Efficacy of Twice Weekly Hemodialysis in Patients With Residual Kidney Function

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1. PURPOSE OF THE STUDY

a. Brief Summary

This study will test whether hemodialysis two times per week is equally effective as hemodialysis three times per week for people who still have some kidney function left. It will hopefully show that twice weekly hemodialysis provides the same quality of life as three times weekly hemodialysis. Such a finding could reduce the burden of hemodialysis and improve people's quality of life.

b. Objectives

More than 100,000 people start hemodialysis every year with the majority getting treatments three days per week. Many of these people, however, have enough remaining kidney function so that they may be able to receive hemodialysis treatments two days per week instead of three. We hope to learn whether a proposed formula for twice weekly dialysis prescription provides effective treatment for patients with residual native kidney function. This knowledge could hopefully reduce the burden on future patients and the cost of their treatment.

c. Rationale for Research in Humans

This study will assess the effect of twice weekly dialysis on the quality of life and on levels of uremic solutes in patients with residual native kidney function. Therefore, we need to include human subjects.

2. STUDY PROCEDURES

a. Procedures

Hemodialysis patients with sufficient residual native kidney function will undergo two 4-week study periods in a cross-over design. During these periods, hemodialysis will be prescribed three times per week and two times per week according to a formula put forward by a National Kidney Foundation Committee.

Screening:
- local nephrologists will be contacted to identify patients with measured residual kidney function or patients who report still producing urine.
- informed consent will be obtained from eligible patients.
- patients who consent will then undergo a run-in period followed by randomization into the cross-over study if they have adequate residual function.

Run-in period:
- patients' residual kidney function (Kru) will be measured by urine and blood collection.
- if Kru is >2.5 ml/min, patients will then proceed into the crossover study periods after completing the following steps:
• receive extra dietary counseling in addition to routine dietary advice provided by the dialysis unit
• diuretic doses will be optimized

Cross-over study with two 4-week study periods.
During each period:
- hemodialysis will be prescribed to achieve adequate treatment according to current National Kidney Foundation Committee guidelines.
- patients will be visited weekly.
- patients will continue to obtain blood work monitoring as per their routine dialysis care.
- hemodialysis and medications will be adjusted by the patients' primary nephrologist as needed.
- receive extra dietary counseling in addition to routine dietary advice provided by the dialysis unit

At the end of each 4-week period:
- patients' residual kidney function will be measured.
- pre- and post-treatment blood samples will be collected at the last treatment of the period. Blood will be collected through the dialysis tubing in the same fashion as the patients' routine lab monitoring.
- waste dialysate, which normally gets thrown away, will be collected during the last treatment.
- patients will complete symptom questionnaires and cognitive function tests.

b. Procedure Risks

Blood would be collected in the same sterile fashion as the patients' routine lab checks. Since the patients are on hemodialysis, blood will be collected in the same fashion as their routine monthly labs through the hemodialysis tubing. We will monitor levels of common blood chemistry such as serum potassium and CO2 as well as monitor blood pressure and weights during the study. We will adjust the hemodialysis prescription and medications based on this monitoring. We will visit the patients weekly to monitor for any symptoms. Hemodialysis will be prescribed according to current National Kidney Foundation Committee guidelines to ensure adequate treatment for the patients.

c. Will it be possible to continue the more (most) appropriate therapy for the participant(s) after the conclusion of the study?

Yes

d. Study Endpoint(s)

The primary endpoint is quality of life as assessed by the KDQOL-36, a questionnaire designed to assess the symptoms commonly experienced with kidney disease. Other endpoints are an additional symptom questionnaire (Dialysis Symptom Index), cognitive testing (Trails Making B and Digit Symbol Substitution Test), and plasma levels of

uremic solutes. We are testing for equivalency between two approved ways of prescribing the hemodialysis. A Data Safety Monitor will review results regularly and report to us and the IRB on any departure from this expectation. If no unexpected differences are detected, the study will end once the projected total subject population has completed the study.

3. BACKGROUND

a. Past Experimental and/or Clinical Findings

We have previously found that the residual native kidney can control plasma levels of secreted solutes better than those of the index solute urea. We subsequently found that plasma levels of secreted solutes were lower or the same in patients on twice weekly hemodialysis compared to anuric patients on thrice weekly hemodialysis.

b. Findings from Past Animal Experiments

N/A

4. DRUGS, BIOLOGICS, REAGENTS, OR CHEMICALS USED IN THE STUDY

a. Commercial Drugs, Biologics, Reagents, or Chemicals

None

5. PARTICIPANT POPULATION

a. Planned Enrollment

Approximately 50 subjects expected to be enrolled from Stanford-affiliated sites including VA Palo Alto, Satellite Healthcare, and Santa Clara Valley Medical Center.

b. Age, Gender, and Ethnic Background

The age range will be 18 to 85 years old. The gender and ethnic background will be representative of the Bay Area population.

c. Recruitment Details

We will notify the primary nephrologists who will help identify patients who are on hemodialysis and have residual kidney function. Residual kidney function (Kru) is not routinely measured. For those patients who do have Kru measured, they will be eligible for the study if Kru is >2.5 ml/min. If no Kru has been measured, a report of urine production greater than 500 ml/day (about 1 cup/day) is sufficient. All patients who consent to be in the study will then provide 24-hour urine and blood collection during the run-in period as described in the study procedures to obtain a Kru measurement before they proceed into the study periods. If the measured Kru is >2.5 ml/min, they can proceed into the study periods. If the measured Kru is <2.5 ml/min, they will not proceed further with the study.

d. Eligibility Criteria

i. Inclusion Criteria

- patients on hemodialysis who have residual kidney function with residual urea clearance (Kru) >2.5 ml/min.

- been on hemodialysis for at least 3 months.
- adherence to regular dialysis treatments.

ii. Exclusion Criteria
- inability to achieve adequate hemodialysis.
- planned revision of hemodialysis vascular access.
- hospitalized within the past 2 months.

e. Screening Procedures

We will notify the primary nephrologists who will help identify patients who are on hemodialysis and have residual kidney function. Residual kidney function (Kru) is not routinely measured. For those patients who do have Kru measured, they will be eligible for the study if Kru is >2.5 ml/min. If no Kru has been measured, a report of urine production greater than 500 ml/day (about 1 cup/day) is sufficient.