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Acute Tolerance to High-Dose Barbiturate Treatment in Patients with Severe Head Injuries

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Barbiturate therapy for severe acute cerebral ischemia has been guided by monitoring intracranial pressure (ICP), electroencephalography (EEG), and blood levels of barbiturate. In barbiturate intoxication, a burst-suppression pattern on the EEG occurs when the duration of the isoelectric periods is within 10 s which is considered to be a good prognostic sign. We have used the barbiturate thiamylal for patients with severe head injuries to decrease ICP and to protect cerebral function by monitoring a burst-suppression pattern with isoelectric periods up to 10 s for 72 h post-trauma. We found acute tolerance to thiamylal a phenomenon that appears to be associated with continuous administration and propose that using a burst-suppression pattern as an exclusive index to determine the effective dose may be risky.

MATERIALS AND METHODS

Five patients with severe head injuries were given thiamylal for 72 h. Coma scores on admission as defined by Glasgow Coma Scale were all below seven points. Tracheas were intubated with nasotracheal tubes and ventilation was controlled to keep Pa_{O_2} between 150 and 200 mmHg, and Pa_{CO_2} between 20 and 30 mmHg. Systolic blood pressure was maintained to at least 100 mmHg with infusions of catecholamines; ICP and EEG were measured continuously and total plasma thiamylal levels were assayed by gas chromatography every 24 h. The dose of thiamylal was regulated to maintain a burst-suppression pattern keeping isoelectric periods up to ten seconds. Statistical analysis was performed utilizing the t test to compare thiamylal concentrations at each period.

RESULTS

A burst-suppression pattern appeared between 12 and 16 minutes after initial injection of thiamylal 15 mg/kg (mean: 15 minutes). At 15 minutes after injection, thiamylal concentrations in plasma were 15.2 to 29.8 μg/ml (20.5 ± 5.8 μg/ml: mean ± SE). However, for the burst-suppression pattern to be maintained required plasma thiamylal concentrations had to be increased for the next 72 h (table 1). On the other hand, the total required dose of thiamylal per 24 h was not significantly decreased (table 2). Four patients have made a good recovery and one is moderately disabled, as defined by the Glasgow Outcome Scale.

DISCUSSION

ICP[1] and EEG monitoring[2] are regarded as convenient and available methods to guide the dosing of barbiturates. Michenfelder and Milde conclude that a barbiturate dose should be tailored to a patient's EEG pattern, such as burst-suppression, which is an indication of relatively deep anesthesia, yet still compatible with adequate hemodynamics.[3] Bruce *et al.*[4] prefer to titrate the dose of barbiturate until a burst-suppression pattern is present on EEG and then keep the burst and suppressions of equal length. They formulated that at this end point, the serum pentobarbital level might vary from 2.5 to 5.0 mg/dl.

We have used high-dose thiamylal treatment using the EEG in patients with severe head injuries since December 1979. We found that the appearance of a burst-suppression pattern implied good prognosis and was associated with low ICP. Increasing doses of thiamylal did not further reduce ICP and only prolonged the silent periods or isoelectric pattern.[5] We now titrate thiamylal with a burst-suppression pattern as a guide for determining the appropriate dose.

TABLE 1. Total Plasma Thiamylal Concentrations (μg/ml) Required to Maintain a Burst-Suppression Pattern in the EEG up to 10 s

	15 min	25 h	48 h	72 h
Maximum	29.8	40.8	48.0	54.8
	22.2	37.6	47.6	54.0
	18.9	28.9	40.2	47.3
	16.4	22.1	37.5	45.2
Minimum	15.2	19.8	30.1	39.7
MEAN ± SD	20.5 ± 5.8	29.8 ± 9.2	40.7 ± 7.5	48.2 ± 6.3

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TABLE 2. Cumulative Doses of Thiamylal during 72-h Period

	Birth Weight (kg)	24 h	48 h	72 h	Total Dose (g)
Patient 1	60	124 mg/kg	220 mg/kg	326 mg/kg	19.56
Patient 2	30	135	267	358	10.68
Patient 3	65	110	208	304	19.76
Patient 4	40	140	232	341	13.64
Patient 5	45	118	190	282	13.19
MEAN ± SD		125.4 ± 12.24	223.4 ± 12.92	322.2 ± 13.41	

In a clinical report of barbiturate intoxication, Brazier found that the duration of isoelectric periods is usually up to 10 s and these episodes are known to occur in cases of acute barbiturate coma with complete recovery.[6] We regulated the doses of thiamylal to keep isoelectric periods in a burst-suppression pattern up to 10 s for 72 h while measuring total plasma thiamylal concentrations. With this EEG end point, the thiamylal concentrations gradually increased reaching two to four times their initial levels. We regard this phenomenon as "acute tolerance." However, tolerance to the hypnotic effects of barbiturates evidently does not significantly increase the lethal dose.[7] Thus, there may be some risk to using a burst-suppression pattern as the sole guide in determining the barbiturate dose and perhaps there is a limitation to the duration of high-dose barbiturate therapy.

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A New Improved Double-Lumen Tube Adaptor

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Previous designs of double-lumen tube adaptors have permitted, with varying degrees of success and ease of use, the application of three major one-lung ventilation/anesthesia management functions/options (without the need for airway disconnection and/or external clamping maneuvers); one-lung ventilation, exposure of one lung to atmospheric pressure and suctioning of one lung at a time.[1-5] None of these double-lumen tube adaptors has the capability of providing the application of three recent major advances in the management of one-lung ventilation/anesthesia; one-lung positive end-expiratory pressure (PEEP) with or without tidal ventilation,[6-8] differential PEEP to both lungs,[8] and one-lung fiberoptic bronchoscopy. This report describes a new, single unit, double-lumen tube adaptor which allows the easy application (no airway disconnection or clamping) of all six of the above one-lung ventilation/anesthesia characteristics by simply turning a dial to the desired setting.

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Key words: Equipment: double-lumen tube adaptor; tubes, endobronchial.

DESCRIPTION

The double-lumen tube adaptor has two round three-way stopcocks placed in parallel inside a plastic-like block [(Delrin,® a heat and solvent resistant synthetic) (fig. 1)]. Each stopcock is fitted with an easily accessible handle. The three passage channels of each stopcock are located at 90° from each other. The anesthesia machine side of the adaptor has three entry ports which allow