Child's Nerv Syst (1993) 9:220–223

Child's Nervous System CNS

Effects of thiopental on middle cerebral artery blood velocities: a transcranial Doppler study in children

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Received: 20 January 1993

Abstract. The effect of an intravenous injection of thiopental on middle cerebral artery blood velocities was assessed by transcranial pulsed Doppler monitoring in 20 children: ten head-injured patients and ten control subjects. Thiopental induced a moderate but immediate decrease of middle cerebral artery blood velocities in both groups; this variation was significant ($P < 0.01$) and more prolonged in the head-injured than in control patients. Transcranial Doppler ultrasonography thus appears to be suitable for monitoring children in intensive care units and could help to avoid the use of thiopental in patients with low cerebral artery blood flow velocity.

Key words: Intracranial pressure – Middle cerebral artery – Blood flow velocity – Thiopental – Transcranial pulsed Doppler – Head injury

Introduction

Intravenous barbiturate therapy is currently prescribed for the treatment of severe traumatic brain edema [13, 17]. At anesthetic concentration, barbiturates reduce intracranial pressure, cerebral blood flow, and cerebral metabolic rate of oxygen by 50% [8, 12, 13]. Barbiturate action is not exactly understood and its benefits in head-injured patients are disputed [17, 18]. The cerebrovascular effects of barbiturate administration in patients have been studied with the xenon 133 method [12]. However, this technique is not suitable for continuous monitoring, and offers a poor time resolution. By contrast transcranial Doppler ultrasonography fills both these requirements and can reach the proximal part of the intracranial vessels [1].

The purpose of this study, therefore, was to use transcranial pulsed Doppler ultrasonography to monitor the effects of an intravenous injection of thiopental on middle cerebral artery blood velocities in children.

This study was approved by our ethical committee.

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Patients and methods

Twenty children (15 boys and 5 girls, with ages ranging from 4.5 to 14 years, mean 9 years), in two groups, were studied by transcranial Doppler ultrasonography in a pediatric anesthesiology department.

Ten head-injured children (8 boys and 2 girls, ages ranging from 4 to 14 years, mean 9 years) were included in the first group. These children had severe brain injuries and were under artificial ventilation. Initial Glasgow coma scale score was less than 8, and arterial CO_2 pressure ($PaCO_2$) was maintained at 4.6 kPa (SD 0.5) after nasotracheal intubation (SV 900 C Siemens ventilator). Six of these ten children had unilateral brain swelling as indicated by cerebral computed tomographic (CT) scanning: their intracranial pressure was measured with an epidural pressure sensor (Plastimed®). The study was performed during the 1st or 2nd day after the children were admitted into the hospital.

The control group was made up of 7 boys and 3 girls (ages ranging from 4 to 14 years, mean 8 years) with limb fractures, with no brain lesions, who had to be subjected to general anesthesia for surgery. Half an hour before the transcranial Doppler study, the children received atropine (0.01 mg/kg subcutaneously), and/or diazepam (0.5 mg/kg i.m.).

The middle cerebral artery blood flow velocities were measured in all children in the supine position using transcranial pulsed Doppler equipment with a 2 MHz probe (TC2-64, EME Society Überlingen). The middle cerebral artery blood velocities were detected and measured according the previously described method [18]. Briefly, proximal middle cerebral artery blood flow velocities were recorded with a surface probe through a transtemporal window at the opposite side to the main cerebral lesions. The pulsed Doppler sample volume was set at a depth of 40–50 mm. The middle cerebral artery Doppler signal was recognized on its positive sign (indicating blood flow directed towards the probe) and its reduction by a short common carotid compression during one or two systoles [18]. The probe was attached to the skull with a head band (EME Society).

After 10 min middle cerebral artery recording in basal conditions, and if the subjects were quiet, intravenous injection of thiopental (5 mg/kg) was performed. In the first group, the $PaCO_2$ was maintained at 4.6 kPa (SD 0.3) during the test. The following parameters were measured each minute for 5 min: peak systolic velocity (SV), end-diastolic maximum velocity (DV) and time-averaged maximum velocity (TAM), Pourcelot resistance index (RI = SV-DV/SV), Gosling pulsatility index (PI = peak-to-peak maximum amplitude divided by TAM), heart rate, and systemic mean arterial pressure (Dynamap®, Critikon). The intracranial pressure was recorded continuously in six head-injured patients, and the

Table 1. Mean baseline measurement values in both groups (mean ± 1 SEM)

	Head-injured patients	Control group
Peak systolic velocity (cm/s)	130±11	110±11
End-diastolic maximum velocity (cm/s)	66.5±6	48±4
Time-averaged maximum velocity (cm/s)	85±8	64+6
Resistance index (RI)	0.49±0.02	0.56±0.03
Pulsatility index (PI)	0.75±0.03	0.97±0.08
Mean arterial pressure (mmHg)	95±4.6	82±2.5
Heart rate (pulse/min)	122±6	119±6
Intracranial pressure (kPa)	2.2±0.2	–

cerebral perfusion pressure (mean arterial pressure minus mean intracranial pressure) was calculated.

