Non-Invasive Diagnosis of Mild to Severe Stenosis of the Internal Carotid Artery

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SUMMARY A prospective masked study of the Langham Ocular Pressure Pulse Amplitude Procedure was made on 20 patients with arteriographically-confirmed completely patent carotid arteries (Group 1) and on 20 patients with either unilateral or bilateral stenoses of the internal carotid arteries (Group 2). The results are compared to similar studies previously reported on 20 patients with radiographically confirmed unilateral or bilateral occlusions of the internal carotid arteries (Group 3). The intraocular pressures, the pulse/intraocular pressure relations, and the ophthalmic arterial pressures were equal in pairs of eyes of Group 1 patients, and similar to those found in normal healthy subjects. The mean ophthalmic/brachial arterial pressure ratio in Group 1 patients was significantly higher than in normal subjects. In the Group 2 patients, the intraocular pressures were normal and all the measured parameters were similar in pairs of eyes, whereas, the ophthalmic/brachial arterial pressure ratios were significantly less than in the eyes of the Group 1 patients. The degree of stenoses of the internal carotid arteries (0 to 100%) as evaluated from arteriography varied inversely with the ophthalmic/brachial arterial pressure ratios (correlation coefficient 0.85). The coefficients of the sensitivity, the specificity, and the accuracy of the ophthalmic/brachial arterial pressure ratios in identifying the presence of stenotic lesions of the internal carotid artery defined by arteriography in the 120 eyes of the three groups were 89, 80, and 86% respectively. The ability of the Procedure to identify hemodynamic lesions of less than 50% is in keeping with published results of theoretical and experimental studies of the pressure gradient across stenoses in arteries with high rates of blood flow.

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MEASUREMENT OF HEMODYNAMIC EVENTS in the ophthalmic artery based on central retinal artery pressures and intraocular pulse volumes are the bases of several non-invasive diagnostic procedures for internal-carotid arterial occlusive disease. The former techniques include ophthalmodynamometry,1-2 and suction cup ophthalmodynamometry,3-5 and the latter techniques include time-delay oculoplethysmography6 and oculopneumoplethysmography.7-9

These methods differ fundamentally from the Langham Pulse/Pressure diagnostic procedure for internal carotid occlusive disease in which direct ocular pulse pressure and tonometric intraocular pressure measurements are made as the intraocular pressure is increased to the level of the ophthalmic arterial pressure.10-13 These measurements give the pulse/intraocular pressure relationships of the eye which are described at their lower limit by the resting pulse amplitude, and the intraocular pressure, and at their upper limit by the value of the intraocular pressure at which the ocular pulse and blood flow into the eye are completely suppressed.10 Using this procedure, the form of the pulse/pressure relation was found to be identical in pairs of eyes of normal subjects, whereas major changes in the shape of the pulse/intraocular pressure relation and in the ophthalmic arterial pressure characterized patients with unilateral and bilateral occlusions of the internal carotid arteries.13

This study extends our previous investigations of normal subjects and of patients with occluded internal carotid arteries to include a series of patients with clinical symptoms of carotid occlusive disease in whom subsequent arteriography revealed fully patent internal carotid arteries and also a series of patients in whom subsequent arteriography revealed a partial stenosis of one or both internal carotid arteries.

Materials and Methods

Patients ranging in age from 49 to 83 years were referred from the neurology services of The Johns Hopkins Hospital for the Ocular Pressure Pulse Amplitude studies. Detailed neurological and ophthalmological studies were made on each patient prior to the Ocular Pressure Pulse Amplitude and arteriographic studies. Only patients who had successful arteriography were included in this study. Most arteriograms were 4-vessel studies performed via a trans-femoral route to give adequate visualization of the aortic arch, both cervical carotid arterial systems, and the intracranial circulation. The grading of the internal carotid artery stenosis was made by an experienced neuro-radiologist who was unaware of the results of the ocular tests. Calculation of the percentage stenoses of the internal carotid arteries from the arteriograms was based on measurements of the smallest diameter of the lumen through the stenosis compared to the diameter of the internal carotid artery at a distal area that was free of post-stenotic dilatation.

