Vasopressin secretion by hypertonic saline infusion during hemodialysis: effect of cardiopulmonary recirculation

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Abstract

Background. Intradialytic hypotension is the most common and severe acute complication of hemodialysis therapy. In our previous study, infusion of 20 mL of 10% saline into the venous line of a dialyzer increased blood pressure during dialysis hypotension by stimulating arginine vasopressin (AVP) secretion, independent of its effect on plasma volume (PV). This study examines the mechanism by which a small amount of hypertonic solution stimulates AVP secretion.

Methods. Hemodialysis patients were infused with 20 mL of 2.5 M saline (100 mOsm) over 5 (Protocol 1) or 2 min (Protocol 2) or with isotonic saline (Protocol 3) into the venous line.

Results. Arterial plasma osmolality (Posm) increased by 28.1 and 16.0 (P < 0.0001), while peripheral venous Posm increased by only 8.6 and 8.9 mOsm/kg H₂O (P < 0.001) in Protocols 2 and 1, respectively. Plasma AVP (P₂AVP) increased significantly by 18.6 and 5.6 pg/mL, PV by 7.2 and 5.5% and mean arterial pressure (MAP) by 15.0 and 7.2 mmHg in Protocols 2 and 1, respectively. Thus, there were large differences in Posm between arterial and peripheral venous blood; osmolar gap, P₂AVP and MAP increased in proportion to the infusion rate. Isotonic saline (30.8 mOsm) infusion increased PV by 8.7% and MAP by 7.2 mmHg.

Conclusions. Our results indicate that by a mechanism similar to cardiopulmonary recirculation, hypertonic saline infusion caused a striking increase in arterial Posm that enhanced AVP secretion and raised blood pressure. The effect of hypertonic saline on PV was less than one-third of isotonic saline under similar osmolar loads.

Keywords: cardiopulmonary recirculation; hemodialysis; hypertonic saline; intradialytic hypotension; vasopressin

Introduction

Intradialytic hypotension is the most common complication of hemodialysis therapy [1]. It is also an independent risk factor for mortality in hemodialysis patients [2]. Intravenous infusion of hypertonic solutions, such as hypertonic saline, is an effective treatment for intradialytic hypotension [1, 3]. Hypertonic solutions have traditionally been considered to act as plasma volume expanders by facilitating the shift of extravascular fluid into the intravascular space [1, 3, 4]. In our previous study, we demonstrated that infusion of a small amount of hypertonic solution (20 mL of 10% saline or 50% glucose) into the venous line of a dialyzer raises blood pressure in intradialytic hypotension by stimulating arginine vasopressin (AVP) secretion, independent of the effect on plasma volume (PV) [5]. The purpose of this clinical study was to clarify the mechanism by which a small amount of hypertonic solution stimulates AVP secretion and raises blood pressure during dialysis. In addition, we studied the relative importance of AVP and PV in controlling blood pressure.

Materials and methods

Subjects

We examined 64 patients on maintenance hemodialysis therapy, who had a high incidence of hypotension during dialysis. Hemodialysis was performed three times a week using bicarbonate dialyze with a sodium concentration of 140 mEq/L and a glucose concentration of 100 mg/dL. Blood flow rate (Qb) and dialyzate flow rate were 200 and 500 mL/min, respectively, as usually used in Japan. All patients had arteriovenous fistulas and underwent ultrafiltration at a constant rate for 4 h until dry weight in each session. This study was approved by the ethics committee of our hospital, and all study participants provided written informed consent.

