Effect of diclofenac on cerebral blood flow velocity in patients with supratentorial tumours

S. J. Jones and J. Dinsmore*

Department of Anaesthesia, St George’s Hospital, Blackshaw Road, London SW17 0NE, UK

*Corresponding author

Background. The aim of this investigation was to determine the effects of diclofenac on cerebral blood flow. Middle cerebral artery blood flow velocity was measured in nine patients with supratentorial tumours.

Methods. Using a transcranial Doppler ultrasound, we measured the baseline mean and systolic cerebral blood flow velocity. Measurements were repeated following administration of diclofenac 75 mg i.v.

Results. There was no significant change in cerebral blood flow velocity. All other physiological variables remained constant.

Conclusion. Diclofenac does not cause a significant change in cerebral blood flow velocity in patients with supratentorial tumours.

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The non-steroidal anti-inflammatory drug (NSAID) diclofenac is used as a perioperative analgesic in our neurosurgical unit for awake craniotomy and supratentorial tumour resections. Indomethacin, another NSAID, is known to significantly decrease cerebral blood flow (CBF) and intracranial pressure without changing cerebral metabolic rate.1 Animal studies using diclofenac show no change in CBF but this has not been studied in man.2 Major changes in cerebral physiology with drugs such as indomethacin have significant clinical implications in neuroanaesthesia and it is important that the cerebral effects of all pharmacological agents are known. The aim of our investigation was to determine the effect of diclofenac on CBF velocity (CBFV) in patients with supratentorial pathology.

Methods and results

After obtaining approval from the Hospital Ethics Committee and written, informed consent, nine patients undergoing elective supratentorial neurosurgery were recruited. Patients were excluded if they had asthma, renal impairment, peptic ulcer disease, bleeding diathesis or had ingested NSAIDs within 24 h. No patient had signs of raised intracranial pressure.

The study was performed in the anaesthetic room before induction of anaesthesia. Patients were not premedicated and were kept in the supine position throughout the study period, with the head resting on a pillow. I.V. and arterial cannulae were inserted under local anaesthesia. Monitors included ECG, continuous arterial pressure, arterial blood gas sampling and axillary temperature.

CBFV was monitored continuously on the ipsilateral side of the intracerebral pathology. The M1 segment of the middle cerebral artery was insonated through the temporal window using a 2 MHz transcranial Doppler (TCD) ultrasound probe (Pioneer EME TCD VER 2.10, Eden Medical Electronics, Überlingen, Germany). The TCD probe was fixed in position to maintain a constant angle of insonation throughout the study. Confirmation of the middle cerebral artery was achieved by increasing sonation depth to visualization of the bidirectional flow pattern typical of the bifurcation of the internal carotid artery to the middle cerebral and anterior cerebral arteries. Insonation depth was then decreased to the point of maximum signal intensity (45–55 mm depth). The TCD frequency spectra, converted into flow velocity (cm s⁻¹), were calculated automatically by the TCD over 4–5 consecutive cardiac cycles.

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Measurements of baseline mean and systolic CBFV were recorded, along with mean arterial pressure, heart rate, temperature, and arterial oxygen and carbon dioxide pressures. Diclofenac, 75 mg in 50 ml normal saline, was then infused over 15 min. The i.v. route was chosen to avoid first-pass metabolism and provide a reliable peak plasma concentration. All measurements were repeated at the end of the infusion (time 15 min) and after a further 25 min (time 40 min), to coincide with the time of peak plasma concentrations.

Anaesthesia was then commenced and surgery continued as normal.

Data are expressed as mean (SD). Data from previous studies indicate that the mean value for CBFV is 65.55 (4.2) cm s \(^{-1}\) under normal physiological conditions. A change of \(>2\) SD was considered significant and with a power of 0.8, \(\alpha=0.05\) and \(\beta=0.2\), we calculated that eight subjects would be required.

Analysis of variance (ANOVA) for repeated measurements was used to compare the values. The changes from baseline to time 15 min and baseline to time 40 min following diclofenac administration were estimated separately. A value of \(P<0.05\) was considered statistically significant.