The present study deals with 40 patients, taken in sequence, who fell into two groups. Group 1 comprised 20 patients in whom arteriography revealed completely patent cervical arteries. All 20 patients, however, had evidence of neurologic deficit and/or cardiovascular pathology. Symptoms included left-sided and/or right-sided motor weakness (11 patients), decreased sensory perception (3 patients), severe frontal and occipital headaches (2 patients), and general
atherosclerosis (3 patients). In addition the group included a healthy 18 year old white male who had sustained bilateral orbital fractures, and a cerebral contusion in a motorcycle accident. He subsequently developed meningitis and a progressive bilateral hemianopia. Skull x-rays were normal except for the orbital fractures; CT scan, pneumoencephalogram, and AP tonogram were normal. Ocular examination of these 20 patients revealed a left optic neuropathy in one patient, bilateral retinal drusen in one patient, and a suspect unilateral glaucoma.

Group 2 comprised 20 patients, taken in sequence, in whom arteriograms showed partial stenosis of one or both internal carotid arteries. Patients with a complete occlusion of one or both internal carotid arteries were excluded, because they had been the subjects of our previous study.\textsuperscript{13} The ocular examination of the 20 patients in Group 2 revealed one case of bilateral diabetic retinopathy and one patient with bilateral hemianopia (defective vision in half of the visual fields). The results from these two groups of patients are compared to the results of similar studies made on 20 patients (Group 3) in whom arteriography revealed a unilateral or bilateral complete occlusion of the internal carotid arteries. This is a group of patients described in our previous study.\textsuperscript{13}

The intraocular pressure and the intraocular pressure pulse were recorded using the Langham pneumatic pressure sensor (Bio-Rad, DigiLab Division, Cambridge, Mass.), and increase of intraocular pressure was produced by using the Langham suction cup system (Bio-Rad, DigiLab Division, Cambridge, Mass.). The instrument used to record the intraocular pressure and the pulse amplitude was developed specifically for the Ocular Pressure Pulse Amplitude Procedure (DigiLab OCVM system, Bio-Rad DigiLab Division, Cambridge, Mass.) and had two recording channels, one for the display of the pulse, and one for recording the average intraocular pressure over successive 2 sec intervals (figs. 1 & 2). The separation of the two components of the intraocular pressure permits the pulse to remain centered on the recording chart as the intraocular pressure is artificially increased (fig. 2).

The Pulse/Pressure Procedure was the same as that described in our previous paper.\textsuperscript{13} Briefly, this included recording of the intraocular pressure and the pulse amplitude on patients in both the seated and supine position prior to the application of the scleral cup. The ocular pulse/pressure relationship was obtained with the patient in the supine position. The brachial blood pressure was measured on both arms immediately before initiation of the procedure using an arm cuff sphygmomanometer and stethoscope. Control studies in which measurements were repeated following completion of the study revealed insignificant change in the brachial arterial pressures during the procedure (less than 5 mm Hg). A red fixation light was used to check vision as the intraocular pressure was increased stepwise using the suction cup system. Five to ten complete pulsations of the intraocular pressure were recorded at each intraocular pressure step. The intraocular pressures and the corresponding average values of the pulse amplitudes were used to plot the pulse/pressure relation (fig. 2). A line of best fit to the observed values was drawn by eye. The point of intersection of this curve with the abscissa (intraocular pressure) was read as the ophthalmic arterial systolic pressure. All results are expressed as the arithmetic mean ± the standard error of the mean. The number for each set of results is shown in parenthesis. Calculation of the coefficients of accuracy, sensitivity, and specificity followed the procedure described by Sumner.\textsuperscript{14}

**Results**

Representative recordings of the intraocular and pulse pressures in pairs of eyes of a patient in Group 1 are shown in figure 1. The intraocular pressures in pairs of eyes of this patient were equal, but the pulse amplitudes of 0.6 mm Hg were less than the range of 2 to 3 mm Hg in eyes of normal healthy subjects.\textsuperscript{10} The
disturbed eyes. One patient had an arrhythmia in the seated position that disappeared on lying supine.

