Sodium Profiling: The Key to Reducing Symptoms of Dialysis?

Paula McLaren
Cheri Hunter

Major advances in dialysis treatment for end stage renal disease have occurred in the last 30 years; and while there have been major improvements in both technology and technique, there remains considerable intra/inter-dialytic morbidity (Bonomini, Coli, & Scolari, 1997; Churchill, 1996; Oliver, Edwards, & Churchill, 2001; Palmer, 2001; Petitclerc & Jacobs, 1995; Sadowski, Alred, & Jabs, 1993; Sang, Kovithavongs, Ulan, & Kjellstrand, 1997; Sherman, 2001; Stiller, Bonnie-Scorn, Grassman, Uhlenbusch-Korwer, & Mann, 2001). This morbidity has been described since the early 1960s and includes a variety of symptoms that may be attributed to physiological changes induced by the process of hemodialysis (Arieff, 1994; Tang et al., 2006).

The symptoms are given different names throughout the literature, including dialysis intolerance, dialysis disequilibrium syndrome, vascular instability syndrome, and dialysis fatigue. For the purpose of this article, the term dialysis intolerance will be used.

Symptoms of dialysis intolerance may present as headache, light-headedness, nausea, vomiting, muscle cramps, and hypotension either during or after the hemodialysis session. The pathophysiological explanation for these symptoms, while multifactorial, remains somewhat unclear, but the following appears to be a generally accepted description of the process among leading researchers (Bonomini, 1995; Levin & Goldstein, 1996; Movilli et al., 1997; Petitclerc & Jacobs, 1995; Sang et al., 1997; Stiller et al., 2001). The total amount of water in the body is approximately 60% of the adult human body weight. Total body water is divided between

NPHROLOGY NURSING JOURNAL ■ July-August 2007 ■ Vol. 34, No. 4

Continuing Nursing Education

Background/Aims: A systematic review was undertaken in order to critically appraise the current knowledge base of sodium profiling in hemodialysis. Between 15%-80% of patients on hemodialysis experience symptoms of dialysis intolerance every dialysis session. The purpose of this review was to identify whether sodium profiling is an effective intervention in removing or reducing these untoward effects.

Methods: A literature search was undertaken using Medline and Embase. Inclusion criteria were primary research or controlled clinical trials published between January 1990 and June 2006 and studies in the chronic dialysis setting and studies that identified sodium profiling as the intervention in hemodialysis or hemodiafiltration. Articles excluded included: those that could not establish whether sodium profiling was the intervention responsible for the outcome; articles on hemofiltration; and review articles and research pertaining to the acute setting. Thirteen articles met the inclusion criteria and were included in the final review.

Results: A number of flaws were identified with methodological adequacy and consistency of findings. It was not possible to determine whether positive effects outweighed negative effects in this review. In the majority of studies, there was a lack of follow-up and the inability to determine long-term outcomes of patients who received sodium profiling.

Conclusion: This evaluative review could not provide evidence to support the clinical use of sodium profiling in the population of patients on hemodialysis who are symptomatic. There remains a theoretical base for the use of sodium profiling, however further studies are needed providing consistency in methodology, looking not only at reduction in morbidity but effects on quality of life, long-term outcomes, and mortality.

Goal
To provide information about sodium profiling in hemodialysis.

Objectives
1. Describe the possible role sodium plays in dialysis intolerance.
2. Explain the reasons sodium profiling is thought to be useful in avoiding dialysis intolerance.
3. Analyze the methods, results, and conclusions provided from a literature review study on sodium profiling.

Note: The authors reported no actual or potential conflict of interest in relation to this continuing nursing education article.
the extra-cellular fluid (ECF) and the intracellular fluid (ICF) compartments. These two compartments differ in their electrolyte composition, with sodium being the main cation of the ECF. Equilibrium is maintained throughout the body compartments by way of osmotic equilibration and the permeability of the cell membranes (Stiller et al., 2001).

The two processes that play a major role in dialysis intolerance are solute disequilibrium and blood-volume depletion (Bonomini et al., 1997). During a dialysis session, fluid is removed via ultrafiltration primarily from the extracellular compartment, thereby reducing the plasma volume and inducing ECF volume contraction (Levin & Goldstein, 1996; Petiçlerc & Jacobs, 1995). The body attempts to compensate for this plasma volume depletion by refilling from the ICF but cannot always keep pace. This fluid shift depletes the available fluid and symptoms occur such as those described above.

Accompanying this process, there is also a rapid decline in solutes (primarily urea) during the initial stage of dialysis, inducing a fall in plasma osmolality (Levin & Goldstein, 1996). This rapid decline in urea causes disequilibrium between the ECF and the ICF, resulting in water moving from the extracellular compartment to the intracellular compartment, which may result in neuronal overhydration and the associated symptoms of dialysis intolerance (Stiller et al., 2001).

Some evidence suggests that autonomic dysfunction, decreased cardiac reserve, changes in serum potassium and calcium concentrations and more recently, accumulation of nitric oxide also play a part in the presence of adverse symptoms during and after dialysis therapy (Dheenan & Henrich, 2001).

