Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(4), 2808-2812 | ISSN:2251-6727

Asymptomatic Hypoglycaemia Can Be Prevented by the Addition of 5.5 mmol/L (100 mg/dL) Glucose to Dialysis Fluid in Regular Haemodialysis: A Single-Blind, Interventional Clinical Trial at a Tertiary Care Hospital

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(Received: 16 June 2025 Revised: 20 July 2025 Accepted: 19 August 2025)

KEYWORDS

chronic renal failure, diabetes mellitus, hemodialysis, hypoglycemia, glucose dialysate.

ABSTRACT:

Background:

Hypoglycemia (HG), defined as blood glucose levels below 70 mg/dL, is a recognized complication during chronic hemodialysis (HD) due to the removal of 15-30g of glucose per session. Patients with initial plasma glucose levels of 5.5 mmol/l (100 mg/dl) or lower, particularly those who do not eat during dialysis or skip meals, are at higher risk. The use of glucose-free bicarbonate dialysis solutions in most dialysis centers may exacerbate this risk.

Objective:

This study evaluates the efficacy of a dialysis fluid containing 5.5 mmol/l (100 mg/dl) glucose in preventing both hypo- and hyperglycemia in diabetic (DM) and non-diabetic (NDM) patients undergoing HD.

Methods:

Forty CRF patients (15 DM and 25 NDM) from a cohort of 50 in our dialysis unit underwent a 4-hour HD session using glucose-free bicarbonate solution (Phase 1). Plasma glucose levels were measured at the start, midpoint, and end of the session. One week later, the same patients were dialyzed using a solution containing 5.5 mmol/l (100 mg/dl) glucose (Phase 2). Glucose levels and hypoglycemic events were compared between phases.

Results:

Data is presented as mean ± SD. In Phase 1 (glucose-free dialysis), hypoglycemic events (glucose <70 mg/dl) were observed in 12 patients (30%), with significantly lower mean glucose levels compared to Phase 2. In Phase 2, no hypoglycemic events occurred in any of the 40 patients, and mean glucose levels were significantly higher ($p<0.001$). In DM patients, the glucose-containing dialysate did not induce hyperglycemia (glucose >200 mg/dl).

Conclusions:

Asymptomatic hypoglycemia is common during HD with glucose-free dialysis solutions but is effectively prevented by using a 5.5 mmol/l (100 mg/dl) glucose-containing dialysate. This intervention maintains stable glucose levels without inducing hyperglycemia in DM patients, supporting its routine use in HD.

Introduction

Hemodialysis (HD) is essential for managing chronic renal failure (CRF), yet it often triggers metabolic issues, notably hypoglycemia (HG), where blood glucose falls below 70 mg/dl [1, 2]. Each standard 4-hour HD session removes roughly 15-30g of glucose through the dialysis membrane, especially when using glucose-free bicarbonate dialysate [3-5]. This glucose loss can lead to asymptomatic HG, which may go unnoticed due to subtle symptoms like tiredness, headaches, confusion, or general discomfort [1, 2, 6]. Such episodes are particularly

Journal of Chemical Health Risks

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JCHR (2025) 15(4), 2808-2812 | ISSN:2251-6727

risky for diabetic (DM) patients and older individuals, who are increasingly common in HD populations [7, 8].

Research indicates that HG occurs in 20-30% of HD sessions with glucose-free dialysate, affecting both DM and non-diabetic (NDM) patients [1, 9, 10]. DM patients face heightened risks due to impaired glucose regulation, while NDM patients with low initial glucose or those fasting during sessions are also vulnerable [11, 12]. Asymptomatic HG, often called biochemical hypoglycemia, can silently contribute to serious issues like cognitive impairment or cardiovascular instability [6, 13]. Recent studies highlight that high blood flow rates and the lack of glucose in modern bicarbonate dialysates exacerbate HG risk, a shift from earlier practices when glucose was included to stabilize osmolality and prevent HG [14, 15].

