Mechanism of the tilt induced increase in collateral arterial resistance in patients with occlusion of the superficial femoral artery

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SUMMARY Resistance in collateral arteries bypassing an occlusion of the superficial femoral artery was studied in five patients before and during epidural blockade. The patients were placed on a tilt table and the measurements were performed with the patients both in supine and tilted position (40° head up). Arterial blood pressure was measured directly in the brachial, common femoral and popliteal artery. Relative and absolute blood flows were calculated as the relative change in arteriovenous oxygen difference and by an indicator dilution technique.

Tilting caused a decrease in relative leg blood flow of 28%. The relative pressure gradient between the femoral and popliteal artery did not change significantly. Calculated relative collateral resistance increased by 49%.

During epidural blockade blood flow increased by 39% in supine position corresponding to a decrease in collateral resistance of 22%.

During blockade tilting caused a decrease in relative blood flow of 22% compared with the value in supine position. The relative pressure gradient over the occluded superficial femoral artery decreased by 14%. The corresponding calculated relative collateral resistance increased by 14%.

The results indicate that the tilt induced constriction of the collateral arteries is mainly neurogenically mediated via the lumbar sympathetic chain, whereas local mechanisms only seems to play a minor role.

In patients with occlusion of the superficial femoral artery, the calf and foot is supplied through collaterals from the deep femoral artery. These collaterals are mainly intermuscular arteries which have a high resistance compared with that of the patent superficial femoral artery. Dornhorst and Sharpey Shafer measured calf flow in patients with occlusive vascular disease in the lower limb before and after sympathectomy. They found a transient increase in hyperaemic flow after the operation indicating collateral dilatation. Beaconsfield and Ludbrook supported this observation except for patients with most severe disease.

Matsubara found that collateral arteries were richly supplied by adrenergic vasoconstrictor fibres. Agerskov et al demonstrated that head up tilt induced constriction of the collateral arteries of the thigh in patients with occlusions of the superficial femoral artery. It was suggested that this collateral vasoconstriction was mainly neurogenically mediated as the response was almost absent in one patient who had had a lumbar sympathectomy 2 years previously. Local factors may also be important. Henriksen showed that venous distension elicited a local vasoconstrictor response in human subcutaneous tissues during lowering the limb probably mediated by a local sympathetic axon reflex mechanism. Similar findings have been obtained in skeletal muscle and cutaneous tissue (Henriksen and Sejrsen). We therefore found it appropriate to study the influence of central versus local nervous reflex mechanisms upon collateral resistance in patients with occlusions of the superficial femoral artery.

Methods

Six patients with multilevel occlusions of the superficial femoral artery verified by angiography participated in the study. None had occlusions proximal to the common femoral artery. The angiography and intra-arterial pressure measurements were a part of the

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was given intravenously prior to blockade. The effect of the epidural blockade was tested by complete analgesia up to the umbilical level and disappearance of the sympathetic galvanic reflex (Daos et al.) and a rise in skin temperature 0.5°C at the ankle and 1°C on the thigh and abdomen within 15 min. None of the patients were able to elevate the legs during blockade. Proximally the block reached the level of the tenth thoracic segment. When the epidural blockade was effective the pressure and flow measurements were repeated as described above.

Relative blood flow in the whole limb was estimated by changes in the arterio-venous oxygen difference. Blood samples were obtained during anaerobic conditions in order to determine the oxygen saturation. Duplicate analysis on each sample were performed on a ABL-2 blood gas analyser.

### Calculations

Relative blood flow during head-up tilt

\[
\frac{F_{\text{test}}}{F_{\text{horizontal}}} = \frac{(S_{\text{aO}_2} - S_{\text{vO}_2})_{\text{horizontal}}}{(S_{\text{aO}_2} - S_{\text{vO}_2})_{\text{test}}}
\]

Assuming that \( O_2 \) consumption remained constant in the horizontal and tilted position \((S_{\text{aO}_2} - S_{\text{vO}_2})_{\text{test}}, \) and \((S_{\text{aO}_2} - S_{\text{vO}_2})_{\text{horizontal}}\), denote the arterio-venous difference in the tilted test position and horizontal position respectively. The calculations were performed for the whole leg by using the difference in oxygen saturation in blood from the femoral artery and femoral vein.

Immediately after blood sampling determination of oxygen saturation, femoral blood flow was measured

**FIG 1** Experimental set-up.
Collateral artery resistance

Table

Absolute and relative blood flow in the common femoral artery in horizontal position and during 40° head-up tilt measured by the indicator dilution technique and by changes in arteriovenous oxygen differences.

