INTRODUCTION

Transcranial Doppler (TCD) is a reliable technique for the non-invasive assessment of cerebral hemodynamics (1,2). In patients with cerebrovascular disease, TCD might identify stenosis or occlusion of the intracerebral arteries and help to evaluate the collateral pathways in patients with extracranial carotid lesions (3-5). However, in approximately 5-20% of patients, particularly in the elderly and in women, a satisfactory study of cerebral arteries is hindered by skull bone hyperostosis (6,7). Recently, transpulmonary echocontrast agents have been developed to overcome this limitation (8). A galactose-based microbubble suspension stabilized by palmitic acid coating, SHU 508 A (Levovist®), proved effective in increasing the reflecting Doppler signal intensity and in improving the signal-to-noise ratio (9-14).

The aim of the study was to evaluate the diagnostic potential of galactose-based microbubble suspension (Levovist®) in patients with acute cerebrovascular disease and inadequate transtemporal acoustic window, when examined by transcranial Doppler (TCD). We studied 10 patients with either transient ischemic attack (no. = 3) or stroke (no. = 7). Inadequate transtemporal acoustic window was unilateral in 3 patients and bilateral in the remaining 7 patients. Signals from middle, anterior, and posterior cerebral arteries (MCA, ACA, PCA) were recorded after injecting Levovist® 300 mg/ml. Six patients needed 3 injections of Levovist®, 1 patient two, and 3 patients one. Mean ± SD duration of optimal signal enhancement was 175.2 ± 53.2 s, range 70-290 s. Doppler waveform analysis was possible in 14 (82.3%) MCA, 11 (65%) ACA, and 9 (53%) PCA. Levovist® improved the reliability of TCD in patients with acute cerebrovascular disease and insufficient transtemporal insonation.

KEY WORDS: Acute stroke, cerebral arteries, contrast media, ultrasonics.

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of neurology. Out of 63 patients arriving within 48 hours of onset of neurological signs and symptoms of focal cerebral ischemia, we identified 10 (15.9%) (4 men and 6 women, mean age ± SD 70.5 ± 7.2 years, range 58 to 79 years) with insufficient Doppler signal from basal cerebral arteries. Three of these patients had suffered a transient ischemic attack and 7 a stroke. No patients presented contraindications to the echocontrast agents, such as galactosemia or galactokinase deficiency.

Each patient underwent a routine ultrasonography study of the extracranial carotid arteries that revealed a carotid occlusion in one, a severe carotid stenosis in two, and no lesions in seven.

TCD was performed by means of an EME TC2-64B device (Überlingen, Germany) with a 2 MHz probe connected to a TC2-Plus upgrade system for computerized Doppler signal analysis. The presence of an insufficient temporal bone window, due to poor Doppler signal or low signal-to-noise ratio, was evident when two experienced sonographers (R.T., S.S.) independently reported that they were unable to evaluate basal cerebral arteries. Upon transtemporal scanning, an insufficient Doppler signal of the cerebral arteries was unilateral in 3 patients and bilateral in 7. In all these patients, TCD examinations were repeated after injecting 2.5 g of Levo - vis® (300 mg/ml) and Doppler signals from middle (MCA), anterior (ACA), and posterior (PCA) cerebral arteries were recorded on videotape for the off-line evaluation. Levo - vis® was injected rapidly in the right cubital vein over 5 to 10 seconds by hand. The injection was repeated if the time of useful enhancement was not sufficient to complete the examination.

RESULTS

The characteristics of the included patients are shown in Table I. Levo - vis® injections were generally well tolerated by all the patients; three patients experienced a transient sensation of warmth on the site of injection after the infusion.

Three patients with unilateral absent transtemporal acoustic window needed one injection of Levo - vis® while 7 patients with bilateral absent transtemporal acoustic window needed two (no. = 1) or three (no. = 6) injections. The Doppler waveform analysis was possible in 14 (82.3%) of the 17 MCA explored, in 11 (65%) of the 17 ACA, and in 9 (53%) of the 17 PCA (Fig. 1).