Protocols

Intradialytic hypotension is defined as a decrease in systolic blood pressure (SBP) to <100 mmHg during dialysis, with a decrease in SBP of at least 20 mmHg from the predialysis value [5]. Under these conditions of intradialytic hypotension, we carried out three infusion protocols. In Protocol 1 (n = 15), 20 mL of 2.5 M (14.6%) saline (100 mOsm) was infused intravenously from the venous sample port of the hemodialysis blood line over 5 min. We obtained blood samples from the arterial blood line sample port just before infusion (t = 0) and at 5 and 10 min after the initiation of infusion. Peripheral venous blood samples were obtained from the contralateral arm at 5 min. Blood pressure and pulse rate were also measured. In Protocol 2 (n = 15), the same solution (20 mL of 2.5 M saline) was infused into the venous line over 2 min. We obtained arterial blood samples at 0, 2, 3, 5 and 10 min. Peripheral venous blood and venous line blood were obtained at 2 and 3 min, respectively. In this group, in order to make the total blood volume removed as small as possible, blood samples were obtained at 2 min from seven patients (Group 2A) and at 3 min from the remaining eight patients (Group 2B). In Protocol 3, 100 mL (n = 10), 75 mL (n = 8) or 50 mL (n = 8) of isotonic (0.9%) saline was infused over 2 min. Arterial blood was obtained at 0, 2, 3, 5 and 10 min. Table 1 lists the numbers and clinical characteristics of patients enrolled in each treatment group.
Table 2. Patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>2.5 M saline infusion (20 mL)</th>
<th>Isotonic saline infusion</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Over 5 min (n = 15)</td>
<td>Over 2 min (n = 15)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>66 (39–86)</td>
<td>69 (56–84)</td>
</tr>
<tr>
<td>Male/female</td>
<td>11/4</td>
<td>5/5</td>
</tr>
<tr>
<td>Dialysis duration (years)</td>
<td>6 (1–21)</td>
<td>6 (1–17)</td>
</tr>
<tr>
<td>Cause of kidney disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Glomerulonephritis</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Nephrosclerosis</td>
<td>4</td>
<td>2</td>
</tr>
</tbody>
</table>

Values expressed as mean (range) or number of patients.

To compare the effect of venous line infusion and peripheral vein infusion, 20 mL of 2.5 M saline was infused over 5 min into a peripheral vein of the non-fistulated arm in six patients (average age, 68 years; four men and two women). Also, in order to prevent access recirculation (AR) in the vascular access, a portion of the vein between arterial and venous needles was occluded using finger pressure during infusion of 2.5 M saline over 2 min in two patients (64-year-old man and 60-year-old woman).

Measurements

Serum sodium and potassium were measured using ion-specific electrodes. We determined plasma osmolality (Posm) by the freezing point depression method using an osmometer. Plasma concentrations of total protein (TP) and urea ([blood urea nitrogen (BUN)]) were measured using an autoanalyzer (Bio Majesty; JEOL, Tokyo, Japan). Plasma samples for AVP were stored frozen at −30°C until hormone levels were measured. We measured plasma AVP concentration using an AVP radioimmunoassay kit (Mitsubishi Chemicals and Yatoron Ltd, Tokyo, Japan) as described previously [6, 7].

Calculations and statistical analysis

Mean arterial pressure (MAP) was calculated as diastolic blood pressure plus one-third pulse pressure. The percent change in plasma volume (%ΔPV) was calculated from before (B) and after (A) hemoglobin (Hb) and hematocrit (Hct) values using the following equation [8]:

\[
\frac{\% \Delta PV_{\text{Hb,Hct}}}{\% \Delta PV_{\text{TP}}} = 100 \left[ \frac{\text{Hb}_A \times \left( 1 - \left( \text{Hct}_A \times 10^{-2} \right) \right)}{\text{Hb}_B \times \left( 1 - \left( \text{Hct}_B \times 10^{-2} \right) \right)} - 1 \right] 
\]

%ΔPV was also calculated from before (B) and after (A) TP [9]:

\[
% \Delta PV_{\text{TP}} = \frac{\text{TP}_A - \text{TP}_B}{\text{TP}_B} \times 100.
\]

Percent recirculation (%R) was calculated using the following equation:

\[
%R = \frac{P - A}{P} \times 100,
\]

wherein P is BUN in peripheral venous blood and A and V are BUN in arterial and venous line blood, respectively. Measured variables are expressed as mean ± SEM. We compared the means using the Student’s t-test.