History

Historically, patients were dialyzed against hyponatremic dialysate (a sodium level of 130–135 mEq/l) on the assumption that this would inhibit sodium accumulation interdialytically, thus preventing hypertension (Kelly, 1996; Palmer, 2001). While this strategy allowed patients to be dialyzed down to dry weight without any significant morbidity, session times were typically 8 to 10 hours long (Kelly, 1996).

Further technological advances and the advent of hollow fibre dialyzers in the late 1980s, allowed dialysis times to be reduced, but patients typically experienced signs and symptoms of dialysis intolerance (Kelly, 1996; Parker, 2000). This was and remains largely due to the rapid removal of plasma volume without adequate refilling with concomitant decreases in blood sodium and osmolality described above (Coli et al., 1998; Kelly, 1996; Sang et al., 1997).

Researchers at this time identified that the symptoms of dialysis intolerance were reduced and hemodynamic stability improved by increasing the dialysate sodium (Kelly, 1996; Palmer, 2001). This was offset against high post-dialysis serum sodium and increased thirst, potentially leading to the development of long-term complications such as left ventricular hypertrophy and congestive cardiac failure (Palmer, 2001).

Ultrafiltration profiling was another method that, at this time, was considered to reduce the hypotension commonly seen towards the end of the dialysis session. It was deduced that if the majority of the fluid removal took place in the beginning of the dialysis session, ending the session with a lower ultrafiltration rate, plasma refill might be able to match the fluid removal rate (Kelly, 1996), and the blood pressure might be more stable (deVries et al., 1990). Clear benefit of ultrafiltration profiling in terms of published studies remains unclear (Parsons, Yuill, Llapitan, & Harris, 1997). Further developments led to the concept of modulating the sodium in the dialysate to reduce the potential complications associated with high sodium dialysate, while keeping the benefits of hemodynamic stability (Kelly, 1996; Palmer, 2001).

What is Sodium Profiling?

Sodium profiling is the means by which sodium in the dialysate fluid is manipulated in order to influence fluid shifts between the ICF and ECF, thus reducing or preventing the changes described earlier. Higher concentration of sodium in the dialysate fluid than in the plasma prevents reduction in ECF osmolality, preventing IC water absorption; it may also support plasma refilling (Bonomini et al., 1997; de Vries et al., 1991; Raja, 1996; Raja & Po, 1994; Stiller et al., 2001) (see Figure 1). During a routine dialysis session sodium is an easy variable to manipulate in order to control the ECF osmolality. Stiller et al. (2001) reported, however, that this increase in ECF volume may be minimal compared to the average blood volume depletion caused by ultrafiltration throughout the hemodialysis procedure.

Sodium profiling consists of changing the dialysate sodium (or conductivity) level from high to low or low to high in stepwise, linear or exponential fashion (see Figure 2). The effects of these profile types have been discussed in the literature, identifying differing effects on symptoms, vascular stability, and osmolality (Stiller et al., 2001). It is possible to see how stepwise sodium profiling delineates clear points at which sodium levels change and thus may ease data collection compared to a constantly changing sodium level seen with exponential and linear sodium profiling.

Current thinking concerning sodium profiling is aimed at modulation of the dialysate sodium over the course of the dialysis session, individually calculated according to a predetermined end sodium balance and the patient’s own predialysis serum sodium (Bonomini, Coli, Feliciangeli, & Scolari, 1996; Di Guilio et al., 1998; Kelly, 1996; Ursino et al., 1998). Mathematical models have been formulated for this, similar to the urea kinetic model in use in many dialysis units today (Bonomini et al., 1996; Coli et al., 1997; Di Guilio et al., 1997).
al., 1998; Flanigan, Khairullah, & Lim, 1997; Jenson, Dobbe, Squillace, & McCarthy, 1994; Pedrini, Ponti, Faranna, Cozzi, & Locatelli, 1991; Raj Dominic, Ramachandran, Somiah, Mani, & Dominic, 1996; Ursino et al., 1997; Ursino et al., 2000). These computerized models have not been widely used and further research is needed to fully evaluate effective methods of achieving this individualization.

**Relevance to Current Practice**

Patients on dialysis have changed over the last 10 years with the current population, including those with high co-morbidity scores. These patients are likely to be at increased risk of dialysis intolerance (Bonomini et al., 1996; Flanigan et al., 1997; Kelly, 1996; Raja, 1996; Raj Dominic et al., 1996) with 15%-80% of patients typically experiencing one or more symptoms of dialysis intolerance each dialysis session (Bonomini, 1996; Bonomini et al., 1996; Bosetto, Bene, & Petitclerc, 1999; Jenson et al., 1994; Kelly, 1996; van Kuijk et al., 1996).

The use of high flux dialyzers is widespread and dialysis times have become shorter as a consequence of this 'more efficient' dialysis. Hemodiafiltration is a technique that has also become popular in some centers and has been reported to improve cardiac stability. This may relate to differing effects on peripheral resistance during the dialysis session (Locatelli et al., 1998) but could also relate to differences in sodium mass removal. Only two studies throughout the literature identify the use of sodium profiling in hemodiafiltration (Locatelli et al., 1998; Pedrini et al., 1991).

Current practice with sodium profiling varies significantly. In a questionnaire of over 2,000 international nephrologists, 26% were in favor of sodium profiling in all patients, 33% for those patients with high interdialytic weight gains, and 38% for select patients (Stiller et al., 2001). This reflects the interest in sodium profiling, but also the reluctance to accept
the evidence on clinical benefit as conclusive.