In Group 2 patients, the average intraocular pressure was 17.70 ± 0.59 (40) mmHg and the mean pulse pressure was 1.58 ± 0.12 (40) mmHg. The latter value is significantly less (p < 0.01) than in normal healthy subjects.

The intraocular pressures in pairs of eyes were equal in 35 of 40 patients in Groups 1 and 2 (table 3), which contrasts with the asymmetry of the intraocular pressures in most patients with severe unilateral internal carotid artery occlusive disease.13

The mean ophthalmic arterial pressure and the ratios of the ophthalmic/brachial arterial pressures in Groups 1 and 2 are summarized in table 4. The mean ratio of 0.78 ± 0.01 (40) in Group 1 patients was significantly higher (p < 0.01) than the mean value of 0.67 ± 0.01 recorded in 13 normal subjects of similar age not given arteriography.13 Table 4 also includes the results of similar studies made on 20 subjects with either unilateral or bilateral occlusions of the internal carotid arteries.13 Group 3a are eyes in which the degree of stenosis in the ipsilateral internal carotid artery was less than 95%; group 3b are the eyes in which the ipsilateral internal carotid artery was completely occluded.

The pulse/intraocular pressure curves were of similar form in pairs of eyes of all 20 patients in Group 1.

TABLE 1 Summary of Measurements on 20 Patients with Zero Stenosis of the Internal Carotid Arteries Based on Arteriographic Studies

<table>
<thead>
<tr>
<th>Age and sex</th>
<th>IOP/PA (mm Hg)</th>
<th>O.A.P. (mm Hg)</th>
<th>Br.A.P. (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>O.D.</td>
<td>O.S.</td>
<td>O.D.</td>
</tr>
<tr>
<td>1. 65 F</td>
<td>16/1.8</td>
<td>17/1.8</td>
<td>95</td>
</tr>
<tr>
<td>2. 51 F</td>
<td>18/2.2</td>
<td>24/2.0</td>
<td>100</td>
</tr>
<tr>
<td>3. 52 F</td>
<td>14/1.6</td>
<td>12/1.2</td>
<td>95</td>
</tr>
<tr>
<td>4. 66 F</td>
<td>17/2.2</td>
<td>18/1.8</td>
<td>110</td>
</tr>
<tr>
<td>5. 31 F</td>
<td>20/2.6</td>
<td>20/2.6</td>
<td>85</td>
</tr>
<tr>
<td>6. 47 F</td>
<td>25/1.8</td>
<td>26/1.7</td>
<td>86</td>
</tr>
<tr>
<td>7. 44 M</td>
<td>15/1.1</td>
<td>16/1.1</td>
<td>110</td>
</tr>
<tr>
<td>8. 64 M</td>
<td>16/1.1</td>
<td>19/1.6</td>
<td>100</td>
</tr>
<tr>
<td>9. 52 F</td>
<td>14/1.3</td>
<td>16/1.4</td>
<td>90</td>
</tr>
<tr>
<td>10. 78 M</td>
<td>12/1.5</td>
<td>15/1.7</td>
<td>98</td>
</tr>
<tr>
<td>11. 41 F</td>
<td>17/1.0</td>
<td>17/0.9</td>
<td>100</td>
</tr>
<tr>
<td>12. 56 M</td>
<td>22/1.8</td>
<td>20/1.6</td>
<td>82</td>
</tr>
<tr>
<td>13. 78 F</td>
<td>14/0.9</td>
<td>13/0.9</td>
<td>105</td>
</tr>
<tr>
<td>14. 60 M</td>
<td>13/1.5</td>
<td>13/1.5</td>
<td>120</td>
</tr>
<tr>
<td>15. 57 F</td>
<td>18/2.2</td>
<td>17/2.4</td>
<td>115</td>
</tr>
<tr>
<td>16. 65 F</td>
<td>17/1.0</td>
<td>16/1.0</td>
<td>90</td>
</tr>
<tr>
<td>17. 52 F</td>
<td>15/0.7</td>
<td>14/0.7</td>
<td>120</td>
</tr>
<tr>
<td>18. 60 M</td>
<td>16/1.3</td>
<td>13/1.8</td>
<td>90</td>
</tr>
<tr>
<td>19. 49 M</td>
<td>13/1.1</td>
<td>14/1.3</td>
<td>94</td>
</tr>
<tr>
<td>20. 18 M</td>
<td>22/2.2</td>
<td>20/2.4</td>
<td>96</td>
</tr>
</tbody>
</table>