Statistical comparison between baseline values and values obtained after intravenous injection of thiopental was performed with Wilcoxon's test for paired data. The middle cerebral artery blood flow velocities at the time of the greatest decrease of mean arterial pressure after thiopental administration were compared to the baseline middle cerebral artery blood flow velocities. We choose the mean arterial pressure as a reference parameter because a significant effect of thiopental on mean arterial pressure has been previously reported [6, 8, 12]. Data were expressed as mean ± 1 standard error of the mean and correlations were considered statistically significant if $P<0.05$.

Results

Mean baseline values are presented in Table 1.

After thiopental injection, there was a significant ($P<0.01$) decrease in mean arterial pressure in both the head-injured group (−14±1.4%) and the control group (−17±1.4%). Heart rate was significantly ($P<0.01$) increased in the head-injured group (+ 6 ±6.5%) but not in the control group. The baseline middle cerebral artery velocities before the pharmacological test were higher in the head-injured group (SV = 130±11 cm/s; DV = 66±6 cm/s; TAM = 85±8 cm/s) than in the control group (SV = 110±11 cm/s; DV = 48±4 cm/s; TAM = 64±6 cm/s). These middle cerebral artery velocities were in agreement with the data in the literature [1] and decreased in both groups after thiopental injection (Fig. 1). These changes were significant in the head-injured group (SV = −15±6.9%, $P<0.01$; DV = −21±6.5%, $P<0.01$; TAM = −20±7.4%, $P<0.01$), but not in the control group (SV = −8±10%; DV = +2±3%; TAM = +1±2%). Reduced middle cerebral artery velocities occurred in 90% of the children 1 min after thiopental was administered. The drop in diastolic velocities lasted 5 min or more in 70% of the head-injured patients, and in only 10% of the control group (Fig. 2). The resistance and pulsatility indices were lower in the head-injured group than in the control group, and were not significantly changed after thiopental injection in either group.

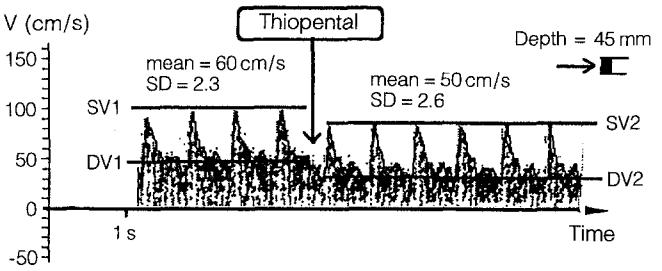

Fig. 1. Middle cerebral artery flow velocity recording after intravenous injection of thiopental in a normal child, showing a drop in systolic and diastolic velocities

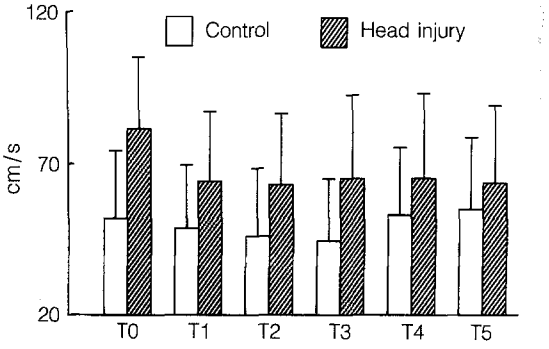

Fig. 2. Effect of thiopental on middle cerebral artery velocities (mean ± SD) in the group of head-injured children and in the control group: immediate reduction of blood flow velocities

The mean intracranial pressure was significantly reduced ($P<0.01$) by 48±16.6%, without significant correlation with middle cerebral artery velocities. The cerebral perfusion pressure was not significantly changed in the six patients with intracranial pressure measurements.