The hospital may be depicted as evolving from a place of treatment to provider of services, and our patients from sick people to customers (Bononimi et al., 1996). Public expectation has moved from patient compliance to patient satisfaction and this has highlighted the need to consider not only morbidity and mortality as final outcomes for patients on dialysis, but also quality of life, patient satisfaction, and social adjustment. It is for this reason that strategies must be implemented in order to eliminate or reduce dialysis intolerance. It would seem that the way forward is to gain an understanding of fluid management variables and the ability to monitor and respond to intradialytic events prior to these events happening, reducing morbidity and, ultimately, increasing the quality of life for patients on dialysis (Kelly, 1996).

**Purpose of This Review**

Primary research on sodium profiling to date has been sparse, with most published studies undertaken in Europe by a small number of researchers with various aims, medical and technological. These studies have had small subject numbers and non-uniformity of methodologies, making it difficult to establish whether evidence exists upon which to base current practice.

Systematic reviews on the subject published to date have been limited and have included much data from the 1970s (Arieff, 1994; Churchill, 1996; Petitclerc & Jacobs, 1995; Stiller et al., 2001). These reviews have included both ultrafiltration and sodium profiling in their methodologies, making it difficult to establish the profile responsible for the change in both physiological and quality of life parameters.

There is a need for a review that specifically addresses the following:

- The effect of sodium profiling on dialysis intolerance;
- The effect of sodium profiling on quality of life;
- The role of sodium profiling in terms of whether the adverse effects outweigh positive effects in clinical practice; and
- To establish whether it is possible to identify those patients who may benefit most from different types of sodium profiling.

The methodology for the review will be outlined, followed by a detailed analysis of the findings of the studies included in the review. Conclusions will then be drawn, gaps identified in the current knowledge base, and recommendations made for future practice.

**Methodology**

**Search Strategy**

A search of databases was undertaken including Medline, Cinahl, and Embase using keywords and limited to articles published after 1990, so as to capture the literature after the advent of hollow fiber dialyzers and bicarbonate dialysis. Grey literature (documentary material that is not commercially published) was searched, including hand searching of reference lists of included papers, as well as National Research Registers in order to identify current and ongoing work. A total of 62 papers were identified.

**Inclusion/Exclusion Criteria**

Primary research studies were included in which it could be established that sodium profiling was the intervention responsible for the outcomes observed. Studies needed to be undertaken in a chronic dialysis setting for inclusion. Although some may argue the benefit of sodium profiling in acutely ill patients, such as those in intensive care, there is much debate about this and this review focused on the chronic setting (Bononimi et al., 1996). A number of systematic reviews were highlighted, however, these included studies in which it was difficult to establish the intervention responsible for the outcomes measured (Arieff, 1994; Churchill, 1996; Petitclerc & Jacobs, 1995; Stiller et al., 2001). Nineteen articles were included after application of inclusion/exclusion criteria.

**Assessment of Methodological Quality**

The 19 papers were assessed for methodological adequacy using both Duffy’s critical appraisal checklist (Duffy, 1985) and Greenhalgh’s adapted checklist (Greenhalgh, 1997). Following critical appraisal, 6 articles were excluded and 13 included in the final review. To ensure subjectivity of the critiquing process, a second reviewer assessed the methodological quality of a selection of the papers included. Following this process and using Spearman’s Rank Correlation Coefficient, a correlation coefficient of $r = 0.95$ ($p < 0.01$) was achieved. Differences were resolved by discussion.

**Results**

Thirteen studies were included in the final review and these are summarized in Table 1. All of the studies were crossover trials with seven being randomized. Subject numbers ranged from 9 subjects (Iselin, Tsinalis, & Brunner, 2001; van Kuijk et al., 1996) to 39 (Acchiardo & Hayden, 1991) and number of dialysis sessions ranged from 1 session (van Kuijk et al., 1996) to 38 sessions (3.5 months) (Flanigan et al., 1997). Six studies compared subjects who had symptomatic hemodialysis at study entry (Coli et al., 1998; Iselin et al., 2001; Jenson et al., 1994; Levin & Goldstein, 1996; Parsons et al., 1997; Tang et al., 2006), 4 studies reported outcomes in subjects who were asymptomatic at study entry (Acchiardo & Hayden, 1991; de Vries et al., 1990; Sadowski et al., 1993; van Kuijk et al., 1996) and 3 studies did not identify whether subjects were symptomatic or asymptomatic at study entry (Flanigan et al., 1997; Raja, 1996; Sang et al., 1997). Symptoms included light headedness, cramps, headache, and thirst. Only one study identified that subjects were blinded to treatment by utilizing...
‘mock’ maneuvers (Levin & Goldstein, 1996), although this is difficult to achieve in practice. Sodium profiles varied from linear, step, exponential, to standard and sodium dialysate levels that ranged from 160 mmol/l to 133 mmol/l throughout the dialysis session.

