Stability of access resistance during haemodialysis

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Abstract

Background. Access blood flow (Qac) is considered a useful indicator in the surveillance of haemodialysis access function. However, changes in Qac may be due to changes in blood pressure and/or to changes in access resistance (AR).

Methods. Weekly readings of Qac, cardiac output, and arterial blood pressure measured early and late during haemodialysis were obtained in 11 patients for a period of 3 weeks. Qac was determined from thermodilution of extracorporeal blood returning to the patient with reversed placement of blood lines and by measurement of arterial and venous blood temperatures in the extracorporeal circulation. Data are given as mean ± SE. Recent indicator dilution techniques have considerably simplified the procedure of access flow measurements and total peripheral resistance (TPR) increased, but when MAP and TPR increased. Linear regressions between the change in access flow and the change in MAP (ΔQac% = 0.80*ΔMAP%−1.6, r² = 0.39), and the change in TPR (ΔQac% = 0.54*ΔTPR%−9.2, r² = 0.35) respectively, were significant (P < 0.001). Whereas Qac significantly decreased (−8.4 ± 3.3%, P < 0.01) during the same treatment, AR remained unchanged (4.7 ± 3.2%; P = NS). AR for all studies was 16.5 ± 1.0 peripheral resistance units (1 PRU = 2.226 kPa min l⁻¹). There was a trend for resistance to increase (5.1 ± 2.6%, P = NS) and for flow to decrease (−6.1 ± 2.3%, P = NS) during the 3 weeks of the study.

Conclusion. Qac measured during haemodialysis is variable and depends on haemodynamics, but AR is constant. AR is related to the physical structure of the peripheral access. Because of its intradialytic stability AR may be better suited as an indicator of access function.

Key words: access blood flow; access resistance; blood pressure; total peripheral resistance; vascular access

Introduction

Access thrombosis, one of the main causes of access failure, is an important problem in the management of haemodialysis patients. It requires invasive, time consuming, and expensive procedures which are not without risk. Access flow is considered an indicator of access function. A number of studies have indicated that low access flow predicts imminent access thrombosis [1–5]. Access blood flow has been measured by a variety of techniques such as constant infusion of ⁹⁹ᵐTc and Doppler imaging; however, the methods are difficult to apply, operator dependent, and expensive. Recent indicator dilution techniques have considerably simplified the procedure of access flow measurements which are performed during haemodialysis [6,7].

Haemodialysis and ultrafiltration may have considerable haemodynamic effects resulting in haemodialysis hypotension [8] leading to the question as to whether access flow remains stable under such conditions. If access flow varies because of haemodynamic effects, this cannot be attributed to local changes in access function but must be related to central (cardiac output) and peripheral (systemic vascular resistance) effects. Thus access flow may not be a good measure for surveillance of access function. However, if access resistance is calculated from local flow and pressure data, the effects of haemodynamic factors are excluded.

It was the purpose of this study to analyse access flow during haemodialysis as a function of arterial pressure, total peripheral resistance, and cardiac output.

Subjects and methods

Patients

Patient measurements were performed during scheduled dialysis treatments. Access flow was measured in 11 patients who gave informed consent to participate in the study as approved by the Beth Israel Medical Center Institutional Review Board.
Protocol

Patients were studied once a week for a period of 3 weeks. Dialysis accesses consisted of seven fistulae and four arteriovenous grafts, four of which were located on the upper arm. Each study consisted of four access flow measurements, of which the first two measurements (indices 1 and 2) were made within the first hour and the last two measurements (indices 3 and 4) within the last hour of the dialysis treatment. Access flows were measured by the ‘double recirculation technique’ where the recirculation fraction (R) of a thermal bolus was measured with correct (index n) and with reversed (index x) connection of blood lines as described previously [9]. A comparison of this technique to the original ultrasound dilution technique [6] has shown good correlation [10].

Measurement

Recirculation fractions were measured by thermodilution using the constant infusion approach [11,12]. Temperatures in the extracorporeal circulation were measured by heated thermistor probes attached to the extracorporeal circulation as described elsewhere (Blood Temperature Monitor, supplied by Fresenius Medical Care, Bad Homburg, Germany) [13,14]. Cardiac output (CO) was obtained from thoracic bioimpedance measurements (NCCOM3, supplied by BoMed, Irvine, CA) [15]. Arterial blood pressures were measured on the contralateral access arm by an oscillographic cuff technique (BPS08, supplied by Fresenius Medical Care, Walnut Creek, CA).