Results

Effect of 2.5 M saline infusion (20 mL over 5 min)

As shown in Table 2 and Figure 1, on average, the infusion increased arterial Posm by 16.0 mOsm/kg H2O, sodium concentration by 8.3 mEq/L, plasma AVP concentration (PAVP) by 5.6 pg/mL and MAP by 7.2 mmHg. The %ΔPV_{Hb,Hct} and %Δ PV_{TP} increased by 5.6 and 5.5%, respectively. Arterial Posm, sodium concentration and %ΔPV_{TP} measured at 5 min were higher than peripheral venous measurements (P < 0.0001, P < 0.001 and P < 0.05, respectively). Hct at 0 min was 36.8 ± 1.5%.

Effect of 2.5 M saline infusion (20 mL over 2 min)

To clarify the effect of infusion rate, the same solution was infused over 2 min. As shown in Table 3 and Figure 1, infusion over 2 min caused a greater increase in arterial Posm (P < 0.001) than infusion over 5 min, indicating that the increase is proportional to the infusion rate rather than the total amount of saline infused. The greater increase in Posm was followed by a greater increase in P_AVP (P < 0.005) and MAP (P < 0.05). In contrast, the effect of infusion rate on PV was relatively small. Thus, while %ΔPV_{TP} showed a significantly greater increase (P < 0.05), %ΔPV_{Hb,Hct} did not (P = 0.5). Arterial Posm was markedly higher than peripheral venous Posm at 2 (P < 0.001) and 3 min (P < 0.01). Furthermore, arterial %ΔPV_{TP} was higher than peripheral venous %ΔPV_{TP} at 2 and 3 min (P < 0.05). Hct at 0 min was 37.2 ± 1.4%. There was no significant difference in any parameter at 0 min between Groups 2A and 2B. Posm of postdialyzer venous line blood (V line Posm) obtained upstream of the infusion point was 280.6 ± 1.97 mOsm/kg H2O (n = 7) at 2 min, indicating that it was in osmotic equilibrium with the dialyzeate.

Changes in plasma osmolality (ΔPosm)

As shown in Figure 2A, arterial ΔPosm increased abruptly by an average of 28.1 mOsm/kg H2O during infusion of 2.5 M saline infusion over 2 min and then decreased to the estimated osmotic equilibrium. The theoretical value of ΔPosm at osmotic equilibrium was estimated to be 3.6 mOsm/kg H2O after infusion in a 50 kg man, assuming total body water (TBW) (55% of body weight) and ΔPosm to be osmolar load added/TBW [10]. Thus, peak arterial ΔPosm was 7-fold greater than the theoretical estimate. On the contrary, peripheral venous ΔPosm was much smaller (8.6 mOsm/kg H2O) than arterial ΔPosm, with a large difference between them (19.5 mOsm/kg H2O). In the two patients in whom AR was blocked, arterial Posm increased similarly by 23 and 27 mOsm/kg H2O, and peripheral venous Posm increased by 4 and 7 mOsm/kg H2O at 2 min. These results suggest that the effect of AR on arterial ΔPosm is small.

As shown in Figure 2B, during a 5-min infusion, arterial ΔPosm was smaller (16.0 mOsm/kg H2O) and, therefore, the difference in ΔPosm was less marked (7.1 mOsm/kg H2O).
Effect of 2.5 M saline infusion (20 mL over 5 min) into a peripheral vein

Four of six patients complained of slight to severe vascular pain during infusion and it was not possible to complete infusion in two patients. The remaining four patients (Table 4) gave average values in each measured parameter similar to those of venous line infusion (Table 2).

![Graphs showing changes in plasma osmolality, MAP, P<sub>AVP</sub>, and ΔPV over time with saline infusion.]