All pressure measurements were made on patients in the supine position. IOP represents the intraocular pressure, PA represents the pulse amplitude, OAP represents ophthalmic arterial pressure, and BrAP represents brachial arterial pressure.
The shape of the curves in 14 of the 20 patients were similar to that shown in figure 3. In 2 patients the pulse/intraocular pressure curves were sigmoid and were typical of those recorded in many normal subjects. In the remaining four patients the pulse amplitudes in the undisturbed eyes were abnormally low resulting in shallow pulse/intraocular pressure curves.

The pulse/intraocular pressure curves in pairs of eyes of Group 2 patients were symmetrical. In 16 patients the curves in pairs of eyes had the form similar to that shown in figure 3. In the remaining 4 cases, either the initial pulse amplitude was abnormally low (2 cases) or the pulse/intraocular pressure curves had the sigmoid shape typical of normal subjects.

A scattergram of the ophthalmic/brachial arterial pressure ratios and the percentage stenoses in the ipsilateral internal carotid arteries is summarized in figure 4. The ratios decreased with increasing stenosis, ranging from the mean of 0.78 ± 0.01 in eyes of patients with fully patent arteries to a mean of 0.31 ± 0.01 in the eyes of patients with a complete occlusion of the ipsilateral internal carotid artery. The coefficient of correlation was 0.85 for the linear regression using the 120 results. Table 3 summarizes the calculated values of sensitivity (the ability to detect the severity of the stenosis revealed by arteriography), specificity (the ability to recognize the absence of the severity of the stenosis revealed by arteriography), and the overall accuracy based on the results on the 120 eyes included in Groups 1, 2, and 3.