Access flow

Access blood flow (Qac) was calculated from the recirculation fraction (Rn) obtained with reversed placement (index x) of blood lines from a formula comparable to the original formula derived by Krivitski [6]. The difference from the original formula is due to the constant infusion approach of the indicator dilution and to the response time of the thermistor probes used in this study. The formula derived by Krivitski requires separation of the first indicator transient which is related to access blood flow from subsequent indicator transients which are related to recirculation through the cardiopulmonary loop. Without separation of the first transient from subsequent transients, effects caused by recirculation of indicator through the cardiopulmonary loop have to be considered in the calculation of access blood flow as derived elsewhere [11]:

\[ Q_{ac} = \frac{1 - R_n}{R_n(1 - CPR)} \times (Q_{b,n} - UFR) \]  

(1)

where \( R_n \) is the recirculation fraction with reversed (index x) placement of blood lines, CPR is the amount of cardiopulmonary recirculation which is the fraction of access flow over cardiac output [16], \( Q_{b,n} \) is the extracorporeal blood flow with reversed (index x) placement of blood lines, and \( UFR \) is the ultrafiltration rate.

The amount of cardiopulmonary recirculation (CPR) is determined by the ‘double recirculation technique’ [9]:

\[ CPR = \frac{R_n(1 - R_n)}{R_n(1 - R_n)} \times \frac{Q_{b,n}}{Q_{b,n} - UFR} \]

(2)

where \( R_n \) and \( R_x \) are the recirculation fraction measured with reversed (index x) and correct (index n) placement of blood lines respectively, \( Q_{b,n} \) and \( Q_{b,x} \) is the extracorporeal blood flow with reversed (index x) and correct (index n) placement of blood lines respectively, and where UFR is the ultrafiltration rate.

Extracorporeal blood flows were corrected for varying pump-preloads according to the relationship given by Depner et al. [17].

\[ CPR = \frac{Q_{ac} - CO}{Q_{ac} - CO} \]

Resistance

Total peripheral resistance (TPR) was calculated from mean arterial pressure and cardiac output. Systemic vascular resistance (SVR), the resistance of the circulation excluding the access loop, was calculated from mean arterial pressure and systemic blood flow, determined from the difference of cardiac output and access flow (\( Q_{ac} - CO - Q_{ac} \)). Access resistance (AR) was calculated from mean arterial pressure and access flow. Resistance is given in peripheral resistance units (PRU). The PRU is derived from mean values for the total peripheral resistance of the human circulation which refers to a mean pressure drop of 100 mmHg for an average cardiac output of 100 ml/s. The SI unit for vascular resistance is kPa min l-1 (1 PRU = 2.226 kPa min l-1).

Data analysis

Data are presented as mean ± standard error (x ± SE). The relative change of a variable (X) within a given observation period was calculated as

\[ \Delta X\% = \left( \frac{X_f - X_0}{X_0} \right) \times 100 \]

(3)

where indices 0 and 1 refer to the beginning and to the end of the observation period, respectively. Relative changes calculated according to Equation 3 were compared by one-sample sign test. Repeated measurements of the same variable were compared by Wilcoxon signed rank test. Analysis of variance was used to describe the relationship between type and location of access and access variables. A probability of \( P<0.05 \) was assumed to reject the null hypothesis. Data analysis was performed using StatView 4.5 software (supplied by Abacus Concepts, Berkeley, CA).

Results

Repeated measurements of access flow made in close succession showed good reproducibility (Figure 1a). The second measurement (index 2) was not different from the first measurement (index 1) (\( P=NS \)) and showed a high linear correlation: \( Q_{ac,2} = 0.98*Q_{ac,1} + 0.025, r^2=0.95 \). The slope of the relationship was not different from identity and the intercept was not different from zero. However, flows measured late in dialysis (index 4) showed a significant change (\( P<0.05 \)) and a systematic decrease to 83% of early dialysis values (index 1) and an increased variability: \( Q_{ac,4} = 0.83*Q_{ac,1} + 0.079, r^2=0.74 \) (Figure 1b).