Discussion

Measurement of middle cerebral artery velocities by transcranial pulsed Doppler ultrasonography appears a convenient method of demonstrating changes in cerebral blood flow [9]. From monitoring data during carotid endarterectomy, Lindegaard et al. [10] have shown that the blood flow velocities in the mean cerebral artery remained proportional to those in the internal carotid artery. The acoustic window available to reach the middle cerebral artery through the temporal bone is rather narrow, thus restricting the possible angles of approach. Anatomical considerations suggest that this angle is less than 30°. Therefore, its cosine will be near 1 and thus negligible for the Doppler frequency / flow velocity translation. Moreover, this angle was maintained unchanged during the whole procedure. Xenon 133 studies have demonstrated that CO_2 responses of intracranial artery blood velocities correlate reliably with changes in cerebral blood flow [3, 14, 15], although there is no significant correlation of these blood velocities with CO_2 level, probably due to the wide variability between patients [3, 15]. Consequently, transcranial Doppler ultrasonography of the cerebral artery has been used to study drug hemodynamic effects in well-defined conditions [5, 7]. Thiopental

administration has a moderate but significant effect on arterial pressure [12, 16], and significantly reduces intracranial pressure [12, 13]. Our results confirm these data. The moderate variations of arterial pressure could explain why heart rate did not significantly increase in our two groups.

Thiopental at an anesthetic dosage induces an immediate and slight reduction of middle cerebral artery blood flow [12]. We observed this reduction in both groups in our present study. The effect was more prolonged in the head-injured group than in the control group. The change was significant in the head-injured group, but not in the control group, where the arterial $PaCO_2$ could not be maintained constant. Nordstrom et al. [12], performing Xenon 133 measurement of blood flow in 19 severely injured patients, also observed that cerebral blood flow and intracranial pressure decreased in patients whose cerebral vasoreactivity was preserved. These results are difficult to compare with ours because transcranial Doppler ultrasonography does not scan the same vascular areas, and because we could not study cerebral vasoreactivity in our patients, for practical and ethical reasons.

We found small and nonsignificant changes in resistance index and pulsatility index values after thiopental injection. These results disagree with those of Piatt and Schiff [13]. Basically, our results suggest that there was a decrease in cerebral artery blood flow velocities without significant change in downstream impedance, probably in proportion to the decrease in arterial pressure decrease, before autoregulation processes took place (or without autoregulation adjustment, in this relatively small range). Nevertheless, there was only a moderate decrease in middle cerebral artery blood velocities, while there were large individual differences between patients as regards base values and heart rate.

The higher blood flow velocities that we observed in the head-injured group could be due to hyperemia and/or vasodilation. Under thiopental at anesthetic concentrations the reduction of blood flow velocities and intracranial pressure was immediate and occurred when electroencephalographic recording reached the level of "burst suppression". The decreases in middle cerebral artery blood flow velocities and intracranial pressure may possibly have been linked, but we did not demonstrate this link in our six patients who did not have very high intracranial pressure. A direct vasodilation effect of thiopental on pial arteries was noticed in cats [2], but these arteries may not be the main site of the vascular resistance which governs the brain circulation. Moreover, vasodilation of the distal cerebral arteries induces an increase in middle cerebral artery flow as recorded by transcranial Doppler, as is well documented by CO_2 testing [3, 14]. Consequently, our data could be consistent with the supposition of a vasoconstriction of the distal cerebral arteries (with a slight increase in resistance index), as were the results of Hatano et al. [7], if not completely explained by the drop in arterial pressure. On the other hand, the drop in arterial pressure seems too small to induce barostatic responses in middle cerebral artery blood velocities, as was demonstrated in the control group.

In the present study, thiopental injection was followed by more marked changes in diastolic than in systolic blood flow velocities. Systolic blood flow velocity is more dependent on cardiac ejection; therefore, an important effect of thiopental on the myocardium is unlikely. Besides, only prolonged treatment at high dosages of barbiturates reduces ventricular filling and impairs barostatic reflexes [13, 16].

Finally, as the main hemodynamic parameters are blood flow, blood pressure, and vascular impedance, isotopic blood flow measurements or Doppler blood velocity measurement, when used separately, are unable to offer a complete understanding of the mechanisms involved in drug effects. However, when compared, their respective data can be complementary.

Conclusion

Our results indicate that the transcranial Doppler technique is suitable for use in anesthesiology and in intensive care for the monitoring of brain-injured patients. We observed a significant although moderate decrease in middle cerebral artery blood velocities after intravenous injection of thiopental, probably as a result of the drop in arterial pressure and/or distal vasoconstriction. Therefore, transcranial pulsed Doppler examination could contribute to better selection of head-injured patients who might benefit from barbiturate therapy, by excluding patients with low blood flow velocities in their cerebral arteries. Although blood flow velocities usually change in the same direction (and even in the same proportions) as volume blood flow, these data are intrinsically different and complementary. Since transcranial Doppler ultrasonography can (via resistance and pulsatility index) demonstrate changes in downstream vascular impedance, isotopic and ultrasonographic methods can be used concurrently for evaluation and monitoring of drug effects on the hemodynamics of cerebral vessels.

Acknowledgements. We gratefully thank K. F. Lindegaard and J. E. Greenleaf for their valuable advice.

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