Indicator Dilution Technique

<table>
<thead>
<tr>
<th>Horizontal</th>
<th>Tilted 40°</th>
<th>Relative blood flow during 40° tilt</th>
<th>SaO₂ - SvO₂</th>
<th>Relative blood flow during 40° tilt</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before epidural blockade (cm³·min⁻¹)</td>
<td>During epidural blockade (cm³·min⁻¹)</td>
<td>Before epidural blockade (cm³·min⁻¹)</td>
<td>During epidural blockade (cm³·min⁻¹)</td>
<td>Before epidural blockade (cm³·min⁻¹)</td>
</tr>
<tr>
<td>478</td>
<td>758</td>
<td>422</td>
<td>691</td>
<td>0.88</td>
</tr>
<tr>
<td>212</td>
<td>288</td>
<td>188</td>
<td>228</td>
<td>0.89</td>
</tr>
<tr>
<td>557</td>
<td>682</td>
<td>297</td>
<td>945</td>
<td>0.85</td>
</tr>
<tr>
<td>548</td>
<td>1082</td>
<td>337</td>
<td>367</td>
<td>0.54</td>
</tr>
<tr>
<td>541</td>
<td>572</td>
<td>442</td>
<td>226</td>
<td>0.62</td>
</tr>
<tr>
<td>425</td>
<td>637</td>
<td>324</td>
<td>520</td>
<td>0.53</td>
</tr>
<tr>
<td>±54</td>
<td>±112</td>
<td>±45</td>
<td>±115</td>
<td>±0.07</td>
</tr>
</tbody>
</table>

Mean ± 1SE
Before epidural blockade P>0.1
During epidural blockade P>0.1

by the indicator dilution technique. Since there was no significant obliteration proximal to the tip of catheter in the femoral artery in the patients studied, the major part of the blood to the leg passed through the common femoral artery (single inlet system).

Blood flow in the femoral artery F could then be calculated as

\[ F = \frac{m_0}{\int_{0}^{t} c(t) \, dt} \]

where \( m_0 \) is the injected dose of indicator and \( \int_{0}^{t} c(t) \, dt \) denotes the area under the curve where concentration of indicator is plotted versus time (Agerskov et al\(^{10}\)).

The result of the flow measurements are shown in the table. There was no difference in the relative blood flow calculated from the isotope studies and arteriovenous oxygen differences, indicating that the assumption of constant O₂ consumption in horizontal and tilted position is valid.

Relative Vascular Resistance

Relative vascular resistance was calculated as the relative pressure gradient

\[ \frac{\Delta P_{\text{test}}}{\Delta P_{\text{horizontal}}} \]

divided by the relative flow in the tilted position,

\[ \frac{F_{\text{horizontal}}}{F_{\text{test}}} \]

For the whole leg \( \Delta P \) represents the difference in mean blood pressure in the common femoral artery and femoral vein.

Relative resistance in collateral arteries was calculated as the relative drop in arterial mean pressure from the common femoral artery to the popliteal artery divided the femoral blood flow (Thulesius\(^{12}\))

\[ \frac{R_{\text{collateral (test)}}}{R_{\text{collateral (horizontal)}}} = \frac{(P_{\text{femoral}} - P_{\text{popliteal}})_{\text{test}}}{(P_{\text{femoral}} - P_{\text{popliteal}})_{\text{horizontal}}} \cdot \frac{F_{\text{test}}}{F_{\text{horizontal}}} \]

Statistics

Student’s t test for paired samples was used to test significance.

The results are given as mean values ± 1SE.

Results

The results in absolute values are summarised in fig 2.

Responses to Head-up Tilt Before Blockade

Passive head-up tilt caused a slight increase in systemic arterial pressure of 3±4% (P>0.4). Total leg
artery of 5±7% (P>0.5). The calculated collateral resistance decreased significantly by 22±8% (P<0.05) (fig 3). Heart rate varied between 72 to 80 beats·min⁻¹, mean 74 beats·min⁻¹.

RESPONSES TO HEAD-UP TILT AFTER EPIDURAL BLOCKADE

During epidural blockade and passive head-up tilt the systemic arterial blood pressure decreased slightly by 4±5% (P>0.4). Total leg blood flow decreased by 22±6% (P<0.02). Total vascular resistance increased on average by 26±9% (P<0.05). Head up tilt caused a significant decrease in the pressure drop over the collateral arteries (P\text{femoral}-P\text{popliteal}) of 14±5% (P<0.05) during epidural blockade. Resistance in the collateral arteries increased by 14±10% (P>0.20) (fig 4).

The ankle pressure remained constant. Heart rate varied between 76 to 84 beats·min⁻¹, mean 80 beats·min⁻¹.
Collateral artery resistance

Collateral artery resistance

FIG 4 A Percentage relative changes during 40º head-up tilt to horizontal values before and during epidural blockade.

Top: Change in pressure gradient between the common femoral artery and vein.
Middle: Change in femoral blood flow.
Bottom: The calculated resistance change in the total leg.

B Top: Change in pressure gradient between the common femoral and popliteal artery.
Middle: Change in common femoral blood flow.
Bottom: The calculated change in resistance in the collateral arteries in the thigh.
○: before epidural blockade
□: during epidural blockade

Discussion

The main result of the present study is that tilting in unblocked patients caused a 30% fall in total leg blood flow without change in the pressure gradient from the common femoral to the popliteal artery, indicating an increase in collateral resistance of 50% (fig 4). Following central sympathetic blockade the tilt induced increase in collateral resistance was reduced by 70% as the femoral-popliteal pressure gradient now decreased by 15% and femoral blood flow decreased by 20%, which corresponded to an increase in collateral resistance of only 15%.

