Physiological Advantages of Cerebral Blood Flow During Carotid Endarterectomy Under Local Anaesthesia. A Randomised Clinical Trial

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Objective: to examine the effects of type of anaesthesia on cerebral blood flow during carotid endarterectomy (CEA).

Design: prospective randomised study.

Methods: thirty-four CEA procedures under local anaesthesia (LA) are compared to 33 procedures under general anaesthesia (GA). Mean middle cerebral artery velocity (MCAVmean) was monitored using Transcranial Doppler (TCD) and mean arterial pressure (MAP) assessed by continuous intra-arterial blood pressure transducer.

Results: pre-op MCAVmean and MAP were similar in both groups. Pre-clamp MCAVmean was similar in both groups and did not differ from pre-op values. With carotid clamping the MCAVmean significantly dropped in both groups. The post-clamp MCAVmean was significantly less in the GA group (p < 0.05), and the percentage reduction in MCAVmean significantly more for GA procedures (p < 0.05). Pre-clamp MAP was significantly elevated in LA procedures and significantly lowered in GA procedures. Pre-clamp MAP was significant less for GA procedures (p < 0.001). Post clamp MAP did not differ from pre-clamp levels in either group. There was no correlation between MCAVmean and MAP. Complication rate, combined death/stroke rates were similar in each group.

Conclusion: LA CEA is associated with better preservation of the ipsilateral cerebral circulation and increased tolerance of the effects of carotid clamping. Changes in MCAVmean cannot be explained by variations in blood pressure between the two techniques.

Key Words: Cerebral blood flow; Carotid endarterectomy.

Introduction

The number of carotid endarterectomy procedures (CEA) performed under local anaesthesia (LA) is increasing. The principle advantage of LA CEA is the ability to accurately monitor patients and to selectively shunt if neurological signs develop during carotid cross clamping. This is reflected in significantly lower shunt rates for LA CEA procedures compared to CEA under general anaesthesia (GA).

Further data suggests that LA may be associated with greater intraoperative cardiovascular stability. LA CEA is associated with less hypotensive episodes, and a higher mean arterial pressure (MAP) at carotid clamping. In addition, one non-randomised study using Near-infrared spectroscopy and jugular venous oximetry demonstrated preservation of cerebral autoregulation associated with a significant rise in MAP at carotid clamping, if the procedure was performed under LA.

Conclusions as to the differing physiological responses of the cerebral circulation to carotid clamping, based on absolute shunt rates, are invalid as the monitoring technique and subsequent selection criteria for shunting differs between the two anaesthetic techniques. Transcranial Doppler (TCD) assessment of the mean middle cerebral artery velocity (MCAVmean) can be used as valid measure of cerebral blood and provide continuous data on cerebral perfusion, particularly during carotid clamping.

The aims of this study were:

(1) to determine if the physiological response to carotid clamping differs between LA and GA using TCD assessment of the MCAVmean, and

(2) to determine if any observed difference was secondary to variation in systemic blood.
Patients and Methods

Patients

Seventy-one patients were prospectively randomised to either LA or GA CEA over a 32 month period (08/98 and 03/01) at the Royal United Hospital, Bath U.K. One patient withdrew after randomisation to GA, and one patient died from a myocardial infarction prior to surgery (GA). One patient in each group was excluded as the internal carotid artery had occluded prior to surgery. One patient had a bilateral procedure, but as this was non concurrent, the analysis is based on the number of procedures performed. Thirty-four LA procedures in 33 patients are compared to 33 GA procedures in 33 patients. Patient demographics are shown in (Table 1). All patients had duplex proven severe (>70%) ipsilateral carotid artery stenosis. All procedures for asymptomatic disease were performed as part of the Asymptomatic Carotid Surgery Trial (ACST).

Anaesthesia

General

Patients received 2–3 mg midazolam (IV) pre-induction and were induced with fentanyl or alfentanil and propofol. Patients were maintained on a mixture of air, oxygen (FiO₂ of 0.5) and an end-tidal isofluorane between 0.8–1.0% with a total gas flow at 11/min to maintain end-tidal pCO₂ between 34 and 38 mmHg.

Regional/local

Patients were premedicated with temazepam (20–30 mg) and promethazine (25 mg). The regional block consisted of local infiltration and a superficial cervical block using a combination of 0.5% bupivacaine and 1% lignocaine containing 1:200 000 adrenaline. No further sedation was given during the procedure, but some patients required additional local anaesthetic, usually because of discomfort during deep dissection (up to 10 ml 1% lignocaine).