Critical Discussion of the Findings of the Studies

Results of the studies will be presented in three sections: (a) those studies whose subjects had symptoms of dialysis intolerance prior to study; (b) those studies whose subjects were asymptomatic at the outset of the studies; and (c) those who did not report whether subjects were symptomatic or asymptomatic at the outset of the studies.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Original Hypothesis</th>
<th>Supported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jenson et al., 1994</td>
<td>Sodium profiling decreases nursing intervention and increases patient comfort</td>
<td>Y</td>
</tr>
<tr>
<td>Levin &amp; Goldstein, 1996</td>
<td>Profiled dialysis will minimize adverse events in select group of patients</td>
<td>Y but only in selected symptomatic patients</td>
</tr>
<tr>
<td>Parsons et al., 1997</td>
<td>Hypovolaemia plays a role in dialysis induced hypotension</td>
<td>N</td>
</tr>
<tr>
<td>Coli et al., 1998</td>
<td>Sodium profiling maintains a more stable blood volume and hemodynamics</td>
<td>Y</td>
</tr>
<tr>
<td>de Vries et al., 1990</td>
<td>Sodium profiling maintains a more stable blood volume, hemodynamic stability and extracellular fluid refill</td>
<td>Y but with caution</td>
</tr>
<tr>
<td>Acchiardo &amp; Hayden, 1991</td>
<td>Sodium profiling results in a reduction in intradialytic cramps, hypotension and associated nursing intervention</td>
<td>Y but profile should be individualized</td>
</tr>
<tr>
<td>Sadowski et al., 1993</td>
<td>Sodium profiling reduces intra/interdialytic morbidity in young patients on hemodialysis without cardiovascular morbidity</td>
<td>Y</td>
</tr>
<tr>
<td>van Kuijk, 1996</td>
<td>Sodium profiling improves hemodynamic stability due to better preservation of blood volume</td>
<td>Y</td>
</tr>
<tr>
<td>Raja, 1996</td>
<td>Sodium profiling reduces morbidity in elderly patients on hemodialysis</td>
<td>Y but profiles should be individualized</td>
</tr>
<tr>
<td>Flanigan et al., 1997</td>
<td>Sodium profiling influences chronic blood pressure management by altering sodium transfer</td>
<td>Y</td>
</tr>
<tr>
<td>Sang et al., 1997</td>
<td>Sodium profiling reduces intra/interdialytic symptoms</td>
<td>N</td>
</tr>
<tr>
<td>Iselin et al., 1997</td>
<td>Sodium profiling improves dialysis tolerance and improves vascular refill in stable patients on chronic HD</td>
<td>N</td>
</tr>
<tr>
<td>Tang et al., 2006</td>
<td>Sodium profiling improves hypotensive episodes and symptoms in patients on chronic HD</td>
<td>Y but at expense of increased IDWG</td>
</tr>
</tbody>
</table>

Studies in Subjects Who Were Symptomatic

Six studies identified symptoms in patients prior to inclusion in studies, varying from large interdialytic weight gains (Parsons et al., 1997), symptomatic intradialytic hypotension (Jenson et al., 1994; Tang et al., 2006) to other symptoms before, during, and after dialysis (Coli et al., 1998; Iselin et al., 2001; Levin & Goldstein, 1996; Tang et al., 2006). Levin and Goldstein (1996) also included 5 out of 16 subjects who were asymptomatic. These studies are summarized in Table 2.

Levin and Goldstein (1996) and Parsons et al. (1997) reported a reduction in headache, while Jenson et al. (1994) reported a trend for the reduction in intradialytic cramps, nausea, and vomiting along with a reduction in symptomatic hypotension ($p < 0.05$) and an associated reduction in normal saline administration and nursing intervention. Parsons et al. (1997) did not find a reduction in pre/during/post-hemodialysis hypotension nor associated decrease in nursing intervention. Tang et al. (2006) reported a significant reduction in hypotensive episodes ($p < 0.05$), cramps ($p < 0.01$), dizziness ($p < 0.05$) and other symptoms, such as chest pain, nausea, and headache ($p < 0.05$) as well as a significant reduction in nursing interventions ($p < 0.01$). Jenson et al. (1994), Parsons et al. (1997) and Coli et al. (1998) reported no increase in pre/post-hemodialysis serum sodium levels with their use of sodium profiling. Iselin et al. (2001) reported no significant reduction in hypotension, cramps, or other dise-
equilibrium symptoms and no significant increase in blood volume reduction, but a trend towards increased interdialytic weight gain.

Levin and Goldstein (1996) reported adverse effects such as an increase in pre/post-hemodialysis serum sodium levels and thirst, but no associated increase in interdialytic weight gain or hypertension. Tang et al. (2006) reported a significant increase in post-dialysis systolic blood pressure ($p < 0.01$) and interdialytic weight gain ($p < 0.001$), but no increase in pre- and post-dialysis serum sodium levels, when subjects received sodium profiling.

