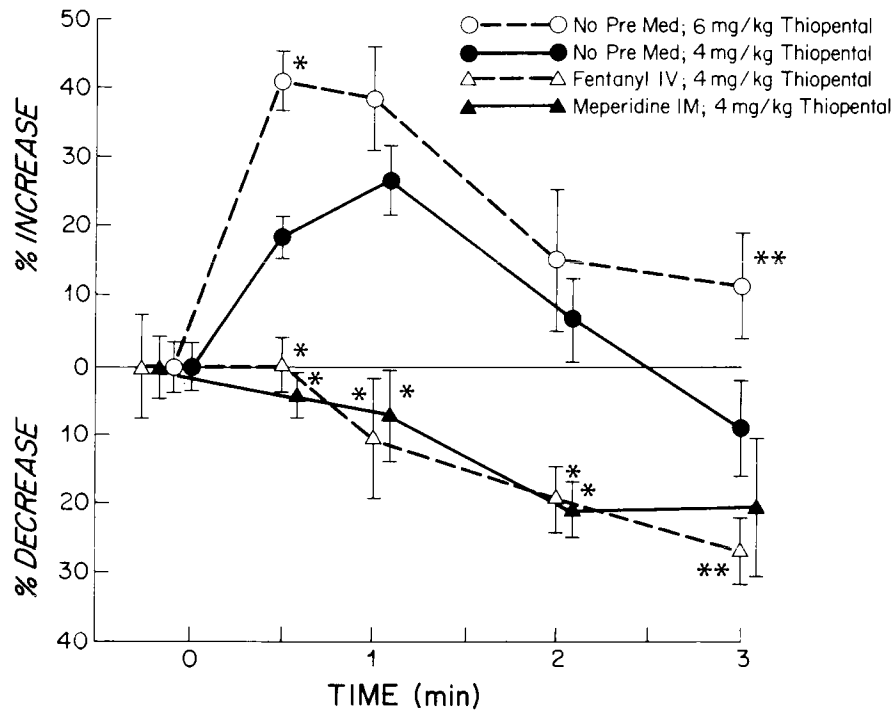


FIG. 2. Per cent change in pupillary diameter following thiopental. Mean \pm standard error of the mean. * $P < .01$ and ** $P < .05$ compared with corresponding times of Group I (● — ●).

author did not attempt to correlate the preinduction state of awareness with the presence or absence of dilation in these Group III patients. A pupillogram from a premedicated patient is shown in figure 1D. A second 4 mg/kg dose of thiopental was given to this patient when she began to resist retraction of the eyelid. This additional thiopental reversed the trend of this pupil to return toward the preinduction diameter and replaced it with a more pronounced phase of constriction.

Of the ten patients given iv fentanyl (Group IV), only one showed an initial dilation. The data from Group IV were definite in showing that narcotics block the initial dilation of the pupil following bolus injections of thiopental. The complete data comparing the four groups is contained in figure 2.

DISCUSSION

These results show that thiopental produces an initial dilation of the pupil in 93 per cent of ASA I

TABLE 1. Age and Pupil Diameters of Each Group. Mean \pm Standard Error of the Mean*

Group	Number of Patients	Age (years)	Pre-induction Pupil Diameter (mm)
I	15	34.3 \pm 2.4	3.4 \pm 0.1
II	15	34.1 \pm 2.8	3.4 \pm 0.1
III	15	35.3 \pm 3.2	2.9 \pm 0.1*
IV	10	32.8 \pm 5.7	2.7 \pm 0.1*

* $P < .01$ as compared to unpremedicated (Groups I and II) patients.

patients. This response is not solely dependent upon the thiopental concentration in the brain since it is blocked by narcotics and is not seen following second injections. The data do not allow one to define the exact mechanisms involved in the pupillary changes. It is possible that dilation of the pupil occurs either through sympathetic activation or by inhibition of the pupilloconstrictor neurons in the midbrain. Both mechanisms may be operative. Their relative contributions will be precisely delineated only by animal experimentation.

In cats, the dilation following thiopental is not affected by transection of the sympathetic nerves innervating the iris.² This suggests that inhibition of the pupilloconstrictor center within the midbrain might be involved. Barbiturates increase inhibitory influences at this site.⁵

Narcotics are commonly used as premedication, and the fact that these agents block the pupillary dilation brought about by thiopental may explain why this dilation has not been reported previously. Narcotics are thought to affect the pupil by an action directly on the pupilloconstrictor nucleus.⁶ This suggests, but does not prove, that the observed pupillary changes reflect drug interactions within the midbrain.

This phenomenon of pupillary dilation during induction of anesthesia may not be unique to thiopental. Guedel described an early reflex dilation of the pupil during ether induction that was blocked by morphine premedication. He further stated that reflex dilation during the first stage of anesthesia occurred also with chloroform, ethyl chloride, ethylene, and nitrous

oxide.⁷ The author does not know of any studies with inhalation agents currently in use.

In summary, thiopental dilates the pupils of most subjects but how the dilation occurs or why it is blocked by narcotics cannot be answered by this study.

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Arterial Pressure Manipulation Alters Spinal Cord Function during Correction of Scoliosis

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Induced hypotension has been employed as a means of improving operating conditions and reducing blood loss during surgery for scoliosis.^{1,2} However, damage to the spinal cord,³ presumably secondary to ischemia, occurs.^{4,5} Effects of hypotension and direct pressure on the cord are additive in producing impairment of spinal cord function^{6,7} and restoration of function with correction of hypotension has been reported.⁸ The purported benefits of deliberate hypotension during operative treatment of scoliosis must be weighed against the possibility that hypotension might increase the risk of acute neurologic complications.

When patients awaken paraplegic after surgery for scoliosis, recovery of neurologic function is unlikely; but immediate removal of Harrington rod instrumentation improves prognosis.³ Assessment of spinal cord

function intraoperatively may therefore be helpful. This can be accomplished using either the "wake up test"^{9,10} or somatosensory cortical evoked potential (SCEP) monitoring.^{11,12} Scalp recorded cortical potentials evoked by stimulation of somatosensory nerves reflect impulse transmission in the dorsal columns of the spinal cord.¹³ Clinically, alterations of these potentials are sensitive indicators of damage to the cord.^{14,15} Studies of cord injury in animals have shown that SCEP changes correlate well with pathologic changes¹⁶ and neurologic outcomes.¹⁷ Though dorsal column transmission and SCEPs may be preserved in the presence of isolated ventral column lesions,¹⁸ traumatic myelopathy usually affects multiple tracts. Transmission of impulses by the dorsal columns often reflects the degree of spinal cord injury.^{15,16,19} Monitoring of evoked potentials has certain advantages over the wake up test. It can be performed continually, while the wake up test can be done only at intervals. SCEP monitoring avoids risks introduced by awakening the patient intraoperatively to check voluntary motor function (risks such as dislodgment of life support and monitoring devices, dislocation of orthopedic instrumentation and air embolism with deep inspiration).

One of our patients demonstrated SCEP changes reproducibly related to arterial pressure during Harrington rod instrumentation for uncomplicated idiopathic scoliosis. Because SCEP monitoring during anesthesia is relatively new and because a number of factors under the control of the anesthesiologist alter SCEPs, we include with this case report a descrip-

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