Table 2

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age Yr.</th>
<th>IOP/PA (mm Hg) O.D.</th>
<th>O.S.</th>
<th>O.A.P (mm Hg) O.D.</th>
<th>O.S.</th>
<th>% Stenosis</th>
<th>Br.A.P (mm Hg)</th>
</tr>
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<tr>
<td>1</td>
<td>68 F</td>
<td>17/2.4</td>
<td>12/2.1</td>
<td>81</td>
<td>81</td>
<td>25</td>
<td>125/68</td>
</tr>
<tr>
<td>2</td>
<td>49 F</td>
<td>17/2.0</td>
<td>17/2.0</td>
<td>80</td>
<td>80</td>
<td>35</td>
<td>130/75</td>
</tr>
<tr>
<td>3</td>
<td>70 M</td>
<td>14/0.5</td>
<td>15/0.5</td>
<td>70</td>
<td>70</td>
<td>0</td>
<td>110/52</td>
</tr>
<tr>
<td>4</td>
<td>75 F</td>
<td>18/1.6</td>
<td>19/1.5</td>
<td>90</td>
<td>97</td>
<td>35</td>
<td>150/68</td>
</tr>
<tr>
<td>5</td>
<td>71 F</td>
<td>22/0.9</td>
<td>20/0.9</td>
<td>90</td>
<td>90</td>
<td>25</td>
<td>182/98</td>
</tr>
<tr>
<td>6</td>
<td>55 M</td>
<td>14/2.3</td>
<td>15/2.3</td>
<td>85</td>
<td>79</td>
<td>55</td>
<td>130/70</td>
</tr>
<tr>
<td>7</td>
<td>55 F</td>
<td>23/1.8</td>
<td>23/1.7</td>
<td>91</td>
<td>85</td>
<td>60</td>
<td>144/80</td>
</tr>
<tr>
<td>8</td>
<td>60 M</td>
<td>15/3.0</td>
<td>13/3.0</td>
<td>103</td>
<td>103</td>
<td>0</td>
<td>160/82</td>
</tr>
<tr>
<td>9</td>
<td>57 M</td>
<td>19/2.0</td>
<td>20/1.9</td>
<td>110</td>
<td>110</td>
<td>25</td>
<td>140/82</td>
</tr>
<tr>
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<td>64 M</td>
<td>20/1.1</td>
<td>20/1.1</td>
<td>72</td>
<td>72</td>
<td>0</td>
<td>130/70</td>
</tr>
<tr>
<td>11</td>
<td>76 M</td>
<td>21/1.4</td>
<td>24/1.4</td>
<td>100</td>
<td>100</td>
<td>25</td>
<td>158/82</td>
</tr>
<tr>
<td>12</td>
<td>62 M</td>
<td>20/0.9</td>
<td>20/0.9</td>
<td>80</td>
<td>80</td>
<td>75</td>
<td>190/105</td>
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<td>55 M</td>
<td>16/1.6</td>
<td>17/1.5</td>
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<td>22/3.0</td>
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<td>100</td>
<td>25</td>
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<td>64 F</td>
<td>18/0.6</td>
<td>18/0.4</td>
<td>75</td>
<td>80</td>
<td>75</td>
<td>153/83</td>
</tr>
<tr>
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<td>57 M</td>
<td>11/1.3</td>
<td>10/1.1</td>
<td>97</td>
<td>96</td>
<td>0</td>
<td>120/70</td>
</tr>
<tr>
<td>19</td>
<td>74 F</td>
<td>19/2.5</td>
<td>19/2.5</td>
<td>110</td>
<td>110</td>
<td>25</td>
<td>150/66</td>
</tr>
<tr>
<td>20</td>
<td>64 F</td>
<td>18/1.2</td>
<td>18/1.2</td>
<td>100</td>
<td>100</td>
<td>35</td>
<td>170/75</td>
</tr>
</tbody>
</table>

All pressure measurements were made on patients in the supine position. IOP is the intraocular pressure, PA is the intraocular pressure pulse amplitude, OAP is the ophthalmic arterial pressure, and BrAP is the brachial arterial pressure.

Discussion

In our previous study, comparison was made of normal subjects without evidence of cardiovascular disease versus patients having either unilateral or bilateral occlusions of the internal carotid arteries. The normal subjects did not have arteriography, and we questioned whether it was justified to use them as a control group. At that time, the symmetry of the intraocular pressures, the pulse amplitudes, the pulse/intraocular pressure curves, and the equal ophthalmic arterial pressures in pairs of eyes of the normal subjects was considered evidence that the members of the "normal" group were free of significant carotid occlusive disease.

The 20 patients in Group 1, with arteriographically-
confirmed fully patent internal carotid arteries, included sixteen patients with symptoms of transient ischemic attacks. The results were similar to those seen in normal subjects in respect to the close symmetry of the intraocular pressures, of the pulse amplitudes, of the pulse/pressure curves, and of the ophthalmic arterial pressures in pairs of eyes. Moreover, the ophthalmic arterial pressures and the ophthalmic/brachial pressure ratios in individual patients were either equal to or higher than in normal subjects. Thus, it appeared to be justified to use the ophthalmic/brachial pressure ratios of this group of patients as controls, in assessing the probability of stenosis of the internal carotid artery.