Four of the studies supported the use of sodium profiling in patients who were symptomatic (Coli et al., 1998; Jenson et al., 1994; Levin & Goldstein, 1996; Tang et al., 2006) with one recommending sodium profiling as maintaining a more stable blood volume and hemodynamics but warning of the need to individualize sodium profiles with the use of a

### Table 2
Symptomatic Subjects at Study Entry

<table>
<thead>
<tr>
<th>Title</th>
<th>Authors</th>
<th>Number of Patients</th>
<th>Hypothesis</th>
<th>Type of Study</th>
<th>Profile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Benefits of High and Variable Sodium Concentration Dialysate in Hemodialysis Patients</td>
<td>Jenson et al., 1994</td>
<td>21; 25 sessions</td>
<td>Decreased nursing intervention; increased patient comfort</td>
<td>Non-randomized, controlled crossover</td>
<td>High to Low Na⁺ 145-140 vs Na⁺ 140 Standard vs. Stepwise</td>
</tr>
<tr>
<td>The Benefits and Side Effects of Ramped Hypertonic Sodium Dialysis</td>
<td>Levin &amp; Goldstein, 1996</td>
<td>16 (11 symptomatic; 5 asymptomatic); 2 week run-in about 3 weeks</td>
<td>Decreased symptoms using thirst to guide profile</td>
<td>Randomized, controlled crossover</td>
<td>High to Low Na⁺ 155-160 (according to thirst)-Na⁺ 140 vs Na⁺ 140 Standard vs. Stepwise</td>
</tr>
<tr>
<td>Sodium Modelling and Profiled Ultrafiltration in Conventional Hemodialysis</td>
<td>Parsons et al., 1997</td>
<td>12; 1 week run-in about 3 weeks</td>
<td>Decreased symptoms and hypotension in those with increased interdialytic weight gain</td>
<td>Randomized, controlled crossover</td>
<td>High to Low Na⁺ 150-140 vs Na⁺ 143 Standard vs. Exponential</td>
</tr>
<tr>
<td>Clinical Use of Profiled Dialysis</td>
<td>Coli et al., 1998</td>
<td>11; 1 session</td>
<td>Sodium profiling will maintain more stable blood volume and hemodynamics</td>
<td>Non-randomized, controlled crossover</td>
<td>High to Low Pre calculated according to individual end sodium balance Na⁺ 138-144 Standard vs. Linear</td>
</tr>
<tr>
<td>Sodium Balance-neutral Sodium Profiling Does Not Improve Dialysis Tolerance</td>
<td>Iselin et al., 2001</td>
<td>9; 321 dialysis sessions (3 months)</td>
<td>Combining a continuously or stepwise decreasing ultrafiltration rate with a similarly decreasing sodium concentration profile will improve vascular refill.</td>
<td>Randomized, controlled crossover</td>
<td>High to Low Na⁺ 145-133 vs. Na⁺ 138 Standard vs. Linear or Step</td>
</tr>
<tr>
<td>Sodium Ramping Reduces Hypotension and Symptoms During Haemodialysis</td>
<td>Tang et al., 2006</td>
<td>13; 4 weeks 8 pts 2x wkly; 5 pts 3x wkly</td>
<td>Decreased hypertensive episodes &amp; disequilibrium symptoms</td>
<td>Non-randomized, controlled crossover</td>
<td>High to Low Na⁺ 150-140 vs. Na⁺ 140 (11 pts) or Na⁺ 135 (2 pts) Standard vs. Linear</td>
</tr>
</tbody>
</table>
mathematical model (Coli et al., 1998), Jenson et al. (1994) supported
the use of sodium profiling as a way of
decreasing nursing interventions and
increasing patient comfort, but rec-
ommended its use only in those
patients where tolerance to the
hemodialysis procedure can be
expected to be improved. Parsons et
al. (1997) further cautioned that many
of the studies undertaken so far that
supported the use of sodium profiling
in patients who were symptomatic
did not utilize a ‘true’ mean sodium
dialysate level as a comparison. This
study, along with Iselin et al. (2001)
did not support the use of sodium
profiling routinely in order to
improve cardiac stability.

Studies in Subjects Who Were
Asymptomatic

Four studies were undertaken on
subjects with no symptoms at study
entry and these are summarized in
Table 3. de Vries et al. (1990) investi-
gated low to high sodium profiling;
van Kuijk et al. (1996) compared a
high sodium dialysate of 144 mEq/l
with a low sodium dialysate of 134
mEq/l. Two studies looked at high to
low sodium profiles (Acchiardo &
Hayden, 1991; Sadowski et al., 1993).

All of the studies used symptoms
dialysis intolerance as a justifica-
tion for undertaking the research
with no corresponding explanation as
to why subjects who were asympto-
tomatic were chosen, although it
could be postulated that sodium pro-
filed may improve clinical parame-
ters in all patients. One study report-
ed a trend for reduction in intradial-
lytic cramps, hypotension and
associated nursing intervention (Ac-
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nificant reduction in intradialytic
and interdialytic symptoms
Sodium Modelling
Ameliorates Intradialytic
and Interdialytic Symptoms
in Young Hemodialysis
Patients

<table>
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</table>
| The Influence of Dialysate Sodium and Variable Ultrafiltration on
Fluid Balance During Hemodialysis Is Sodium Modelling             | de Vries et al., 1990 | 15; 3 sessions     | Effect on blood volume, blood pressure and IC/EC fluid movement | Non-randomized, controlled crossover | Low to High Na⁺ 140-148 vs. Na⁺ 140          |
| Necessary in High Flux Dialysis?                                    | Acchiardo & Hayden, 1991 | 39; 9 weeks       | Decreased cramps, hypotension and nursing
interventions                                        | Non-randomized        | High to Low Na⁺ 149 (decreasing by machine calculation) vs. Na⁺ 140 |
| Sodium Modelling Ameliorates Intradialytic and Interdialytic Symptoms in Young Hemodialysis Patients | Sadowski et al., 1993 | 16; 2 weeks       | Decreased intra/interdialytic morbidity         | Randomized, controlled crossover    | High to Low Na⁺ 148-138 vs. Na⁺ 138         |
| Vascular Reactivity During Combined Ultrafiltration Hemodialysis-the Influence of Dialysate Sodium | van Kuijk, 1996       | 9; 1 session       | Increased hemodynamic stability and blood volume preservation | Randomized, controlled crossover    | N/A                                          |