Monitoring

An anaesthetist was present during all procedures and monitored the systemic blood pressure and heart rate from a radial cannula and electrocardiogram. Systemic blood pressure was manipulated pharmacologically to maintain the blood pressure within 30% of pre-op values. Hypertension was defined as MAP greater than 30% of pre-op value, and hypotension as a greater than 30% fall in MAP.

Mean blood flow velocity was measured in the ipsilateral middle cerebral artery using the Sci-Med PC-Dop 842 with a 2 MHz pulsed wave Doppler transducer (Sci-Med Ltd, U.K.) through a trans-temporal window. The probe was secured with an elastic headband.

In addition patients in the local anaesthesia group were monitored by direct neurological examination (awake patient monitoring). Patients were asked to squeeze a squeaky ball held in the contralateral hand, move the contralateral lower limb, perform simple mental arithmetic and to recite their name, age and address at regular intervals. This function was performed by a vascular technologist.

Surgery

A standard endarterectomy was performed. The carotid sinus was blocked with 1 ml of 1% lignocaine before full mobilisation of the carotid arteries. Intravenous heparin (50 IU/kg) was administered prior to cross clamping, which were applied in the following sequence; external, common and internal.

Clinical selective shunting

A policy of selective shunting was used during this study. Shunts were inserted in the GA group, if TCD monitoring was not possible, or there was a greater than 50% reduction in the velocity of the middle
cerebral artery with carotid clamping. Shunts were inserted in the LA group, if patients were unable to move a contralateral limb (Focal deficit) or who became unresponsive to questioning (Global deficit). Distal tacking sutures and Dacron patching were performed as necessary. Completion duplex examination was performed as a quality control measure.

**Data**

The mean middle cerebral artery mean velocity (MCAV\textsubscript{mean} (cm/s)) and mean systemic arterial pressure (MAP (mmHg)) were continuously monitored but for the purposes of data presentation and analysis the procedure was divided into three phases: preoperative (day prior to surgery), pre-clamp (immediately prior to clamping) and clamp (clamping of common and external carotid artery). Maximum and minimum intraoperative mean systemic arterial pressures were recorded.

**Sample size estimation**

Based on published data for MCAV\textsubscript{mean} for GA procedures and observational data from 105 non-randomised procedures in our institution, 26 patients in each group would have a 80% chance of detecting a difference with a 5% significance level (Table 2).7±10

**Statistics**

Discrete variables were analysed with the Pearson Chi-squared test and Fisher’s exact test where appropriate. Continuous variables are expressed as medians with interquartile ranges. Graphical data expressed in box and whisker diagrams shows median, interquartile ranges, minimum and maximum values. Continuous variables were analysed by the Mann–Whitney U-test for unpaired data (inter-group analysis) and the Wilcoxon signed rank test for paired data (intra-group analysis). Correlation was assessed using Spearman’s nonparametric analysis. Statistical significance was taken at the 5% level.

**Results**

**Mean middle cerebral artery velocity (MCAV\textsubscript{mean})**

Transcranial Doppler monitoring was possible in 23/33 (70%) GA procedures and 30/34 (88%) LA procedures, (p > 0.05). The MCAV\textsubscript{mean} data are summarised in Table 3 and Figure 1. Pre-op MCAV\textsubscript{mean} was similar in both groups, (40 cm/s GA, 45 cm/s LA, p > 0.05). Anaesthesia had no significant effect on MCAV\textsubscript{mean} in either group, (45 cm/s GA, 46 cm/s LA, p > 0.05). The MCAV\textsubscript{mean} significantly dropped in both groups with clamping of the carotid artery, however the percentage reduction was significantly more in the GA procedures (58% GA, 27% LA, p < 0.05), and post-clamp MCAV\textsubscript{mean} was significantly lower in the GA group (20 cm/s GA, 32 cm/s LA, p < 0.05).

**Mean systemic arterial pressure (MAP)**

The MAP data are summarised in Figure 1. Pre-op MAP was similar for the two groups, (104 mmHg GA, 108 mmHg LA, p > 0.05). With GA, the pre-clamp MAP significantly fell in spite of pharmacological intervention (104 mmHg GA pre-op, 93 mmHg GA pre-clamp, p < 0.05). In LA procedures the pre-clamp MAP was significantly elevated compared to pre-op MAP levels, (108 mmHg LA pre-op, 120 mmHg LA pre clamp, p < 0.05). Pre-clamp MAP were significantly lower in the GA group (93 mmHg GA, 120 mmHg LA, p < 0.001). Carotid cross clamping had no effect on MAP in either group.

