

# A Prospective Cross-over Study Examining the use of 5% Dextrose in people receiving Haemodialysis

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## Abstract

**Background:** Intradialytic hypotension is a frequent haemodialysis complication.

**Aim:** This multicentre, prospective, cross-over interventional study aims to compare the effectiveness of 5% Dextrose for priming, reinfusion and treatment of intravascular volume depletion symptoms against 0.9% normal saline in non-diabetic people receiving haemodialysis therapy. The primary objective is to reduce interdialytic weight gain thereby preventing rapid ultrafiltration during haemodialysis. The secondary objective is to minimise symptoms of intravascular volume depletion during haemodialysis treatments. **Methods:** The study population will include adult haemodialysis patients who are able to provide informed consent and who have been receiving haemodialysis for a minimum of 6 months with a permanent vascular access. Fifty participants will be recruited. Participants will continue to receive 0.9 percent Normal Saline for priming, reinfusion and treatment of symptoms during haemodialysis treatments for 3 months. Participants will then cross-over using 5% Dextrose for the following 6 months. The measurement of treatment effects includes interdialytic weight gain, vital signs, symptoms of intravascular volume depletion, blood volume monitoring and blood sugar levels. Adverse events will be tracked and monitored. This study has been designed to provide evidence and assist renal clinicians in determining the optimal strategy for preventing the need for rapid ultrafiltration during haemodialysis therapy.

## Background

Haemodialysis is the most common form of renal replacement therapy used in dialysis units around the world. Although haemodialysis is effective in removing excess solutes and fluid, it is frequently accompanied by intradialytic complications such as hypotension, muscle cramps, dizziness and light-headedness (Nette, Krepel, van den Meiracker, Weimar, & Zietse, 2002). Hypotension occurs in approximately 25 to 55 percent of haemodialysis treatments

(Holley, 2010). Intradialytic cramping has been reported as occurring in 5 to 20 percent of haemodialysis treatments (Holley, 2010). These complications are generally caused by multiple underlying factors. These factors include an excessive reduction in blood volume due to rapid fluid removal; the need for a high ultrafiltration rate due to excessive interdialytic weight gain, target weight set too low, intake of food during treatments, ingestion of antihypertensive medications during treatment; and poor contractility

## Key Words

Haemodialysis, hypovolaemia; blood volume; interdialytic weight; hypotension; dry weight

due to age and/or cardiac disease (Holley, 2010; Sherman, Daugirdas, & Ing, 2007). These complications often occur simultaneously. Hypotension is usually accompanied by cramping, light-headedness, and sometimes nausea and vomiting (Sherman, *et al.*, 2007). In severe cases, hypotension can lead to more serious complications such as cardiac or cerebral ischaemia (Van Der Sande, Luik, Kooman, Verstappen, & Leunissen, 2000).

The patients who are most prone to hypotensive episodes are the elderly and those with a compromised cardiovascular system. Patients with a compromised cardiovascular system are also more prone to the serious consequences of hypotensive episodes during their haemodialysis treatment (Van Der Sande, *et al.*, 2000).

An important contributing factor for these complications is hypovolaemia due to the removal of fluid from the intravascular space during the haemodialysis treatment and the inadequate refilling from the extravascular compartment (Nette, *et al.*, 2002). Other contributing factors include the

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inadequate constriction of the venous & arterial vascular beds and dysfunction of the autonomic nervous system (Nette, *et al.*, 2002; Schroeder, Sallustio, & Ross, 2004). The treatment of hypotension includes placing the patient in the trendelenburg position, the administration of a bolus dose of 0.9 percent normal saline and reducing as near to zero as possible the ultrafiltration rate (Daugirdas, Blake & Ing, 2007). These treatments however lead to decreased dialysis efficiency, inadequate fluid removal and consequently increases the patient's morbidity and a decreased quality of life (Holley, 2005). Hypotensive episodes can also be treated with the administration of hypertonic fluids such as hypertonic saline. This is not widely practiced due to side-effects such as thirst, interdialytic weight gain and hypertension, which have a great clinical effect in patients with compromised cardiovascular status (Van Der Sande, *et al.*, 2000).