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Event</th>
<th>Stroke onset (hours)</th>
<th>Absent acoustic window</th>
<th>No. of injections</th>
<th>Duration of amplification (seconds)</th>
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<tbody>
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<td>61</td>
<td>F</td>
<td>TIA</td>
<td>12</td>
<td>bilateral</td>
<td>3</td>
<td>250-210-150</td>
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<tr>
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<td>58</td>
<td>F</td>
<td>TIA</td>
<td>20</td>
<td>unilateral</td>
<td>1</td>
<td>150</td>
</tr>
<tr>
<td>3</td>
<td>73</td>
<td>M</td>
<td>stroke</td>
<td>6</td>
<td>bilateral</td>
<td>3</td>
<td>180-200-150</td>
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<tr>
<td>4</td>
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<td>stroke</td>
<td>48</td>
<td>bilateral</td>
<td>3</td>
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<tr>
<td>5</td>
<td>75</td>
<td>M</td>
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<td>48</td>
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<td>3</td>
<td>220-210-200</td>
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<td>48</td>
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<tr>
<td>7</td>
<td>70</td>
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<td>TIA</td>
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<tr>
<td>8</td>
<td>72</td>
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<td>stroke</td>
<td>15</td>
<td>bilateral</td>
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<td>3</td>
<td>170-180-190</td>
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<tr>
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<td>79</td>
<td>M</td>
<td>stroke</td>
<td>48</td>
<td>bilateral</td>
<td>3</td>
<td>120-140-110</td>
</tr>
</tbody>
</table>

Abbreviations: TIA = transient ischemic attack.
Mean ± SD duration of optimal signal enhancement was 175.2 ± 53.2 s, range 70-290 s. Distribution of the signal enhancement duration of the 23 injections is reported in Fig. 2 (see over). The duration of the signal enhancement was between 121 and 240 s after the majority of injections (74%) and shorter than 120 s after 3 injections (13%).

In one patient, early examination after stroke onset allowed us to identify only the ACA and PCA ipsilateral to the stroke side, suggesting MCA trunk occlusion. The diagnosis was also indicated by the appearance of signs of recanalization at 24 and 48 hours. Activation of the collateral blood supply through the anterior communicating artery was detected in the patient with carotid occlusion and in the two patients with severe carotid stenosis. In the remaining 6 patients no alterations of cerebral blood flow velocity were found.

**DISCUSSION**

Recent technical improvements have led to morphological imaging of intracranial vessels by transcranial color-coded real-time sonography (TCCS) (15,16). However, TCD remains a suitable technique for the evaluation of cerebral hemodynamics. Technical obstacles such as inadequate acoustic window, examiner inexperience, low flow velocity, or vessel depth might contribute to limiting the use of TCD. Among these obstacles, inadequate acoustic window due to hyperostosis is the most frequent. Our results, in agreement with previous studies performed by TCD and TCCS (17-21), indicate that the limitations due to poor ultrasound reflection might be overcome by echocontrast agents. Minor adverse reactions such as sensation of warmth were experienced by three pa-

![Fig. 1 - Identification of vessel segment after Levovist® administration. MCA, middle cerebral artery; ACA, anterior cerebral artery; PCA, posterior cerebral artery.](image-url)
tients. The absence of serious adverse reactions confirmed that the administration of Levovist® was generally well tolerated (11,19).

Levovist® was injected rapidly, over 5-10 seconds, and improved the acoustic signal from intracranial arteries for up to 180 seconds in the majority of patients (11,13,14,17). The enhancement curve showed the typical pattern of a rapid increase in Doppler signal, a short plateau, and a rapid decay (22). In our series, to obtain a complete examination, 7 patients needed at least two injections of echocontrast agent. A slow infusion of echocontrast agent might reduce or abolish saturation artifacts, increase the duration of the enhancement with no need of further injections in the same patient (19,22,23). However, some examinations might remain inconclusive even after echocontrast agent infusion (19). In the present series, contrast-enhanced TCD did not allow identification of the Doppler signal from 18% of the explored MCA, 35% of the ACA, and 47% of the PCA (11,14,17,19,21,23).

When the Doppler signal from the MCA is not detectable, difficulty differentiating between vessel occlusion and technical problems represents a limitation of TCD. Successful insonation of the remaining ipsilateral basal cerebral arteries is mandatory to indicate an MCA occlusion (3-5). The diagnosis of MCA occlusion in our patient was possible since contrast-enhanced TCD permitted the identification of ipsilateral ACA and PCA. Contrast-enhanced TCD might be a reliable method to identify, in acute stroke patients with poor ultrasound window, occlusions of the major cerebral arteries that might benefit from thrombolytic therapies (5,19,20,23-25). Moreover, contrast-enhanced TCD allowed the evaluation of collateral flow through the circle of Willis in two patients with high grade carotid stenosis. Non-invasive evaluation of collateral supply by TCD might be helpful in pa-
tients with internal carotid lesions and for the preoperative assessment of candidates for carotid endarterectomy (26,27).

In conclusion, echo enhancement with Levovist® improved the reliability of TCD in patients with acute cerebrovascular disease and insufficient transtemporal insonation reducing the need for more invasive or expensive vascular neuroimaging techniques.

REFERENCES

18. Goertler M, Kross R, Baeumer M et al. Diagnostic impact and prognostic relevance of early contrast-enhanced transcranial color-