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Trends towards an increase in pre/post-hemodialysis serum sodium (Ac-
chiardo & Hayden (1991), an increase in post-hemodialysis serum sodium
(p < 0.05) (de Vries et al., 1990), but no associated increase in
intradialytic weight gain or hyperten-
sion (de Vries et al., 1990; van Kuijk
et al., 1996). Sadowski et al. (1993)
reported an increase in post-
hemodialysis thirst with stepwise
sodium profiling (p < 0.05).

One study concluded support of
their original hypothesis and stated
that sodium profiling should always
be used in high flux dialysis
(Acchiardo & Hayden, 1991). van
Kuijk et al. (1996) supported their
original hypothesis of sodium profil-
ing in hemodialysis, improving
hemodynamic stability due to better
preservation of blood volume, and de
Vries et al. (1990) supported their
original hypothesis with caution due
to the small number of measure-
ments made throughout the study.
Sadowski et al. (1993) supported the
use of sodium profiling to reduce

Table 3
Asymptomatic Subjects at Study Entry

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| The Influence of Dialysate Sodium and Variable Ultrafiltration on
Fluid Balance During Hemodialysis Is Sodium Modelling             | de Vries et al., 1990 | 15; 3 sessions     | Effect on blood volume, blood pressure and IC/EC fluid movement | Non-randomized, controlled crossover | Low to High Na⁺ 140-148 vs. Na⁺ 140          |
| Necessary in High Flux Dialysis?                                    | Acchiardo & Hayden, 1991 | 39; 9 weeks       | Decreased cramps, hypotension and nursing
interventions                                        | Non-randomized        | High to Low Na⁺ 149 (decreasing by machine calculation) vs. Na⁺ 140 |
| Sodium Modelling Ameliorates Intradialytic and Interdialytic Symptoms in Young Hemodialysis Patients | Sadowski et al., 1993 | 16; 2 weeks       | Decreased intra/interdialytic morbidity         | Randomized, controlled crossover    | High to Low Na⁺ 148-138 vs. Na⁺ 138         |
| Vascular Reactivity During Combined Ultrafiltration Hemodialysis-the Influence of Dialysate Sodium | van Kuijk, 1996       | 9; 1 session       | Increased hemodynamic stability and blood volume preservation | Randomized, controlled crossover    | N/A                                          |
They also stated that sodium profiling effects both intra- and interdialytically. Their original hypothesis and found that in cramps with sodium profiling (disequilibrium in the form of reduction in pre-dialysis serum sodium levels and an increase in thirst (worst in dialysis serum sodium levels and an increase in pre-hemodialysis serum sodium levels, but Sang et al. (1997) reported a significant increase in post-dialysis serum sodium levels and an associated increase in thirst (worst in stepwise profile), interdialytic weight gain, and hypertension (p < 0.05).

Sang et al. (1997) did not support their original hypothesis and found that 10 out of 23 subjects did not benefit from sodium profiling in terms of side effects both intra- and interdialytically. They also stated that sodium profiling may be detrimental to those patients with few or no dialysis intolerance symptoms.

Raja (1996) supported the original hypothesis of sodium profiling reducing morbidity in elderly patients on hemodialysis, but warned of the potential for sodium retention in linear sodium profiling and the need for profiles to be individualized. Caution should be advised here too. Although the studies were identified as elderly, in only 5 out of the 11 studies were subjects over age 60, skewing the mean age. Flanigan et al. (1997) supported their original hypothesis that sodium profiling did alter chronic blood pressure management.

Studies in Which The Symptomatic State Was Not Reported

Three studies did not identify whether their subjects were symptomatic or asymptomatic at study entry (Flanigan et al., 1997; Raja, 1996; Sang et al., 1997). All three studies reported a significant reduction in nursing interventions (p < 0.05), but only one (Raja, 1996) reported better blood volume preservation with high sodium constant dialysate (p < 0.05). Sang et al. (1997) identified reduction in osmotic disequilibrium in the form of reduction in cramps with sodium profiling (p < 0.05). These studies are summarized in Table 4.

None of the studies reported an increase in pre-hemodialysis serum sodium levels, but Sang et al. (1997) reported a significant increase in post-dialysis serum sodium levels and an associated increase in thirst (worst in stepwise profile), interdialytic weight gain, and hypertension (p < 0.05).