**Correlation between MCAV\textsubscript{mean} and MAP**

The correlation data are summarised in Table 4. There was no statistical relationship between MAP and MCAV\textsubscript{mean} in either group, either before or after carotid clamping.

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Table 2. Data used in sample size estimation.

<table>
<thead>
<tr>
<th>Reference</th>
<th>MCAV\textsubscript{mean} (cm/s)</th>
<th>Standard deviation</th>
<th>Numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bass\textsuperscript{8}</td>
<td>24</td>
<td>13.0</td>
<td>49</td>
</tr>
<tr>
<td>Halsey\textsuperscript{7}</td>
<td>21</td>
<td>11.7</td>
<td>31</td>
</tr>
<tr>
<td>Schneider\textsuperscript{9}</td>
<td>22</td>
<td>14.8</td>
<td>23</td>
</tr>
<tr>
<td>Bath LA data\textsuperscript{10}</td>
<td>35</td>
<td>14.2</td>
<td>105</td>
</tr>
</tbody>
</table>

Table 3. MCAV\textsubscript{mean} (cm/s) for GA and LA procedures.

<table>
<thead>
<tr>
<th>MCAV\textsubscript{mean}</th>
<th>GA</th>
<th>LA</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-op</td>
<td>40 (38–55)</td>
<td>45 (39–55)</td>
<td>ns</td>
</tr>
<tr>
<td>Pre-clamp</td>
<td>45 (32–56)</td>
<td>46 (35–55)</td>
<td>ns</td>
</tr>
<tr>
<td>Post-clamp</td>
<td>20 (14–32)</td>
<td>32 (20–50)</td>
<td>p = 0.023</td>
</tr>
<tr>
<td>Percentage reduction</td>
<td>58 (18–69)</td>
<td>29 (4–44)</td>
<td>p = 0.043</td>
</tr>
</tbody>
</table>

Median (IQR). Mann–Whitney U-test. ns = non significant.
The highest recorded intra-operative systemic pressure was significantly higher in the LA group (107 (94–123) GA, 128 (113–142) LA, \(p < 0.01\)). The lowest recorded intraoperative MAP was lower in the GA group, (77 (68–91) GA, 97 (82–110) LA, \(p < 0.001\)). There was no difference in the highest or lowest recorded post-operative blood pressure between the two groups Table 5. The incidence of hypotension was significantly higher in the GA group. There was no difference in the incidence of hypertension.

### Shunt rates

The clinical shunt rate was 67% (22/33) in the GA group and 15% (5/34) in the LA group (\(p < 0.0001\)). Ten patients were shunted in the GA group because of an inadequate temporal window. If patients without temporal windows are excluded and the same theoretical TCD shunt criteria applied to both groups, the shunt rates would still be significantly different (GA 12/23 (52%), LA 6/30 (20%), \(p < 0.05\)).

### Clinical outcome

There was one death in each group. In the GA group a 72-year-old male with ischaemic heart disease had a myocardial infarction on day 5 post-op and died. In addition there was a further myocardial infarction in the GA group (male 70 with known ischaemic heart disease, recovered). In the LA group a 65-year-old male with ischaemic heart disease had a myocardial infarct on day 3 post-op and died. There were no strokes in this study population. The combined death/stroke rate for this study was 3% for each group.
Shunting during carotid endarterectomy remains controversial and while there is no conclusive data to support or refute the use of routine or selective shunting in carotid surgery, there is consensus that either policy is preferable to a policy of routine non-shunting.\(^\text{11,12}\) Shunts can give rise to complications and the finite risk of stroke associated with their use is reason enough to avoid using them when possible.\(^\text{13,14}\)

The principle advantage of LA CEA is the ability to monitor patients more accurately with direct neurological assessment and selectively shunt if they develop neurological signs.\(^\text{15±17}\) This study confirms that LA CEA is associated with a clinically lower shunt rate compared to CEA performed under GA. This difference almost certainly reflects more accurate assessment with awake patient monitoring compared to TCD monitoring during GA procedures. However, if identical TCD shunt criteria had been applied to the two groups, the shunt rate would still be significantly less in LA procedures. This study using TCD assessment of MCAV\text{mean} demonstrates that the cerebral vascular response to carotid clamping is less pronounced in procedures performed under LA. Carotid clamping was associated with a more significant reduction in MCAV\text{mean} and a lower post-clamp MCAV\text{mean} if the procedure was performed under GA. These data suggest that LA CEA is associated with a better preservation of the ipsilateral cerebral circulation, and that the lower shunt rate reported for LA procedures is a combination of this physiological protective mechanism as well as more accurate monitoring.