The results on Group 1 patients did differ from those in normal subjects both in respect to the pulse pressure and in respect to the mean value of the ophthalmic/brachial arterial pressure ratios. The mean ocular pulse amplitude in these patients was significantly less and the mean ophthalmic/brachial arterial pressure ratio was significantly higher \((p \lt 0.001)\) than in healthy age matched subjects. This relative increase in the ophthalmic arterial pressure could be due either to a decreased flow resistance in the cervical arteries, or to an increased flow resistance in the vascular network of the brain. The latter explanation is consistent with the observations of Weigelin and co-workers. In meticulous studies using a modified procedure of retinal ophthalmodynamometry and the nitrous-oxide clearance technique of Kety and Schmidt to measure cerebral blood flow, Weigelin showed that the ophthalmic arterial pressure increased proportionately with the cerebral vascular resistance in a series of 53 patients.

In order to maximize the accuracy of the non-invasive procedures it has been found necessary to relate the ophthalmic/brachial arterial pressure ratio to the degree of internal carotid artery stenosis. This accuracy is greatest when the systolic values of the ophthalmic and brachial arterial pressures are used rather than the diastolic or mean pressure values. The ratios may then be used either to derive a linear regression relating the degree of stenosis to the ophthalmic/brachial arterial ratio or to derive a relation between stenosis and the difference of the ratios between pairs of eyes. The application of the linear regression analysis to the results of compression ophthalmodynamometry, suction ophthalmodynamometry, and oculoplethysmography was found to yield coefficients of sensitivity of 63, 56, and 24\% respectively for stenosis exceeding 50\%. The latter approach, based on the degrees of asymmetry of the ophthalmic/brachial arterial pressure ratios, has been found to give increased predictive value over the use of a linear regression equation. Using compression and suction ophthalmodynamometric techniques, Sanborn et al reported that the sensitivity (percentage of true positives), and specificity (percentage of true negatives) was 63\% and 87\% respectively in patients with more than 50\% internal carotid artery stenosis when a pressure difference greater than 20\% between pairs of eyes was considered to be diagnostic. Similar values for the sensitivity and for the specificity in patients with internal carotid artery stenoses exceeding 50\% have been reported using Doppler supraorbital examination, photoplethysmography, pulse delay oculoplethysmography, and suction cup oculoplethysmography by other investigators.

The diagnostic value of non-invasive procedures based on the asymmetry of the measured parameters in pairs of eyes is good for internal carotid artery stenoses exceeding 75\%, but is only moderately valuable for the diagnosis of internal carotid artery stenoses in the range of 50 to 75\%; and little, if any, diagnostic value for internal carotid artery stenotic lesions of less than...
TABLE 5

The Sensitivity (ability to detect stenosis), Specificity (ability to detect stenoses that do not fall into the category), and Accuracy of the Ophthalmic/Brachial Arterial Ratios of Patients in Groups 1, 2, and 3 in Diagnosing the Degree of Stenosis of the Internal Carotid Artery Based on Arteriography

<table>
<thead>
<tr>
<th>Arteriography</th>
<th>OAP/BrAP ratios</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Accuracy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stenoses &gt;50%</td>
<td>(R &lt; .4)</td>
<td>76</td>
<td>99</td>
<td>93</td>
</tr>
<tr>
<td>Stenosis &gt;75%</td>
<td>(R &lt; .5)</td>
<td>93</td>
<td>89</td>
<td>90</td>
</tr>
<tr>
<td>Stenoses &gt;50%</td>
<td>(R &lt; .5)</td>
<td>78</td>
<td>89</td>
<td>84</td>
</tr>
<tr>
<td>Stenoses &lt;50%</td>
<td>(R &lt; .6)</td>
<td>91</td>
<td>41</td>
<td>80</td>
</tr>
<tr>
<td>All stenoses</td>
<td>(R &lt; .6)</td>
<td>83</td>
<td>91</td>
<td>86</td>
</tr>
<tr>
<td>All stenoses</td>
<td>(R &lt; .68)</td>
<td>89</td>
<td>80</td>
<td>86</td>
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</tbody>
</table>