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Table 4
Not Stated Symptomatic/Asymptomatic at Study Entry

<table>
<thead>
<tr>
<th>Title</th>
<th>Authors</th>
<th>Number of patients</th>
<th>Hypothesis</th>
<th>Type of Study</th>
<th>Profile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium Profiling in Elderly Hemodialysis Patients</td>
<td>Raja, 1996</td>
<td>10: 1 session</td>
<td>Decreased morbidity in elderly patients</td>
<td>Non-randomized, controlled trial</td>
<td>High to Low Na+ 160-140 vs. Na+ 150-140</td>
</tr>
<tr>
<td>Dialysate Sodium Delivery Can Alter Chronic Blood Pressure Management</td>
<td>Flanigan et al., 1997</td>
<td>18: 3.5 months</td>
<td>Improved blood pressure control</td>
<td>Randomized, controlled crossover</td>
<td>High to Low Na+ 155-135 vs. Na+ 140</td>
</tr>
<tr>
<td>Sodium Ramping in Hemodialysis - A Study of Beneficial and Adverse Effects</td>
<td>Sang et al., 1997</td>
<td>23: 2 weeks</td>
<td>Decreased intra/interdialytic symptoms</td>
<td>Randomized, controlled crossover</td>
<td>High to Low Na+ 155-140 vs. Na+ 140</td>
</tr>
</tbody>
</table>

Discussion

The routine use of sodium profiling in clinical practice is a topic that is still much debated and this review has highlighted some of the inconsistencies in the research to date. Methodological problems with the studies reviewed included lack of follow-up of the subjects, inability to determine long-term outcomes and mortality for those patients who receive sodium profiling, and lack of consistency in research design. The overall significance of the outcomes of the studies is included in Table 5.

Four studies reported a reduction in headaches with the use of sodium profiling (Levin & Goldstein, 1996; Parsons et al., 1997; Sadowski et al., 1993; Tang et al., 2006); three a reduction in cramps (Sadowski et al., 1993; Sang et al., 1997; Tang et al., 2006), and two a reduction in nausea and/or vomiting (Sadowski et al., 1993, Tang et al., 2006). Four studies reported a reduction in nursing interventions (Jenson et al., 1994; Raja, 1996; Sang et al., 1997; Tang et al., 2006); four a reduction in blood volume changes (Coli et al, 1998; de Vries et al., 1990; Raja, 1996; van Kuijk et al., 1996), and four a reduction in intradialytic hypotension (Coli et al., 1998; Jenson et al., 1994; Sang et al., 1997; Tang et al., 2006).

Three studies reported an increase in post-dialysis thirst (Levin & Goldstein, 1996; Sadowski et al., 1993; Sang et al., 1997); six reported no increase in interdialytic weight gain (Flanigan et al, 1997; Jenson et al., 1994; Levin & Goldstein, 1996; Parsons et al., 1997; Sadowski et al., 1993; van Kuijk et al., 1996; ), with two studies reporting a significant increase in interdialytic weight gain with sodium profiling (p < 0.05) (Sang et al., 1997; Tang et al., 2006). One study reported a significant increase in pre dialysis serum sodium level in the sodium profiled subjects (p < 0.05) (Levin & Goldstein, 1996) and four reporting a significant increase in post-dialysis serum sodium in the sodium profiled groups (p < 0.05) (de Vries et al., 1990; Levin & Goldstein, 1996; Sang et al., 1997; van Kuijk, 1996). Two studies reported a signifi-
Table 5
Overview of Significance of Outcomes of Studies in Review

<table>
<thead>
<tr>
<th>Study</th>
<th>Positive Outcomes</th>
<th>Negative Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Reduction Headache</td>
<td>Reduction Cramp</td>
</tr>
<tr>
<td>Symptomatic at Study Entry</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jenson et al., 1994</td>
<td>N</td>
<td>N but trend</td>
</tr>
<tr>
<td>Levin &amp; Goldstein, 1996</td>
<td>Y</td>
<td>Trend</td>
</tr>
<tr>
<td>Parsons et al., 1997</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Coli et al., 1998</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Iselin et al., 2001</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Tang et al., 2006</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Asymptomatic at Study Entry</td>
<td></td>
<td></td>
</tr>
<tr>
<td>de Vries et al., 1990</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Acchiardo &amp; Hayden, 1991</td>
<td>N/A</td>
<td>Trend</td>
</tr>
<tr>
<td>Sadovski et al., 1993</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>van Kuijk, 1996</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Symptoms Not Stated at Study Entry</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Raja, 1996</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Flanigan et al., 1997</td>
<td>N/A</td>
<td>N</td>
</tr>
<tr>
<td>Sang et al., 1997</td>
<td>N/A</td>
<td>Y</td>
</tr>
</tbody>
</table>
cant increase in hypertension in the sodium profiled subjects (p < 0.05) (Sang et al., 1997; Tang et al., 2006).

Many of the studies included in this review had small numbers of subjects included and varied considerably in the length of the study. The majority of the included studies did not follow up with subjects and it was difficult to establish long-term outcomes for those receiving sodium profiling. A number of studies included subjects who were either asymptomatic at study entry or in whom no symptoms were stated, making it difficult to establish whether sodium profiling had an effect on intra/interdialytic symptoms. Only six studies included symptomatic subjects at study entry, and it is arguable that only these studies could begin to provide evidence of the effects of sodium profiling in the symptomatic hemodialysis population. None of the studies included in this review investigated quality of life as an outcome measure and so the effect of sodium profiling on quality of life could not be established.

Overall, this review does not provide evidence to support the routine clinical use of sodium profiling in the hemodialysis population suffering from dialysis intolerance nor in the wider hemodialysis population. While benefits of sodium profiling could be recognized, there was no consistency in the findings. The studies included could not establish whether positive effects outweighed negative effects, nor whether individuals could be identified who may most benefit from sodium profiling in practice, although some researchers attempted to identify particular profiles that may eliminate specific symptoms (Raja, 1996; Sadowski et al., 1993).