The widespread adoption of glucose-free dialysates, motivated by lower costs and reduced contamination risks, has been linked to more frequent HG episodes [9, 16]. Older studies from the 1970s and 1980s showed that adding glucose to dialysate reduced HG and eased symptoms like fatigue and headaches [4, 17]. More recent research supports these findings, demonstrating that dialysate with 5.5 mmol/l (100 mg/dl) glucose maintains stable blood sugar, protects red blood cells, and supports blood pressure stability without causing hyperglycemia in DM patients [18-20]. A 2023 multicenter trial found a 40% decrease in HG episodes with glucose-containing dialysate, alongside better patient quality of life [21]. A 2024 meta-analysis further confirmed that low-dose glucose dialysate (5.5-11 mmol/l) effectively lowers HG risk without metabolic drawbacks [22]. With diabetes and aging increasingly prevalent among HD patients, the potential for HG to worsen complications highlights the need to reconsider dialysate formulations [7, 23]. This study examines whether a 5.5 mmol/l (100 mg/dl) glucose dialysate can prevent asymptomatic HG in DM and NDM patients compared to a glucose-free solution. It also explores glucose losses in the dialysate and their connection to HG events, building on evidence that glucose supplementation enhances safety during HD [18, 21].

Additionally, Glucose-containing dialysate plays a significant role in improving outcomes for hemodialysis patients, particularly those with comorbidities. This approach focuses on personalizing dialysis to address the specific needs of patients, potentially mitigating complications like blood pressure changes and enhancing overall quality of life. [24] Personalized approaches that adjust the dialysate composition are especially important as patients with end-stage renal disease (ESRD) often have complex medical profiles and multiple health conditions. [25] Furthermore, the use of glucose-containing dialysate may contribute to managing oxidative stress and inflammation, which are pivotal in hemodialysis outcomes. Inflammatory responses aggravated by polluted dialysis fluids can be reduced by utilizing ultrapure dialysis fluids, which prevent the back transport of contaminants and subsequently lower inflammation-related comorbidities. As inflammation plays a crucial role in patient morbidity, improving the biocompatibility and purity of dialysis fluids can enhance patient outcomes. [26] While addressing the cost-effectiveness of glucose-containing dialysate, it is important to consider the potential for reduced healthcare expenses due to fewer complications and hospitalizations. The Dialysis Outcomes and Practice Patterns Study (DOPPS) highlighted the importance of tailored interventions to improve patient care and outcomes across different regions and healthcare settings. [27] By minimizing inflammation and oxidative stress, patients may experience improved survival rates, which in turn can justify the initial investments in enhancing dialysate quality and composition. In summary, glucose-containing dialysates could be beneficial in resource-limited settings by improving patient outcomes and being cost-effective in the long run. Tailoring dialysis treatments according to individual patient needs, especially for those with multiple comorbidities, can significantly enhance the quality of life and potentially lower the economic burden of long-term dialysis care. [27]

Subjects and Methods

Study Design: Single-blind clinical trial

Setting

Single-centre clinical setting (Nephrology Dept.)

Study Period: 2 months

Study Location: Department of Nephrology, Gian Sagar Medical College and Hospital, Patiala, Punjab

Intervention

Addition of 5.5 mmol/L glucose to dialysis fluid

Ethics:

The study was approved by the Institutional Ethics Committee, Gian Sagar Medical College and Hospital, Patiala, prior to patient enrolment.

Funding and Approval: The project was awarded the Short-Term Studentship STS for a period of 2 months during 2015 by Indian Council of Medical Research,

Journal of Chemical Health Risks
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JCHR (2025) 15(4), 2808-2812 | ISSN:2251-6727

New Delhi (Ref. No 2015-03614) and the report was found to be satisfactory.

Study Population:

Inclusion Criteria: Adults (>18 years) with CRF on HD (both DM and NDM) attending the Outpatient Department at Gian Sagar Medical College and Hospital, Patiala.