50%.12,14 These conclusions are consistent with our findings using the Ocular Pressure Pulse Amplitude Procedure. Symmetry of intraocular pressure, pulse amplitude, ophthalmic arterial pressure, and the pulse/pressure relations was present in nearly all patients with stenosis of less than 50%. In patients with stenosis of 50 to 75%, asymmetry of the measured parameters was present in some but not all patients. In patients with unilateral or bilateral internal carotid artery occlusions or internal carotid artery stenoses exceeding 75%, asymmetry was present in all patients. This asymmetry was present even when arteriography showed identical stenoses in pairs of internal carotid arteries. The persistence of the asymmetry under these conditions presumably reflects the variable degree of severity of the disease in adjacent arteries.

The capability of the Ocular Pressure Pulse Amplitude Procedure to extend the range of the occlusive diagnosis to include internal carotid artery stenosis of less than 50% results from the accuracy of the pneumatic tonometer to record intraocular pressure and the pressure pulse amplitude both in the undisturbed eye and in the eye with experimentally induced increased intraocular pressure.15-21 This contrasts with the techniques of ophthalmodynamometry, suction cup ophthalmodynamometry, and oculoplethysmography in which the intraocular pressure cannot be directly measured but has to be derived from calibration tables relating intraocular pressure to the value of the force applied to the eye. These procedures rely on the amount of force or suction applied to the eye to evaluate the ophthalmic arterial pressure. Unfortunately, this indirect evaluation of both the intraocular pressure and the ophthalmic/brachial pressure ratio has serious limitations especially in eyes with a decreased vascular perfusion pressure. A major source of error arises from the fact that the increment of intraocular pressure induced by the externally applied force is largely determined by the vascular compliance and the vascular perfusion pressure of the eye, i.e. by the parameters which will change with stenosis of the carotid artery.10,11,22-24

The present results are in agreement with those of Russell et al28 who employed the Langham procedure to study 19 patients who subsequently had arteriography. In eight patients with stenoses greater than 50% the ophthalmic/brachial pressure ratios were reported to be less than 0.6 in all cases (100% sensitivity). In the remaining 11 patients with stenosis less than 50%, the ophthalmic/brachial arterial ratios were less than 0.6 in 7 patients. On the assumption that lesions of less than 50% would not be hemodynamically significant the authors concluded that the results on the 7 patients were false positives (see below).

The identification of minimal to moderate lesions of the internal carotid artery by the present technique contrasts with the widely held view that a stenosis of less than 50% would have no hemodynamically significant effect distal to the lesion.11,12,25-29 However, the experimental and the theoretical studies of Berguer and Hwang30 have shown that the influence of arterial constriction on the distal pressure depends on the basal rate of blood flow, and that the distal pressure decreases significantly with constriction below 50% in arteries with high rates of blood flow; this is true of the internal carotid arteries.31 Using the generalized equation of energy conservation $E_r = h + \frac{V^2}{2} g + P/\gamma$ where h is gravitational potential energy, $V/2 g$ is the kinetic energy (Ek) of unit weight of blood, $P/\gamma$ is the lateral pressure energy (Ep), and $\gamma$ is density, they were able to predict the effect of increasing stenosis of an artery on the lateral pressure in the poststenotic
(distal) region. In their in vivo experimental arterial system the critical amount of constriction of the stenosis corresponded to 60 to 70%, i.e.; the lateral pressure began to fall rapidly as the constriction exceeded this value (fig. 5). Based on the close agreement between theory and experiment, these authors showed how the form of the relation between flow and stenosis changed with low and high basal flow rates, the length and geometry of the stenotic lesion, and with the distal resistance (fig. 5). In arteries with low rates of blood flow the critical amount of constriction is well defined, whereas in vessels with high flow rates this value is less well defined, and the lateral pressure in the poststenotic region changes significantly with lesser degrees of constriction (fig. 5).