**Table 2. Effect of 2.5 M saline infusion (20 mL over 5 min)**

<table>
<thead>
<tr>
<th>Time after starting infusion (min)</th>
<th>Arterial blood</th>
<th>Peripheral venous blood</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
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<tr>
<td>10</td>
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**Table 3. Theoretical estimation of plasma osmolality difference between arterial (A) and peripheral venous blood (P) [Posm (A − P)]**

Theoretical estimation of plasma osmolality difference between arterial (A) and peripheral venous blood (P) [Posm (A − P)]

Theory: We considered that the difference in Posm between arterial and peripheral venous blood (Figure 2) can be explained as follows: venous line blood infused with hypertonic saline enters the heart rapidly, where it mixes

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Fig. 1. Effect of infusing hypertonic or isotonic saline on plasma osmolality (Posm), plasma vasopressin concentration (P<sub>AVP</sub>), MAP and percent change in plasma volume (ΔPV) calculated from changes in hemoglobin and hematocrit. Open circles denote infusion of 2.5 M saline (20 mL over 2 min), solid circles denote infusion of 2.5 M saline (20 mL over 5 min) and triangles denote infusion of isotonic saline (100 mL over 2 min). *P < 0.05, **P < 0.01 - isotonic saline infusion.
with systemic venous blood. Here, the volume of blood entering the heart equals cardiac output. It then passes through the heart and pulmonary blood vessels without osmotic equilibration with the extravascular fluid. A portion of blood then returns to the vascular access. These events significantly increase Posm in arterial blood compared to peripheral venous blood because the latter has passed through the systemic capillary microcirculation, where it approaches osmotic equilibrium with TBW.

This process is similar to a phenomenon called cardiopulmonary recirculation (CPR) [11, 12]. CPR occurs when blood with reduced BUN concentration that has just left the dialyzer outlet port returns to the dialyzer inlet port via cardiopulmonary circulation, bypassing the systemic microcirculation. This process leads to lower arterial BUN than peripheral venous BUN because urea diffuses into the blood from the extravascular space during the systemic microcirculation.

CPR is a flow phenomenon not necessarily related to hemodialysis itself.

However, the effect of CPR is manifested when the BUN concentration of outlet blood is reduced by dialysis or, similarly, when the venous line NaCl concentration is increased by hypertonic saline infusion. Under these conditions, Posm \((A - P)\) can be calculated using the following formula:

\[
\text{Posm}(A - P) = \frac{\text{NaCl infusion rate} - (\text{peripheral venous Posm} - \text{V line Posm}) \times Qb \times (1 - \text{Hct} \times 10^{-2})}{\text{cardiac output} \times (1 - \text{Hct} \times 10^{-2})}
\]

wherein the numerator indicates net osmolar load added to venous plasma per minute (mOsm/min) and the denominator indicates cardiac output expressed as liters of plasma per minute.

For simplicity, if the difference between peripheral venous Posm and V line Posm is neglected:

\[
\text{Posm}'(A - P) = \text{NaCl infusion rate} \times \frac{1}{\text{cardiac output}} \times \frac{1}{(1 - \text{Hct} \times 10^{-2})}
\]

Calculations: If 20 mL of 2.5 M saline is infused over 2 min (50 mOsm/min), the calculated Posm \((A - P)\) or Posm’ \((A - P)\) is 19.3 or 19.8 mOsm/kg H2O, respectively, assuming a cardiac output of 4 L/min and given the following values: peripheral venous Posm = 290.5, V line Posm = 280.6 mOsm/kg H2O, Qb = 0.2 L/min and Hct = 37%. If infused over 5 min, the calculated result is 7.4 or 7.9 mOsm/kg H2O, respectively. Thus, calculated values were quite similar to measured values, indicating that a mechanism similar to CPR assumed above is actually taking place.