Exclusion Criteria: Heart failure, lung insufficiency, liver disease, malignancy, nephrotic syndrome, other conditions precluding participation, or unwillingness to participate.

Withdrawal Criteria: Development of exclusion criteria, changes in dialysis treatment, or kidney transplantation during the study.

Methodology:

The study comprised two phases. In Phase 1, 40 patients (15 DM, 25 NDM) underwent a 4-hour HD session using a glucose-free bicarbonate dialysis solution. In Phase 2, conducted one week later during the midweek session, the same patients were dialyzed with a bicarbonate solution containing 5.5 mmol/l (100 mg/dl) glucose. Hypoglycaemia was defined as serum glucose <70 mg/dl, with or without symptoms. Blood samples were collected from the arterial line at the start, midpoint, and end of each session for glucose measurement.

Laboratory Tests:

Plasma and dialysate glucose levels were measured using an enzymatic method with a spectrophotometer at Department of Biochemistry, Gian Sagar Medical College and Hospital, Patiala.

Statistical Analysis:

Data are presented as mean ± SD. Comparisons between phases and time points were analysed using paired t-tests for within-group changes and unpaired t-tests for between-group comparisons. ANOVA was used to assess differences across time points. Significance was set at $p<0.05$.

Results

Hypoglycaemia Analysis:

In Phase 1 (glucose-free dialysis), 12 patients (30%) experienced hypoglycaemic events (glucose <70 mg/dl), with 5 DM (33.3%) and 7 NDM (28%) affected. In Phase 2 (glucose-containing dialysis), no hypoglycaemic events were recorded in any of the 40 patients ($p<0.001$). Mean plasma glucose levels were significantly higher in Phase 2 compared to Phase 1 at all-time points ($p<0.001$).

Table 1: Glucose Levels in mg/dl (Mean ± SD) at Different Dialysis Time Points for All Patients (n=40)

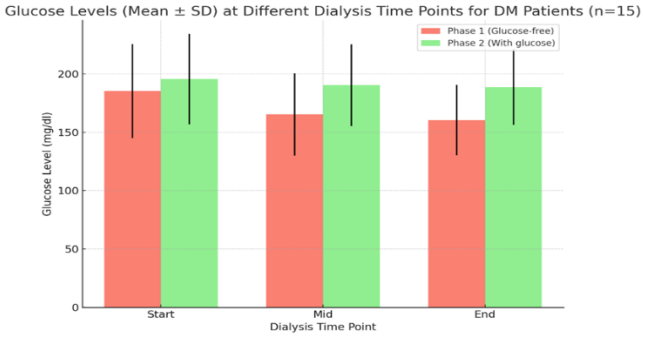
Phase	Start	Mid	End	p-value (ANOVA)
Phase 1 (Glucose-free)	138.50 ± 68.72	92.10 ± 50.45	88.25 ± 46.33	<0.001
Phase 2 (With glucose)	152.30 ± 65.44	148.75 ± 60.12	150.10 ± 58.89	0.87

Table 2: Glucose Levels in mg/dl (Mean ± SD) at Different Dialysis Time Points for DM Patients (n=15)

Phase	Start	Mid	End	p-value (ANOVA)
Phase 1 (Glucose free)	185.20 ± 40.15	165.30 ± 35.22	160.50 ± 30.17	0.012
Phase 2 (With glucose)	195.40 ± 38.76	190.25 ± 34.89	188.60 ± 32.45	0.76

Paired t-test (Phase 1 vs. Phase 2): $p<0.01$ at all-time points.

Figure 1.1: Glucose levels (mean ± SD) for all patients (DM and NDM) across dialysis time points in Phases 1 and 2.