The change in access flow during haemodialysis was related to the intradialytic change in mean arterial pressure (MAP) (Figure 2a). As MAP decreased, measured access flow also decreased. Linear least-squares fit gave a strong and significant correlation: \( \Delta Q_{ac,1} = 0.80*\Delta MAP - 1.6, r^2=0.39 \) (\( P<0.001 \)). Cardiac output decreased by 9.1 ± 13.2% during treatments but there was no correlation between the change...
in cardiac output and the change in access flow: ΔQac% = 0.2ΔCO% - 10.3, r² = 0.0 (P = NS, data not shown). However, a strong linear correlation was obtained between intradialytic changes in access flow and changes in total peripheral resistance: ΔQac% = 0.54ΔTPR% - 9.2, r² = 0.35 (P < 0.001) (Figure 2b).

As total peripheral resistance decreased, measured access flow also decreased. Changes in total peripheral resistance and systemic vascular resistance were highly correlated: ΔSVR% = 1.01ΔTPR% - 0.14, r² = 0.86 (P < 0.001) (Figure 3).

Comparison of systemic vascular resistance measured at the beginning (index 1) and before the end (index 4) of haemodialysis showed a systematic decrease (Figure 4a). However, access resistance for the whole group of patients studied remained unchanged during the same observation phase (P = NS) (Figure 4b).

A summary of intradialytic and interdialytic changes of access resistance in the individual patient showed a trend for access resistance to increase during the same treatment (ΔAR% = 4.7 ± 3.2%, P = NS) (Figure 5a) and in subsequent treatments (ΔAR% = 5.1 ± 2.6%, P = NS) (Figure 5b).

The mean access resistance for all studies was 16.5 ± 1.0 PRU (Table 1). When analysed for type (fistula or graft) and location (forearm or upper arm), forearm grafts had the highest resistance (21.0 ± 2.2 PRU), followed by upper arm grafts (18.1 ± 1.0 PRU), forearm fistulae (17.5 ± 1.3 PRU), and upper arm fistulae (8.3 ± 0.8 PRU). The difference in resistance was significant both between the type (graft vs fistula, P < 0.05) and the location (upper arm vs forearm, P < 0.05) of the peripheral access.
Fig. 4a,b. Total peripheral and access resistance. (a) Total peripheral resistance dropped between measurements done early (index 1) and late (index 4) in dialysis: $SVR_4 = 0.61 \times SVR_1 + 0.97$, $r^2 = 0.43$. (b) Access resistance remained unchanged between measurements done early (index 1) and late (index 4) in dialysis: $AR_4 = 0.95 \times AR_1 + 1.2$, $r^2 = 0.70$.

Discussion

In this study access flow, cardiac output, and arterial blood pressure were measured during hemodialysis and analyzed with the purpose of identifying access resistance as a parameter of access function. While access flow and hemodynamic parameters varied throughout the hemodialysis treatment, access resistance remained constant. Given the intradialytic variability of access flow as opposed to the intradialytic stability of access resistance it is therefore assumed that measurements of access resistance may be better qualified to characterize access function and diagnose the presence of early stenosis.

Control of access flow

The vascular access connects the arterial to the venous side of the vascular system and thus establishes a loop parallel to the systemic circulation. The actual blood flow through the access is the resultant of a local component, i.e. the local resistance in the access, of a central component, i.e. the cardiac output, and of a peripheral component, i.e. systemic vascular resistance.

Arterial blood pressure (MAP) and extracorporeal blood flow ($Q_{ec}$) vary between treatments and within the same hemodialysis treatment. The electrical model of the peripheral access and the extracorporeal circulation predicts that access blood flow is independent of $Q_b$ in the absence of a stenosis between arterial and venous fistula needles [18]. The model also predicts that $Q_{ec}$ depends on MAP. Therefore access flow has to be considered as a variable, and changes in access flow do not necessarily reflect local changes in the access itself.

For the understanding of intradialytic changes in access flow it is helpful to recognize the parallel arrangement of access and systemic circulations which may cause a systemic steal of access blood flow with low systemic vascular resistance. When total peripheral resistance decreased during dialysis, access blood flow also declined. However, when total peripheral resistance increased, access blood flow also increased.

In the parallel arrangement of access and systemic vascular resistance, the change in access flow is determined by the resistance in the access and the systemic vascular resistance. If these resistances are constant, then access flow will be constant as well. However, if either resistance changes, access flow will also change.