Two studies (Nette, *et al.*, 2002; Van Der Sande, *et al.*, 2000) have compared various intravenous solutions such as albumin, hydroxyethyl starch, 3 percent hypertonic saline, 20 percent mannitol, 7.5 percent hypertonic saline, 23 percent saturated hypertonic saline, 7.5 percent hypertonic saline with 6 percent dextran, 5 percent dextrose, 20 percent dextrose, and 0.9 percent normal saline. The studies examined the effects of these various intravenous solutions on relative blood volume, blood pressure and the relief of symptoms of volume depletion in people receiving haemodialysis treatment. Both of these studies confirmed that the use of hypertonic solutions increased blood volume (thus increasing blood pressure) in hypotensive-prone patients. However, these studies did not examine the effects of these solutions in regards to interdialytic weight gain.

A study done by Nette *et al* (Nette, *et al.*, 2002) compared the specific effects of 20 percent dextrose, 20 percent mannitol, 0.9 percent normal saline & 5 percent dextrose on blood volume during haemodialysis. The results showed that an increase in relative blood volume was greater after the infusion of 20 percent dextrose than with other solutions ( $p < 0.05$ ). A major limitation of this study was the sample size. Only six clinically stable patients were included in the study and the study duration was six consecutive weeks. Again, this study did not include the effects of the solutions in regards to interdialytic weight gain.

Normal saline (0.9 percent) has traditionally been used as the priming fluid for extracorporeal circuits, to relieve symptoms of volume depletion (cramps, hypotension, etc.) and for reinfusion at the end of haemodialysis. This study will examine that the use of 5 percent dextrose, instead of 0.9 percent normal saline, in the priming and reinfusion of the extracorporeal circuit and to relieve symptoms of volume depletion will reduce the interdialytic weight gain in non-diabetic people receiving haemodialysis treatment.

### Hypothesis

The use of 5 percent dextrose instead of 0.9 percent normal saline for priming the extracorporeal circuit in haemodialysis will reduce the patient's interdialytic weight gain thus reducing the need for high ultrafiltration rates and preventing subsequent episodes of intravascular depletion during haemodialysis.

### Aim

To compare the effectiveness of using 5 percent dextrose for priming, reinfusion of the extracorporeal circuit and treatment of intravascular volume

depletion symptoms against 0.9 percent normal saline in non diabetic people receiving haemodialysis treatment.

### Objectives

- To minimise/reduce symptoms of intravascular volume depletion during haemodialysis treatments
- To minimise/reduce patient's interdialytic weight gain, thereby preventing rapid ultrafiltration during haemodialysis

### Overview

This is a 9 month, prospective, cross-over, interventional study of 50 participants in five haemodialysis units across an Area Health Service, examining the use of 5 percent dextrose for priming, reinfusion of the extracorporeal circuit and for the treatment of intravascular volume depletion symptoms, in reducing the incidence of hypotension and cramps in people receiving haemodialysis treatment. A randomised control trial was considered for the study design not enough potential eligible participants will be available for the study due to the rigorous exclusion criteria (diabetics, patients receiving haemodiafiltration, and patients with temporary vascular catheters). Unfortunately, a large proportion of patients receiving haemodialysis in the renal unit have diabetes (approximately 50 percent) and 30 percent of patients receive haemodiafiltration as treatment modality. A convenience sample size of 50 subjects was selected and power calculation was not done as this is a cross-over design study. Ethics approval has been sought. Participants who are receiving maintenance conventional haemodialysis for 6 months or more will be invited to participate in the study.

## Study Setting and Sample

Participants will be recruited from five haemodialysis units located within one Area Health Service.

## Inclusion criteria

Participants will be included in the study and must meet the following criteria: age 18 years or above at entry to the study, have the ability to provide informed consent, receiving maintenance haemodialysis for at least 6 months and who have permanent haemodialysis vascular access (i.e. native arteriovenous fistula or graft)

## Exclusion criteria

Participants will be excluded if they have a temporary access (e.g. vascular catheter, either tunneled or non-tunneled), receiving acute haemodialysis (i.e. patients receiving dialysis in intensive care unit & coronary care unit), diabetes (insulin dependent and non-insulin dependent) or receiving haemodiafiltration.

## Study Design

Participants included into the study will continue to receive usual treatment (i.e. 0.9 percent normal saline for priming, reinfusion of the extracorporeal circuit and treatment of the intravascular volume depletion symptoms during haemodialysis treatments) for the first 3 months. There will be no washout period prior to crossover to 5 percent dextrose as these subjects have been using normal saline for their previous dialysis sessions. Following the two day break from haemodialysis, participants will then cross-over to 5 percent dextrose for priming, reinfusion of the extracorporeal circuit and treatment of the intravascular volume

depletion symptoms during haemodialysis treatments for the following 6 months.