Nine patients were recruited. The mean age was 49.6 (range 25–72) and the mean weight was 73.2 (13.8) kg. The effects of diclofenac on physiological variables are shown in Table 1. There was no statistical difference between measurements of CBFV at 15 and 40 min compared with baseline. No statistical differences were found between the physiological variables of mean arterial pressure, heart rate, temperature, and arterial oxygen and carbon dioxide pressures. Results of the tissue analysis in the nine volunteers revealed five gliomas, two astrocytomas, one lymphoma and one inflammatory tissue.

Comments

We find that diclofenac provides useful perioperative analgesia in a select group of neurosurgical patients but we were unsure of its effects on cerebral physiology. Animal studies have shown that diclofenac has no effect on cerebral haemodynamics but this had not been confirmed in humans, or in this patient population. The results of this study demonstrate that diclofenac does not cause significant changes in CBFV. We compared mean and systolic CBFV before and after the administration of diclofenac in patients with supratentorial pathology. Other physiological parameters that might have affected CBF remained constant. The patients were awake during the experiment and received no pharmacological agents other than diclofenac in normal saline 50 ml, thus avoiding potential alterations of CBF or intracerebral vessel diameter.

Indomethacin, another NSAID, is a potent cerebral vasoconstricter. It decreases CBF by up to 40% without a change in cerebral metabolic rate, similar to the effects of hypocapnia. However, this effect appears to be unique among the NSAIDs. Its mechanism of cerebral vasoconstriction is still uncertain, but seems to result from mechanisms other than prostaglandin inhibition. The role of NSAIDs in the management of cerebral injury has also been investigated. NSAIDs may improve collateral circulation in ischaemic brain and prevent cerebral vasospasm following subarachnoid haemorrhage. Indomethacin has been used to control intracranial pressure and improve operating conditions in patients with cerebral tumours.

We chose to study patients with intracerebral pathology as this may alter CBF and its regulation, and for the practical reason that this reflects our clinical patient population likely to receive diclofenac. As our numbers are small, we may have overlooked a significant response to diclofenac with a given tumour type, although no trend was seen.

Absolute CBF cannot be inferred from measurements of CBFV because the diameter of the insonated vessel segment is unknown. Despite this, the use of the TCD to measure CBFV has been shown to provide a good correlation between changes in flow velocity and cerebral blood flow as long as measurement conditions such as insonation angle and depth remain constant.

In conclusion, we have shown that there is no significant change in CBFV after the administration of diclofenac in a small group of patients with supratentorial tumours.

References


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Table 1 The effect of diclofenac on physiological variables. Data are mean (SD). CBFV=cerebral blood flow velocity

<table>
<thead>
<tr>
<th></th>
<th>0 min (baseline)</th>
<th>15 min after diclofenac</th>
<th>40 min after diclofenac</th>
<th>P-value (40 min vs baseline)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean arterial pressure (mm Hg)</td>
<td>100 (11)</td>
<td>103 (10)</td>
<td>104 (8)</td>
<td>0.48</td>
</tr>
<tr>
<td>Heart rate (beats min(^{-1}))</td>
<td>62 (14)</td>
<td>61 (12)</td>
<td>61 (13)</td>
<td>0.94</td>
</tr>
<tr>
<td>Arterial oxygen pressure (mm Hg)</td>
<td>10.9 (1.2)</td>
<td>11.5 (1)</td>
<td>11.4 (0.8)</td>
<td>0.31</td>
</tr>
<tr>
<td>Arterial carbon dioxide pressure (mm Hg)</td>
<td>4.8 (0.2)</td>
<td>4.7 (0.3)</td>
<td>4.7 (0.4)</td>
<td>0.99</td>
</tr>
<tr>
<td>Temperature (°C)</td>
<td>36.3 (0.4)</td>
<td>not measured</td>
<td>36.2 (0.5)</td>
<td>0.78</td>
</tr>
<tr>
<td>Mean CBFV (cm s(^{-1}))</td>
<td>51.6 (11.7)</td>
<td>53.2 (12.6)</td>
<td>52.6 (11.7)</td>
<td>0.85</td>
</tr>
<tr>
<td>Systolic CBFV (cm s(^{-1}))</td>
<td>83.4 (14.7)</td>
<td>85.2 (16.6)</td>
<td>83.2 (15.8)</td>
<td>0.81</td>
</tr>
</tbody>
</table>
Sator-Katzenschlager et al

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