Calculation of relative resistance in the collateral arteries as the relative pressure drop over the collateral vessels divided by relative blood flow in the femoral artery is based upon the assumptions that the pressure drop is mainly influenced by blood flow in the thigh, and that head up tilt causes an uniform relative decrease in thigh blood flow.

Blood flow in the thigh is most important for the pressure drop over the collateral arteries because circulatory arrest below the knee reduces the pressure drop by only 30% (Agerskov submitted). If the blood flow in the thigh was of only minor importance to the pressure drop over the collateral arteries then it would be expected that circulatory arrest below the knee would eliminate the pressure drop. Thus, blood flow to the thigh plays the dominant role in the pressure drop over collateral arteries. In a comparative group of patients it has been shown that blood flow in the thigh muscle as measured by the local 133Xe washout technique changed uniformly while tilt (Agerskov, submitted). Furthermore, Henriksen found, in patients with proximal arterial occlusion and rest pain, that the vasocostriction in subcutaneous tissue just below the knee during lowering was not different from that seen in normal individuals. Thus the above mentioned assumptions for calculating relative collateral resistance seem to be valid. This also rules out the possibility that the observations were due only to changes in arteriolar tone during tilt. If so, it would be necessary to assume that the decrease in total leg blood during tilt alone is due to arteriolar constriction in tissues above the level where the pressure drop occurs whereas blood flow in the collateral arteries with the significant flow resistance should remain constant.

Thus the observation that the pressure drop over the collateral arteries remained constant despite the decrease in total leg blood flow during head up tilt suggests that tilt causes constriction of the collateral arteries by-passing a superficial femoral occlusion.

If the tilt induced constriction of the collateral arteries alone was due to a myogenic response to increase in vascular transmural pressure (Bayliss, Folkow, Johnson, Grande and Mellander) this observation could be explained by a smaller increase in transmural pressure in the collateral arteries caused by a fall in systemic arterial pressure in the tilted position during epidural blockade. The increase in transmural pressure in the common femoral artery during head up tilt was, however, reduced by only 4% during epidural blockade. This indicates that only a minor part of the reduction of the tilt induced constriction of the collateral arteries during epidural blockade can be explained by a less pronounced increase in transmural...
pressure in the collateral arteries. The diminished constriction seems therefore mainly to be due to the central nervous blockade. This taken together with the observation that intra-arterial administered phentolamine in low doses, which induces a selectively α-receptor blockade, caused a similar reduction in the constriction of the collateral vessels during tilt (Agerskov and Henriksen), strongly suggests that the observed constriction of the collateral arteries during tilt is mainly neurogenically mediated by means of a reflex arc comprising the spinal cord and/or higher centres in the brain. This is compatible with the observation that adrenergic sympathetic vasoconstrictor fibres richly innervate the collateral arteries (Matsubara).

Local sympathetic reflex mechanisms (Henriksen) do not seem to be important for the tilt induced increase in collateral resistance since there was only a small difference in the results obtained by epidural blockade and by local α-receptor blockade.

The remaining increase in collateral resistance during tilt and epidural blockade might be caused by a myogenic response of the vascular smooth muscle cells to the increase in vascular transmural pressure (Bayliss, Folkow, Johnsen, Grände and Mellander).

The evidence obtained further suggests that the tone of the collateral arteries in the resting supine position is influenced by centrally elicited sympathetic vasoconstrictor activity. Epidural blockade caused a decrease in calculated collateral resistance of 20% in the horizontal position. This cannot be explained by a decrease in myogenic vasoconstrictor activity since blood pressure in the common femoral artery remained constant.

The calculated reduced collateral resistance in supine position following epidural blockade may partly be due to a fall in blood viscosity following isotonic saline infusion. However, only a slight insignificant decrease in haematocrit of about 7% was seen after the saline infusion, indicating that changes in blood viscosity did not contribute significantly to the calculated decrease in collateral resistance.

Thus, the decrease in collateral resistance seems to be caused mainly by the central blockade of the sympathetic outflow to the collateral arteries.

The conclusion that sympathetic reflex mechanisms play an important role for the tone in the collateral arteries is compatible with the findings of Thulesius, who induced occlusion of the femoral artery in cats.

In normal subjects the tilt induced decrease in leg blood flow can be ascribed to constriction of the arterioles because the tone of the main arteries is without importance for the total vascular resistance. In the patients, with occlusion of the superficial femoral artery, however, the collaterals bypassing the occlusion make a significant contribution to the total flow resistance in the part of the leg supplied by the collaterals so that augmented constriction of the collateral arteries during head up tilt seems to contribute to the observed decrease in total leg blood flow.

References