**Effect of isotonic saline infusions**

To elucidate the relative importance of AVP and PV on blood pressure after hypertonic saline infusions, we examined the effect of PV alone by infusing isotonic saline (Table 5). As illustrated in Figure 3, infusions of 100, 75

<table>
<thead>
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<th>Time after starting infusion (min)</th>
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<th>Peripheral venous blood</th>
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<tbody>
<tr>
<td>0</td>
<td>88.6 ± 1.9</td>
<td>89.2 ± 2.0</td>
</tr>
<tr>
<td>2</td>
<td>68.3 ± 2.6</td>
<td>71.8 ± 2.3</td>
</tr>
<tr>
<td>3</td>
<td>58.3 ± 2.3</td>
<td>63.2 ± 2.3</td>
</tr>
<tr>
<td>5</td>
<td>48.2 ± 3.1</td>
<td>54.3 ± 2.6</td>
</tr>
<tr>
<td>10</td>
<td>38.2 ± 3.2</td>
<td>45.4 ± 2.9</td>
</tr>
</tbody>
</table>

\(P = P\)-values compared with baseline values \(t = 0\), \%\(\Delta\)PV_{10-Hct}, percent change in plasma volume calculated from changes in hemoglobin and hematocrit; \%\(\Delta\)PV_{TP}, percent change in plasma volume calculated from changes in total plasma protein concentration; DBP, diastolic blood pressure; PR, pulse rate.

<table>
<thead>
<tr>
<th>Time after starting infusion (min)</th>
<th>Arterial blood</th>
<th>Peripheral venous blood</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>38.2 ± 3.2</td>
<td>45.4 ± 2.9</td>
</tr>
<tr>
<td>2</td>
<td>38.2 ± 3.2</td>
<td>45.4 ± 2.9</td>
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<tr>
<td>3</td>
<td>38.2 ± 3.2</td>
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<td>10</td>
<td>38.2 ± 3.2</td>
<td>45.4 ± 2.9</td>
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Effect of infusing 20 mL of 2.5 M saline over 2 (A) or 5 (B) min on the average change in plasma osmolality ($\Delta$Posm). Open circles denote $\Delta$Posm of arterial blood and solid circles denote $\Delta$Posm of peripheral venous blood. Triangles denote $\Delta$Posm of theoretical estimates at osmotic equilibrium. *$P < 0.01$, **$P < 0.001$ versus $\Delta$Posm of peripheral venous blood.

and 50 mL of isotonic saline increased $\%\Delta$PV$_{\text{TP}}$ by 8.7, 6.5 and 3.4% (each $P < 0.001$) and raised MAP by 5.8 ($P < 0.01$), 5.5 ($P < 0.05$) and 1.3 mmHg ($P = 0.5$) at 3 min, respectively, without any significant changes in $P_{AVP}$. On the other hand, infusing 20 mL of 2.5 M saline over 2 min raised MAP $>2$-fold of that predicted from an increase in PV alone, suggesting a combined or synergistic effect of AVP and PV on blood pressure.

As illustrated in Figure 1, 100 mL of isotonic saline increased PV to a similar extent as 20 mL of 2.5 M saline, but the 2.5 M saline raised MAP higher and longer than the isotonic saline. This suggests that on average, AVP is relatively more important than PV, especially with rapid hypertonic saline infusion.

Although the values of $\%\Delta$PV at 2 min are quite small (Table 5), this seems to indicate that uniform mixing of blood constituents throughout the vascular space did not occur at this time and accurate measurements could not be made [9].

**Percentage of recirculation**

To assess the effect of AR on arterial $\Delta$Posm, we measured percentage of recirculation ($\%R$) using the traditional urea method. When 20 mL of 2.5 M saline was infused over 2 min, $\%R$ was 12.5 ± 1.6% (range, 4.6–17.5%) at 2 min ($n = 7$) and 13.6 ± 2.0% (7.8–16.5%) at 3 min ($n = 4$).