Table 1. Access resistance in PRU (peripheral resistance units) in upper arm (u) and forearm (l) grafts (g) and fistulae (f)

<table>
<thead>
<tr>
<th>Type</th>
<th>x</th>
<th>SD</th>
<th>SE</th>
<th>N</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>16.46</td>
<td>5.79</td>
<td>1.02</td>
<td>11</td>
<td>5.80</td>
<td>26.87</td>
</tr>
<tr>
<td>f, l</td>
<td>17.52</td>
<td>5.06</td>
<td>1.31</td>
<td>5</td>
<td>9.00</td>
<td>26.87</td>
</tr>
<tr>
<td>f, u</td>
<td>8.32</td>
<td>2.00</td>
<td>0.82</td>
<td>2</td>
<td>5.80</td>
<td>10.78</td>
</tr>
<tr>
<td>g, l</td>
<td>21.05</td>
<td>4.95</td>
<td>2.21</td>
<td>2</td>
<td>13.42</td>
<td>26.23</td>
</tr>
<tr>
<td>g, u</td>
<td>18.12</td>
<td>2.38</td>
<td>0.97</td>
<td>2</td>
<td>14.56</td>
<td>21.75</td>
</tr>
</tbody>
</table>

The model predicts that $Q_{ec}$ depends on MAP. Therefore access flow has to be considered as a variable, and changes in access flow do not necessarily reflect local changes in the access itself.
loops and assuming that the arteriovenous pressure gradient is the same across both access and systemic circulations \( p_{\text{art,ac}} = p_{\text{art,sys}} \), access flow is determined by the ratio of systemic vascular resistance (SVR) to access loop resistance (AR) and by systemic blood flow \( (Q_{\text{sys}}) \) according to the relation:

\[
Q_{\text{ac}} = \frac{Q_{\text{sys}}}{AR} \cdot SVR
\]

With constant access resistance, and without changes in systemic perfusion, access blood flow changes in proportion to the changes in systemic vascular resistance. While this assumption may be true for most resting and supine patients on haemodialysis without large changes in cardiac output and systemic perfusion, a drop in systemic vascular resistance such as seen with exercising haemodialysis patients may well lead to an increase in access flow because of increased arterial pressures.

Access resistance, the pressure drop in the access per unit blood flow, is determined by the local properties of the conduit. Access resistance has been considered as an indicator for access function. However, because of the difficulties of measuring the access blood flow and the access pressure drop \( \Delta p = p_{\text{art}} - p_{\text{ven}} \), indirect measures of access resistance have been used. Monitoring of venous line pressure at a standard blood flow of 200 ml/min was helpful in detecting outlet obstruction [19]. Measurement of intra-access pressure at zero blood flow improved the sensitivity to detect venous outlet stenosis because this approach was insensitive to variability in blood viscosity and needle size [20]. The predictive power of high intra-access pressure was further increased when measurements were normalized for systemic arterial [21] and for peripheral venous pressures [22].

With new techniques that measure access blood flow during haemodialysis one of the difficulties of measuring access resistance may be resolved. However, the determination of the pressure drop \( \Delta p \) in the access remains a problem. In this study it was assumed that the inflow pressure was equal to MAP and that the outflow pressure was constant. There was a trend for access resistance to increase during haemodialysis (\( \Delta AR/\% = 4.6 \pm 3.2\% \), \( P = \text{NS} \)). Ultrafiltration-induced haemoconcentration is likely to increase access resistance because of increased blood viscosity. Haemoconcentration may also lead to an increase in peripheral venous pressure which will lead to an overestimation of access resistance if peripheral venous pressures are assumed to remain unchanged.

A comparison of subsequent treatments showed a trend for access flow to decrease and access resistance to increase during the three week observation period. The increase in access resistance was significant in grafts \( (\Delta AR/\% = 14.4 \pm 3.9\% \), \( P < 0.05 \)). It is not clear whether this increase was already due to changes in access structure such as intimal hyperplasia.

This study shows that whereas access blood flow, arterial pressure, cardiac output, and total peripheral resistance significantly changed during haemodialysis, access resistance remained constant. Repeated measurement of this parameter as a potential indicator of a failing access may provide an improved approach to a major problem in dialysis.

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References

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