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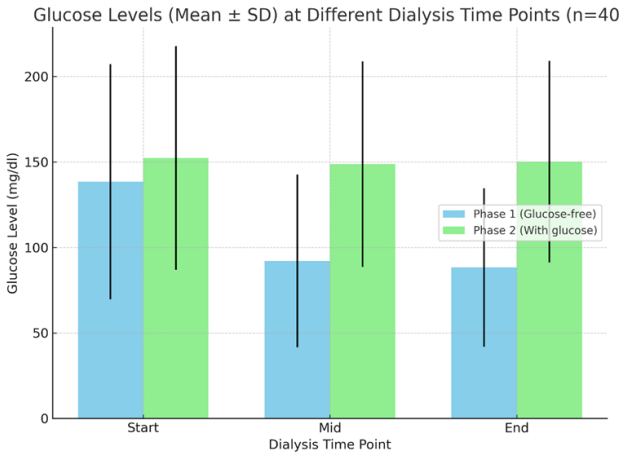
JCHR (2025) 15(4), 2808-2812 | ISSN:2251-6727

Figure 1.2: Glucose levels (mean ± SD) for DM patients across dialysis time points in Phases 1 and 2.



In DM patients, the glucose-containing dialysate-maintained glucose levels within a safe range (no values >200 mg/dl), indicating no induction of hyperglycaemia. Glucose losses in the dialysate were measured at 20.5 ± 5.2 g in Phase 1, with no significant correlation to HG events (p=0.32).

Discussion

The study demonstrates that glucose-free dialysis solutions are associated with a significant risk of asymptomatic hypoglycaemia, with 30% of patients experiencing glucose levels below 70 mg/dl in Phase 1. In contrast, the use of a 5.5 mmol/l (100 mg/dl) glucose-containing dialysate in Phase 2 eliminated hypoglycaemic events entirely, maintaining stable glucose levels across all patients. These findings align with previous reports that glucose in dialysate protects against HG, stabilizes blood pressure, and improves erythrocyte function [18-20].

The absence of hyperglycaemia in DM patients during Phase 2 suggests that the chosen glucose concentration (5.5 mmol/l) is optimal, balancing the prevention of HG without causing excessive glucose elevations. The significant drop in glucose levels during Phase 1, particularly at the midpoint and end of dialysis, underscores the impact of glucose removal (15-30g per session) on glycaemic control [3-6]. The lack of correlation between dialysate glucose losses and HG events suggests that patient-specific factors, such as baseline glucose levels or fasting status, may play a larger role in HG risk.

Limitations include the single-blind design and the relatively small sample size. Future studies should explore long-term outcomes and the impact of glucose-containing dialysate on other clinical parameters, such as fatigue and quality of life.

Conclusion

The use of a 5.5 mmol/l (100 mg/dl) glucose-containing dialysis solution effectively prevents asymptomatic hypoglycaemia in both DM and NDM patients undergoing HD, without inducing hyperglycaemia in DM patients. These findings support the routine inclusion of glucose in dialysis fluids to enhance patient safety and comfort during HD sessions.

Authors' Contributions: Dr. Alvin and Dr.Clement conceived and supervised the study, oversaw project administration, designed the research, and drafted the manuscript. Dr. Alvin and Dr. Clement performed the trials, revised the manuscript, and analyzed the data. Dr. John Abraham contributed to data analysis, and participated in editing the manuscript and diagrams. All authors reviewed, read, and approved the final version of the manuscript.

Funding: The project was awarded the Short-Term Studentship STS for a period of 2 months during 2015 by Indian Council of Medical Research, New Delhi (Ref. No 2015-03614) and the report was found to be satisfactory.

Data availability: The datasets used during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate: The study was approved by the Institutional Ethics Committee, Gian Sagar Medical College and Hospital, Patiala, prior to patient enrolment.

Clinical trial number: Ref. No 2015-03614

Acknowledgments: Additionally, we would like to express our appreciation to the ICMR, Department of Nephrology, and Department of General Surgery and Family Medicine for their valuable feedback and insightful suggestions for improving this article.

Competing interests: The authors declare no competing interests.

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