Evidence that the internal carotid artery responds to increasing stenosis in a similar manner to the experimental and theoretical findings in an artery with a high rate of blood flow is shown in figure 5. The ordinate is the pressure gradient between the common carotid and the ophthalmic arteries. With the internal carotid artery fully patent the pressure gradient is small (approximately 3–4 mmHg); based on the present observations this gradient increases to a mean of approximately 50 mmHg in patients with normal blood pressure and arterial stenosis of approximately 100%. The dotted line in figure 5 reflects the relation between the degree of stenosis and the pressure gradient in the internal carotid artery found in the present study. This dotted line corresponds closely to the upper solid line which is taken from the paper of Berguer & Hwang and represents the theoretical result for arteries with high rates of blood flow.

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FIGURE 5. Comparison of the theoretical and experimental curves relating the effect of increasing arterial stenosis on the arterial pressure gradient. The ordinate (arterial pressure gradient) of 50 mm Hg reflects the decrease in the ophthalmic arterial pressure induced by a complete stenosis of the proximal portion of the internal carotid artery. In the fully patent artery the corresponding pressure gradient is assumed to be 3 mmHg. The dotted line reflects the present results on Groups 1, 2, and 3 patients. The continuous lines are the theoretical results for arteries with either high (upper line) or low (lower line) flow rates respectively as reported by Berguer & Hwang.

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Naloxone Therapy During Focal Cerebral Ischemia
Evaluation in a Primate Model

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SUMMARY Conflicting reports have appeared in the literature regarding the effect of the opiate antagonist naloxone on ischemic neurologic deficits. We report the results of a study using naloxone in our model of focal cerebral ischemia in the awake primate. A total of 14 adult baboons were subjected to six-hour occlusion of the left middle cerebral artery (MCA). Seven animals served as controls and seven received treatment with naloxone (5 mg/kg) beginning 30 min after MCA occlusion and continuing until two hours after reperfusion. All animals developed profound hemiparesis and homonymous hemianopsia within seconds of inflating the MCA occluder.

Acutely, treatment with naloxone partially reversed ischemic neurologic deficits in five of the seven treatment animals. Within minutes of receiving the loading dose of naloxone, responding animals were more alert and demonstrated improvements in motor function.

Naloxone did not affect mortality: Three animals in the treatment group and two in the naloxone group died secondary to malignant intracranial pressure within 48 hours of the ischemic episode. In animals surviving the ischemic insult however, treatment with naloxone significantly improved neurologic outcome at 10 days (p < 0.05). Neuropathologic examinations in these animals revealed amelioration of ischemic tissue damage, with three of the five suffering only small focal areas of infarction. (All control animals suffered large infarcts of the MCA territory.) Our results verify that naloxone can reverse ischemic deficits, and more importantly may improve the outcome from focal ischemic insults.

In order to investigate these issues, we studied the effects of naloxone after MCA occlusion in our standardized primate model. Specifically, we sought to determine whether naloxone would reverse acute neurologic deficits during and/or improve the final outcome after six hours of MCA occlusion.

Material and Methods

A total of 14 adult baboons (Papio anibus) were used for this study. Animals weighed from 15 to 28 kg. Both control and treatment groups were subjected to a six-hour period of MCA occlusion. Seven animals were randomly assigned to receive treatment with naloxone and seven served as controls. We have previously reported the details of this experimental model. Briefly, animals were prepared as follows. After induction of general anesthesia with thiopental, the animal was intubated and placed on a volume cycled respirator. Anesthesia was maintained with thiopental infusion. The left orbit and scalp were prepped and draped using sterile technique, and with the aid of an operating microscope, the left MCA was exposed...
Non-invasive diagnosis of mild to severe stenosis of the internal carotid artery.
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