Study Protocol

Study Title: Adherence as a moderator of phosphorus education effectiveness in hemodialysis patients: an exploratory study.

IRB Number: JMRPGJP0071

Institution: Jen-Ai Hospital, Taiwan

Principal Investigator: Wei-Hua Chen, Senior Dialysis Technologist

Date: July 29, 2024

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1. Background and Rationale

Chronic kidney disease (CKD) patients must maintain serum phosphorus (P) levels within 3.5–5.5 mg/dL and a calcium-phosphorus product below 55 mg^2/dL^2, as recommended by the National Kidney Foundation (KDOQI). Hyperphosphatemia can lead to complications such as secondary hyperparathyroidism, renal osteodystrophy, and cardiovascular issues. Despite regular dialysis, phosphorus control remains suboptimal in many patients.

Recent reports from the Taiwan Renal Registry Data System (TWRDS) indicate that over 28% of dialysis patients exceed the recommended phosphorus threshold. In the Ren-Ai Hemodialysis Unit, approximately 36.27% of patients had serum phosphorus levels above 5.5 mg/dL over a recent six-month period, indicating room for improvement in current care strategies.

Educational interventions targeting dietary control and phosphate binder use have shown promise, but little research has explored how the **content and intensity** of such education affects patient outcomes. This study seeks to address this gap.

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2. Objectives

- To evaluate the impact of different educational content modules (dietary education vs. phosphate binder education) on serum phosphorus levels

in dialysis patients.

- To examine the role of educational intensity (number of sessions) in influencing patient outcomes.
- To identify the most effective combination of education type and frequency.

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3. Study Design

This is a 3×3 factorial experimental study involving:

- **Independent variables:** Educational content (A = dietary education, B = phosphate binder education, A+B = combined) and educational intensity (1, 2, or 3 sessions).
- **Outcome variable:** Change in serum phosphorus levels.
- **Control variables:** Age, gender, dialysis vintage, blood pressure.

Subjects will be randomized into 9 groups (3 content types × 3 intensities), with approximately 5 patients per group.

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4. Participants

- **Inclusion criteria:**
    - Diagnosed with CKD and receiving maintenance hemodialysis
    - Using phosphate binders
    - Cognitively capable of understanding educational materials
- **Exclusion criteria:**
    - Receiving dialysis for less than 6 months
    - Not currently prescribed phosphate binders
    - Significant cognitive impairment

5. Intervention Procedures

Educational interventions will be delivered using short video modules (3–5 minutes each), reinforced by brief discussions led by trained nurses. Modules cover:

- Dietary phosphorus management
- Proper use of phosphate binders
- Understanding phosphorus test results and dialysis principles

The intervention period will last two months. Education will be delivered during dialysis sessions. Blood samples will be collected biweekly to monitor serum phosphorus and calcium levels.

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6. Data Collection and Analysis

Blood phosphorus levels will be collected at baseline and every two weeks throughout the study. The primary endpoint is the change in serum phosphorus levels after completion of the intervention.

Statistical methods will include:

- One-way ANOVA and factorial ANOVA
- Post-hoc testing (e.g., Tukey's test) for multiple comparisons
- Effect size estimates and p-value thresholds at $\alpha = 0.05$

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7. Ethical Considerations

This study has been approved by the Jen-Ai Hospital Institutional Review Board (IRB No. JMRPGJP0071). All participants will provide informed consent before enrollment. Participant privacy will be protected by assigning research codes and omitting all personal identifiers from data files. All data will be stored

securely and destroyed two years after publication.

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8. Timeline

- **Month 1:** Recruitment, baseline labs, educational session 1
- **Month 2:** Continued intervention, biweekly labs
- **Month 3:** Final blood test, data analysis

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9. Expected Outcomes

- Identification of an optimal educational model
- Improved serum phosphorus control in dialysis patients
- Reduction in nursing workload due to ineffective education
- Contribution to precision education in nephrology care

Statistical Analysis Plan (SAP)

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1. Study Overview

This is a 3×3 factorial randomized experimental study involving hemodialysis patients who are prescribed phosphate binders. The study aims to evaluate how different educational interventions (type and frequency) affect serum phosphorus levels over a two-month period.

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2. Objectives

- To assess the effectiveness of different educational content (dietary education, phosphate binder education, or both) on serum phosphorus levels.
- To examine how varying frequencies (1, 2, or 3 sessions) of education influence outcomes.
- To identify any interaction effects between content and frequency.

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3. Study Endpoints

- **Primary Endpoint:** Change in serum phosphorus levels from baseline to study completion (after 2 months).
- **Secondary Endpoints:** Change in calcium-phosphorus product levels;

variation in response across different subgroups (e.g., adherence levels).

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4. Hypotheses

- **H1:** There is a statistically significant difference in serum phosphorus levels across different educational content types.
- **H2:** Increasing the number of educational sessions improves phosphorus control.
- **H3:** There is an interaction effect between education content and frequency.

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5. Analysis Sets

- **Full Analysis Set (FAS):** All participants who completed at least one educational session and provided both baseline and follow-up lab data.
- **Per-Protocol Set (PPS):** Participants who completed the full intervention as assigned.

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6. Statistical Methods

- Descriptive statistics will summarize baseline characteristics and outcome distributions.
- **Primary analysis:**
    - Factorial ANOVA (3 × 3 design) to evaluate main and interaction effects on phosphorus levels.
    - Post-hoc comparisons using Tukey's HSD test.
- **Secondary analysis:**
    - One-way ANOVA for subgroup comparisons (e.g., adherence level).

- Pearson correlation analysis between adherence scores and phosphorus levels.

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7. Missing Data Handling

- Missing outcome data will be imputed using Last Observation Carried Forward (LOCF) if dropout is <10%.
- Sensitivity analysis will be conducted to assess the robustness of results to different missing data assumptions.

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8. Software and Tools

- Statistical analysis will be conducted using SPSS version 28 and G*Power 3.1.9.7.
- Significance level is set at $\alpha = 0.05$.

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9. Sample Size Justification

- Estimated using G*Power for ANOVA, fixed effects, with an assumed effect size f = 0.4 (large), $\alpha = 0.05$, power $(1 - \beta) = 0.80$.
- Minimum sample size per group: 5
- Total sample size: 45 (9 groups × 5 participants)

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10. Reporting

- All findings will be reported in accordance with CONSORT guidelines.
- Both point estimates and 95% confidence intervals will be presented.
- All statistical assumptions will be checked and reported.