Since it has been suggested that the method used actually measures the combined effects of both AR and CPR [12], we measured $\%R$ in two patients in whom AR was blocked. Under these conditions, $\%R$ was 13.9 and 9.3% at 2 min and 11.9 and 6.7% at 3 min, respectively. Thus, $\%R$ was just as great whether AR was blocked or not. The results suggest that the effect of AR on measured $\%R$ and, therefore, on arterial $\Delta$Posm is likely to be small, at least, in these patients.

**Discussion**

The present study clearly demonstrates that hypertonic saline infusion into the venous line raises blood pressure during dialysis hypotension by stimulating AVP secretion, confirming and extending the results of our previous study [5].

In the previous study, 20 mL of 10% saline was infused over 5 min. Arterial $\Delta$Posm at 5 min was more than 3-fold greater (9.6 mOsm/kg H$_2$O) than the theoretical estimate under osmotic equilibrium (2.5 mOsm/kg H$_2$O) [10], raising $P_{AVP}$ by 3.9 pg/mL before subsequently decreasing to the estimated value. Assuming that there is no difference in Posm between arterial and peripheral venous blood, this change in Posm seemed to contrast to the response in healthy subjects, in which 1.2 mL of 10% saline per kilogram of body weight was infused into a peripheral vein over 5 min, and venous blood samples were obtained from the contralateral arm. Under these conditions, $\Delta$Posm at 5 min (8.1 mOsm/kg H$_2$O) was almost the same as the theoretical value of osmotic equilibration (7.5 mOsm/kg H$_2$O), with $P_{AVP}$ increasing by 3.4 pg/mL [13]. Thus, it seemed that the excessive increase in arterial Posm during dialysis effectively stimulated AVP secretion. Osmotic equilibration appeared to be delayed under these conditions. However, the exact mechanism could not be determined from previous data because we did not measure arterial Posm in these normal subjects and peripheral venous Posm in these hemodialysis patients.

In the present study, we also observed a transient and striking increase in arterial Posm during hypertonic saline infusion. In addition, we demonstrated for the first time that there is a large difference in Posm between arterial blood and simultaneously obtained peripheral venous blood and that this difference increases in proportion to the infusion rate. Furthermore, we indicated that these observations can be explained by a mechanism similar to CPR.

These findings may explain how a small amount of hypertonic solution can cause a striking increase in arterial Posm and, in turn, efficiently raise $P_{AVP}$ to a sufficient level to elevate blood pressure [5]. It may also explain why hypertonic solutions are clinically more effective in correcting dialysis hypotension when administered per bolus injection or rapid infusion. On the other hand, because these changes in Posm are underestimated, the secretion of AVP as a result of hypertonic solution infusion might have been overlooked for many years.

Peripheral venous infusion of hypertonic saline had a similar effect as venous line infusion. Thus, NaCl may have entered the cardiopulmonary circulation at a similar rate. However, this procedure caused vascular pain, indicating the clinical importance and specificity of the venous line infusion. Similarly, in normal subjects, intravenous hypertonic saline infusion may also increase arterial Posm compared to peripheral venous Posm. In fact, if we take this possibility into consideration, the findings from the normal subjects described above may not necessarily contrast to...
the findings from hemodialysis patients, although we did not measure arterial Posm in these normal subjects. In this study, we measured %R by the traditional urea method to assess the possible effect of AR on arterial DPosm. It has been shown that this method overestimates AR and actually measures the combined effects of AR and CPR [12]. Recent studies using indicator techniques demonstrated that the majority of patients have, in fact, a very low degree of AR [14–16]. According to Tattersall et al. [14], although the traditional urea method indicated a mean %R of 12.5%, no AR was found when measured using saline dilution methods. In this study, blocking AR did not significantly affect %R, which suggested that the effect of AR on %R or on arterial DPosm is, if present, small.