Transcranial Doppler monitoring of the MCAV\text{mean} is not synonymous with absolute blood flow. According to the Hagen–Pouiseille law, absolute blood flow is proportional to the fourth power of the radius while the velocity is proportional to the radius squared. Theoretically it is possible that GA caused cerebral vasodilatation and the same total volume flow passed through the brain as during LA procedures but at a lower velocity. However previous data has demonstrated that provided end-tidal CO\textsubscript{2} remains stable, as in this study, relative changes in middle cerebral artery velocity may be used as a valid index of change in associated blood flow.\(^\text{5,6}\)

In this study changes in MCAV\text{mean} could not be accounted for by changes in MAP with clamping. The MAP did not change with carotid clamping in either group. This appears to be in contradiction of other published data.\(^\text{3,4}\) In McCleary’s study, the increase in MAP with carotid clamping was only witnessed in the LA group, whereas in other studies it has been reported with GA.\(^\text{18}\) In Hayes large series of 548 CEA procedures performed under GA, the mean systolic blood pressure increased by 5 mmHg with carotid clamping. Although the data for diastolic and mean blood pressures are not given in this paper, the data from this paper, if used for a power/sample size estimation suggest that at least 466 patients would be required in each group to detect a statistical difference with a 90% power. We therefore believe that our study was not sufficiently powered to detect such a moderate rise in blood pressure, and this was not a primary end point.

In McCleary’s prospective non-randomised study, assessing cerebral metabolism during anaesthesia, LA patients demonstrated a spontaneous recovery of oxyhaemoglobin and oxidised cytochrome oxidase to normal indicating return to normality of cerebral oxygenation.\(^\text{4}\) In this study both a higher intraoperative systemic blood pressure and a significant rise in MAP with carotid clamping in the LA procedures were thought to contribute to the preservation of autoregulation. The authors suggest that this phenomenon appears to depend on a reflex rise in blood pressure.
that is not seen in general anaesthetic compared to local anaesthesia patients. Hayes data, however, would contradict this hypothesis. The data in our study support the phenomenon of preservation of the cerebral circulation with LA and suggests that the higher MCAVmean seen in LA CEA is independent of the mean arterial pressure. This finding is supported by Hayes data which also failed to show a relationship between MAP and MCAVmean. 18

Several studies have shown that intraoperative blood pressure during CEA behaves differently under LA and GA.3,4,19,20 This study confirms that the mean arterial pressure tends to elevated in LA CEA and decreased in GA CEA throughout the procedure, particularly at the time prior to carotid clamping.19 In addition, episodes of hypotension, when both cerebral and cardiac perfusion may be compromised are more frequent with GA.21 Some authors have expressed concerns that whilst the higher MAP during LA CEA may improve cerebral perfusion it may also increase the cardiac risk during the procedure, but evidence from a metaanalysis of non-randomised trials suggests that LA CEA is associated with a 50% reduction in mortality and major morbidity and a 60% reduction in the relative risk of perioperative myocardial infarction.3 There is however no evidence from randomised studies that LA CEA is associated with a lower incidence of cardiac events.2,21 The reason for the observed difference in cardiac morbidity is unclear, but some authors believe it may be due to the higher incidence of hypotension in GA CEA and the associated reduction in coronary artery perfusion.20

Three possible theoretical explanations exist to account for the differences in response of the cerebral circulation to carotid clamping. Firstly, the extent of cerebral cross flow may have been different between the two groups. We believe this is unlikely as the patients were randomised and had a similar degree of contralateral carotid disease. A second explanation may be that a cerebral circulation with pre-existing ischaemic damage and impaired autoregulation may be more susceptible to decreases in cerebral perfusion pressure and the lower pre-clamp MAP in the GA group may well potentiate the problem. Finally, a third explanation as suggested by McCleary et al. is that GA blocks cerebral perfusion receptors which then prevent the normal autoregulatory response.4,20

In conclusion, this study demonstrates a physiological advantage to the ipsilateral cerebral circulation which is independent of MAP if the procedure is performed under LA. This response may prevent cerebral hypoperfusion injury during CEA. In addition this study confirms that intraoperative hypotension is more common in GA CEA. Evidence from non-randomised trials suggests potential benefits with LA CEA including a reduction in mortality, major morbidity and perioperative cardiac events. There is not enough evidence from randomised trials comparing CEA performed under local as opposed to general anaesthesia, and only the results of a prospective randomised trial will confirm if these physiological advantages lead to any significant clinical benefit.

References
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