Treatment effects will be compared for the entire study periods. Data collection includes:

1. Interdialytic weight gain will be measured with the difference in weight between the last and current haemodialysis treatment)
2. Vital signs (blood pressure, pulse & temperature) will be recorded at the commencement and the end of the haemodialysis treatment.
3. Symptoms of intravascular volume depletion will be monitored which include signs of dizziness, cramps, hypotension (i.e. blood pressure of less than 90/60).
4. Blood volume will be monitored via the Fresenius BVM module once every midweek, noting the minimum relative blood volume at the end of the haemodialysis treatment.
5. Blood glucose levels will be monitored using a glucometer at a random time during the mid week dialysis session. Blood will be aseptically collected from the arterial line.
6. Monthly full blood count and biochemistry will be taken during the study.

Adverse events will be tracked, recorded and monitored. All hospital care will be recorded routinely on the case report forms at study visits.

## Time and Events Schedule

The Time and Events Schedule summarises the frequency and timing of measurements and the introduction of the study intervention (Table 1). The

following section describes in detail procedures to be completed.

Participants will be evaluated for entry as they become available. Eligible subjects will have visits scheduled at regular time intervals after inclusion in the study according to the Time and Events Schedule. The study protocol ends after nine months, upon voluntary withdrawal, transplantation, infection and/or loss of patent access or death of the participant.

## Screening and Recruitment

Following study initiation, potential participants will be evaluated for entry criteria during a screening visit. Researchers will discuss the study with potential participants prior to commencement of their dialysis session. The study will be explained to potential participants and/or their family members and informed consent will be sought in writing. The participant information sheet and consent form will only be available in English. Interpreters will be accessed if required. The following procedures will be initiated at the screening visit: informed consent, participant demographics such as age and gender, medical history, vital signs such as blood pressure, pulse and temperature, body weight, hypotensive episodes as per treatment record and blood glucose level at a random time during the mid week dialysis session.

Procedures to be completed during subsequent visits are described in detail in the following sections. A final visit will be scheduled after nine months when the participant has completed the study according to protocol or upon withdrawal.

Eligible participants who sign informed consents will be recruited to the study. After baseline data is collected the

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Time and Events Schedule (Table 1)

	Screening	Study Baseline Month 0	Intervention Baseline 5% Dextrose Month 3									End of Study Month 9
				W 13	W 14	W 15	M 4	M 5	M 6	M 7	M 8	
Informed Consent	X											
Subject Demographics	X											
Weight – Pre & Post		X	X	X	X	X	X	X	X	X	X	X
Medical History & Co-morbidities	X											
BP – Pre & Post (Sitting & Standing)	X	X	X	X	X	X	X	X	X	X	X	X
Pulse – Pre & Post (Sitting & Standing)	X	X	X	X	X	X	X	X	X	X	X	X
Body Weight (Ideal Body)	X	X	X	X	X	X	X	X	X	X	X	X
Interdialytic Weight Gain		X	X	X	X	X	X	X	X	X	X	X
Blood Volume Monitoring (Relative Blood Volume %) – middle or last day of the week		X										X
Hypotensive Episodes		X	X	X	X	X	X	X	X	X	X	X
Blood Sugar Level (Glucometer reading at 2 hrs into dialysis during 1st midweek session of month)		X	X	X	X	X	X	X	X	X	X	X
Full blood count and Biochemistry		X	X				X	X	X	X	X	X
Adverse Event Reporting		X	X	X	X	X	X	X	X	X	X	X

W = Week BP = blood pressure

Time and Events Schedule will be initiated. The following baseline data will be collected at recruitment, (using 0.9 percent Normal Saline): vital signs (temperature, pulse & blood pressure), body weight, interdialytic weight gain, blood volume monitoring (mRBV percent [minimum relative blood volume percent] at end of dialysis), blood sugar level (random glucometer reading midweek dialysis session), hypotensive episodes and records of any adverse events such as hospitalisation, infection.

### **Intervention Phase (5% Dextrose)**

Documentation of all study procedures, required parameters and adverse events will be recorded in the case report forms during the study visits. Data will be collected weekly for four weeks following conversion to 5 percent dextrose at month three. Data will then be collected monthly at months four, five, six, seven and eight. The following data will be collected: vital signs, body weight, interdialytic weight gain, blood volume monitoring (mRBV percent at end of dialysis), blood glucose level (random glucometer reading midweek dialysis session), hypotensive episodes and records of any adverse events such as hospitalisation or infection.