**Strengths of This Review**

This review investigated the effects of sodium profiling specifically on intra/interdialytic symptoms. Others reviews have included studies that have investigated ultrafiltration profiling in combination with or as being solely responsible for the reduction in symptoms. The review offers an overview of contemporary research and current techniques.

**Limitations of This Review**

This review was a systematic review, and a meta-analysis was not undertaken due to the difficulty in directly comparing results that utilized a wide variety of differing methodologies. Standardization of results and meta-analysis may have allowed for a more direct comparison of results.

**Implications for Practice**

Inconsistencies are evident in the literature to date on the effect of sodium profiling in the hemodialysis population. The future would seem to suggest that technology needs to assist practitioners to accurately determine individual sodium removal strategies that enable not only reduction in morbidity but also mortality. The current use of sodium profiling limits the ability to individualize the profile, and suggestions have been made in order to overcome these technical difficulties (Coli et al., 1998; Locatelli et al., 1998; Petitclerc, Hamami, & Jacobs, 1992; Petitclerc, Trombert, Coevert, & Jacobs, 1996). Current sodium profiles do not have the aim of achieving net zero sodium balance, which could potentially lead to excess in sodium mass and increase the risk of long-term complications. Attaining the optimal total body sodium content should become just as important as achieving correct dry weight in practice (Palmer, 2001).

There remains a theoretical basis for the use of sodium profiling and further research is required in order to provide evidence to support its use in clinical practice. Sodium profiling has the potential for optimization of mass sodium removal, thus achieving net sodium balance post-dialysis. The effect on osmotic disequilibrium, vascular instability, quality of dialysis sessions, and nursing intervention has yet to be realized.

**Questions Raised and Future Research**

The individualization of the sodium profile in order to achieve sodium balance should be considered as a fundamental target. Researchers suggest that this individualization may be achieved in a number of ways. Flanigan et al. (1994) suggested the use of an active interface that can sense serum sodium activity, and Bonomini et al. (1996) envisioned the use of mathematical and biofeedback models that can automatically respond and adjust to intradialytic changes in mass sodium and volume. These techniques involve the use of extensive computer software with the specific capabilities of determining not only dialyse sodium conductivity but also serum sodium levels throughout the dialysis session (Coli et al., 1998; Kelly, 1996; Stiller et al., 2001; Ursino et al., 1997). Although software is becoming more readily available, technical problems continue to make clinical application difficult.

There remains a gap in knowledge about the long-term effects of sodium profiling in patients on hemodialysis. Research suggests that sodium accumulation may increase the risk of LVH or CCF but clear evidence is required in order to establish this effect on morbidity and mortality with the clinical use of sodium profiling (Kelly, 1996; Palmer, 2001; Stiller et al., 2001).

There is also a gap in research identifying the effect of sodium profiling on quality of life. Clinical experience would suggest that patients on hemodialysis suffer often intolerable symptoms and report a poorer quality of life, but direct evidence is lacking. The National Research Register (2006) lists two ongoing projects looking into quality of life, utilizing the SF-36 Kidney Disease Quality of Life questionnaire.

Only two studies throughout the literature identify the use of sodium profiling in hemodiafiltration (Locatelli et al., 1998; Pedrini et al., 1991) and these studies were not included in this review as they reported mathematical model formulation, rather than the effect of sodium profiling on symptoms. Locatelli et al. (1998) suggested that hemodiafiltration may improve cardiovascular stability, perhaps due to the different effect on...
Peripheral resistance. Further research is needed in the use of sodium profiling in those patients receiving hemodialfiltration.

There remains a lack of consistency in study design and methodology and further investigation is required into the role of sodium profiling in today’s hemodialysis units in relation to quality of life, clinical effects, morbidity, and mortality, including the use of sodium profiling in hemodiafiltration and high flux dialysis. Further research is also needed to establish whether particular profiles may be of benefit to particular symptoms and to develop models that may aid the determination of sodium mass balance and achievement of net balance.

References


Sodium Profiling: The Key to Reducing Symptoms of Dialysis?


Complete the Following:

Name: ____________________________________________________________
Address: __________________________________________________________
__________________________________________________________________
Telephone: ______________________ Email: _____________________________

CNN: ___ Yes   ___ No   CDN: ___ Yes   ___ No   CCHT: ___ Yes   ___ No

Payment:

ANNA Member: ____ Yes   ____ No    Member #___________________________
☐ Check Enclosed   ☐ American Express   ☐ Visa   ☐ MasterCard

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GOAL
To provide information about sodium profiling in hemodialysis

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Evaluation

2. By completing this offering, I was able to meet the stated objectives
   a. Describe the possible role sodium plays in dialysis tolerance. 1 2 3 4 5
   b. Explain the reasons sodium profiling is thought to be useful in avoiding dialysis intolerance. 1 2 3 4 5
   c. Analyze the methods, results, and conclusions provided from a literature review study on sodium profiling. 1 2 3 4 5

3. The content was current and relevant.

4. This was an effective method to learn this content.

5. Time required to complete reading assignment: ____________ minutes.

I verify that I have completed this activity _____________________________
(Signature)