It now seems clear that hypertonic saline infusions raise blood pressure by increasing both PAVP and PV. As to the relative importance of these two factors, we found that on average, AVP is more important than PV, especially...
with rapid infusions (Figure 1). However, we observed considerable individual variability in the response of blood pressure, P_AVP and PV, as well as in the pressor response to exogenous AVP infusions [5]. Therefore, the relative importance may vary by patient depending on underlying pathophysiological conditions of dialysis hypotension, and AVP and PV may act synergistically rather than additively under these conditions. However, we cannot also rule out the possibility that an increase in Posm may raise blood pressure through mechanisms independent of AVP or PV [17].

On the other hand, we found that the contribution of infused hypertonic saline to the increase in PV was much smaller (less than one-third) than that of isotonic saline when compared under similar osmolar load. For example, 100 mL of isotonic saline (30.8 mOsm) increased PVT by 8.7%, whereas 20 mL of 2.5 M saline (100 mOsm) increased PVT by only 7.6%. Similarly, in our previous study [5], 200 mL of isotonic saline (61.6 mOsm) increased PVT by 12.2%, while 20 mL of 10% saline (68.4 mOsm) increased PVT by only 2.8%. This degree of increase in PVT (3.5%) did not raise blood pressure significantly (Table 4 and Figure 3).

Arterial %ΔPV_TP was significantly higher than simultaneously measured peripheral venous %ΔPV_TP (Table 3). This may be explained by considering that some of the serum sodium diffused down its concentration gradient into the extravascular compartment during systemic capillary microcirculation.

Hemodynamic stability during dialysis depends, at least, on both preservation of PV and an appropriate cardiovascular compensatory reaction [1, 3, 18]. It has been shown repeatedly that hypertonic saline infusions improve hemodynamic stability [19–23]. For example, an injection of 20 mL of 10% saline every hour during dialysis can prevent intradialytic hypotension [19]. Although these effects have been explained primarily by better preservation of PV, our results strongly suggest that osmotically stimulated AVP secretion or an increase in P_AVP also plays an important role in the control of blood pressure under these conditions.

On the other hand, the failure of baroreflex-mediated AVP secretion during hemodialysis has been reported in several studies [5, 24–26], suggesting that it may contribute, at least in part, to intradialytic hypotension. Based on these findings, adequately manipulating P_AVP by several treatments may also help improve hemodynamic stability during dialysis [5, 25–28].

In conclusion, the present study is the first to demonstrate that a large difference in Posm occurs between arterial and peripheral venous blood during hypertonic saline infusion into the venous line and that this difference increases in proportion to the infusion rate. The results indicate that through a mechanism similar to CPR, the hypertonic saline infusion causes a striking increase in arterial Posm, which efficiently enhances AVP secretion and thus raises blood pressure during dialysis hypotension. The effect of hypertonic saline infusion on the increase in PV was less than one-third of isotonic saline under similar osmolar loads.

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Conflict of interest statement. None declared.

References

Exploration of the difference in incidence of renal replacement therapy between Flanders and the Netherlands—investigation of explanatory variables

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Abstract

Aim. This study investigates the difference in the incidence of renal replacement therapy (RRT) between Flanders and the Netherlands and possible explanations for this difference.

Methods. End-stage renal disease incidence data were obtained from the European Renal Association-European Dialysis and Transplant Association (ERA-EDTA). Additional sources were the National Institute of Statistics (NIS), the Central Bureau of Statistics (CBS), the Organisation for Economic Cooperation and Development (OECD) health data and the WHO Health For All database (WHO-HFA).

Results. There is remarkable difference in incidence rate of RRT between Flanders and the Netherlands, with a higher rate in Flanders. This difference is already present in patients aged 45–64 years and increases with age, being ≥2-fold higher in subjects of ≥75 years. With respect to the renal diagnoses leading to need for RRT, a higher share of especially diabetes mellitus type 2 and renovascular disease was observed in Flanders. Remarkably, the difference in incidence rate of RRT is not associated with a difference in survival on RRT, not even in the elderly, arguing against a restricted access to RRT in the Netherlands. In the general