### **Completion of Study**

The final visit will be attended at month nine. The final data collection and procedures will include: vital signs, body weight, interdialytic weight gain, blood volume monitoring (mRBV percent at end of dialysis), blood glucose level (random glucometer reading midweek dialysis session), hypotensive episodes as reported in the treatment record. Data collection, procedures, adverse events and safety evaluations will not be

monitored or recorded by designated study personnel after completion of the study protocol.

### **Statistical Methods**

Data will be entered into and analysed using SPSS. Chi square test and t-tests will be used to examine the difference in the nature and number of untoward events between the groups. Nominal data will be analysed using percentages/chi square. Chi square and t-tests will be used to examine the difference in the clinical data.

### **Safety Evaluations**

Patient safety will be monitored through the evaluation and monitoring of any changes to patients' interdialytic weight gain, frequency of hypotensive episodes, pre-post dialysis blood pressure readings, blood volume monitoring, and blood glucose level monitoring. Any changes detected will be discussed with the participant's medical physician and the participant will be withdrawn from the study at the direction of the medical physician.

The following safety evaluations will be performed during the study to measure, monitor and evaluate the use of 5 percent dextrose for priming, wash-back of the extracorporeal circuit and treatment of intravascular volume depletion symptoms, such as hypotension, cramps, dizziness, etc. during haemodialysis treatments: vital signs, changes to patients' interdialytic weight gain, frequency of hypotensive episodes, blood volume monitoring (mRBV percent at end of dialysis), blood glucose level monitoring and all adverse events occurring during the study period will be reported and investigated during the study period.

All persisting adverse events at the study completion will be followed until a clinically stable resolution is achieved.

### **Limitations/Discussion**

High interdialytic weight gain (IDWG) has been associated with intradialytic complications, such as hypotension and cramps, due to rapid ultrafiltration (Sherman, *et al.*, 2007). IDWG of greater than 3 percent can increase the risk of myocardial infarction, coronary artery by-pass graft (CABG) operation or coronary artery dilatation, and death amongst chronic haemodialysis population (Holmberg & Stegmayr, 2009). Similarly, high IDWG and non-compliance with the treatment are independent risk factors for higher blood pressure amongst this population (Sarkar, Kotanko, & Levin, 2006). Various strategies have been suggested to minimise or reduce patient's interdialytic weight gain, such as salt and fluid restriction (Sarkar, *et al.*, 2006) and yet normal saline (0.9%) is still being used in priming and wash-back of extracorporeal circuits.

This study only includes non-diabetic adults who are receiving haemodialysis treatment via a permanent vascular access. Considering that the leading cause of end-stage kidney disease is diabetes mellitus (McDonald, Excell, & Dent, 2009), this study excludes the majority of the haemodialysis population. Further studies that include this population would be beneficial in assisting dialysis nurses to provide the best possible care available, thus improving the patient's quality of life. In addition, this study excludes patients with vascular catheters (either tunneled or non-tunneled) to reduce the variable in the patients' hypovolaemic episodes. Vascular catheters have been known to increase the chance of septic episodes amongst these patients (McDonald, *et al.*, 2009; VAS, 2002), thus leading to vasodilatation and hypotensive episodes that could or could not be related to high ultrafiltration rate. Unfortunately,

the dialysis units that will be involved have a high incidence of tunnelled vascular catheters use for patients who are unsuitable to have an arteriovenous fistula (AVF) or arteriovenous graft (AVG) created or patients who have had multiple access failure. This accounts for approximately 20% of the current haemodialysis population. This is above the recommended guideline of less than 10% (Choi & Frankel, 2007). Considering the tunnelled vascular catheter is the permanent access for these patients, it maybe worthwhile including this group of patients in future studies.

### Conclusion

Haemodialysis has limitations and disadvantages due to complications that could occur during treatment. Symptoms of volume depletion such as hypotension, muscle cramps, dizziness, nausea and vomiting. Hypotension is the most common intradialytic complication in dialysis. The cause of this is multi-factorial, such as high ultrafiltration rate, and/or inaccurate assessment of dry weight. Prevention or minimising these complications is one of the goals of haemodialysis. This study has been designed to provide evidence and assist renal clinicians in determining the optimal strategy for preventing rapid ultrafiltration and the subsequent complications during haemodialysis.

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