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A Comparative Study of Intradialytic vs. Pre-Dialysis Physical Therapy Interventions in Individuals
Undergoing Dialysis: Randomized Controlled Trial
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Title: A Comparative Study of Intradialytic vs. Pre-Dialysis Physical Therapy Interventions in Individuals Undergoing Dialysis: Randomized Controlled Trial

Introduction:

Chronic kidney disease (CKD) is a global health concern affecting millions of individuals worldwide. End-stage renal disease (ESRD) often necessitates dialysis, which can significantly impact patients' quality of life and physical function. Physical therapy interventions have shown promise in improving outcomes for individuals undergoing dialysis, but the optimal timing of these interventions remains uncertain. This study aims to compare the effectiveness of intradialytic versus pre-dialysis physical therapy in improving physical function and other outcomes among individuals undergoing dialysis.(1, 2)

Objectives:

To compare the effectiveness of intradialytic and pre-dialysis physical therapy interventions in improving physical function among individuals undergoing dialysis.

To assess the impact of intradialytic and pre-dialysis physical therapy on secondary outcomes including hemoglobin levels, electrolyte balance, quality of life, and pain scores.(3)

To evaluate the safety and feasibility of intradialytic and pre-dialysis physical therapy interventions in individuals undergoing dialysis.

Study Design:

This study will be a randomized controlled trial conducted at Mubarak Al-Abdullah Al-

Jaber Al-Sabah Dialysis Center
[Mubarak Al-Kabeer Hospital, State of Kuwait].
Participants will be randomly assigned to either the intradialytic physical therapy group or the pre-dialysis physical therapy group.

The study duration will be 12 months, including an intervention period of 2 session pre week for 3 months and a follow-up period of 6 months.

Participants:

Sample Size

The sample size required per group is approximately 36 participants.

Therefore, for two groups (intradialytic and pre-dialysis), you would need a total of 72 participants (36 in each group).

The sample size for this study was determined using G*Power software, a widely used tool for statistical power analysis. The calculation was based on detecting a clinically meaningful difference in physical function between the intradialytic and pre-dialysis physical therapy groups. A two-tailed t-test for independent samples was selected, assuming an effect size (Cohen's d) of 0.8, a statistical power of 80% (1-β = 0.80), and a significance level (α) of 0.05 to minimize Type I and Type II errors. Using the formula:

$$n = \frac{2(\sigma 2)(Z\alpha/2 \quad + Z\beta \quad)2}{\Delta 2}$$

Where σ is the estimated standard deviation from previous studies, Δ is the expected difference between groups, and Z values correspond to the chosen significance level and power, the required sample size was found to be 36 participants per group. Thus, a total of 72 participants (36 per group) were needed to ensure sufficient statistical power for detecting differences in physical function between interventions.

Inclusion Criteria:

Adults aged 21 years to 65 years diagnosed with ESRD undergoing hemodialysis. Stable medical condition suitable for participation in physical therapy interventions.

Exclusion Criteria:

Individuals with contraindications to physical therapy or exercise (4) as following:

- Poorly controlled hypertension
- Uncompensated heart failure
- Cardiac arrhythmia requiring treatment
- Recent unstable angina
- Persistent hyperkalemia before dialysis
- Significant valvular heart disease
- Myocardial infarction within the past 6 months
- Significant cerebral or peripheral arteriosclerosis
- Bone disease with a risk of fracture
- Orthopedic or musculoskeletal limitations
- Weight gains > 4 kg from Friday to Monday or from Saturday to Tuesday.
- A recent significant change in the resting echocardiography
- Third degree atroventricular heart block without pacemaker
- Severe aortic stenosis
- Cardiac tamponade
- Suspected or known dissecting aneurysm
- Active or suspected myocarditis or pericarditis
- Thrombophlebitis or intracardiac thrombi
- Recent systemic or pulmonary embolus
- Acute infections
- Pregnancy
- Unstable medical conditions that may affect participation or outcomes.

Procedure and Protocol

In this randomized controlled trial comparing intradialytic versus pre-dialysis physical therapy interventions, the roles and tasks of the team members working with the patients are clearly defined to ensure a smooth and effective study process.

Doctor's Responsibilities:

- **Selection and Education:** The doctor will select patients based on the inclusion and exclusion criteria. They will explain the study in detail, educate the patients about the procedures and expected outcomes, and address any initial questions.

All participants in the study will receive **the same educational session** about the **benefits and safety of exercise** for individuals undergoing dialysis. This ensures that both groups have equal knowledge and understanding of how physical activity can support their health, without introducing bias between the intradialytic and pre-dialysis groups.

Education Topics Covered:

1. **Benefits of Exercise for Dialysis Patients**
    - Improves muscle strength and endurance
    - Enhances cardiovascular health
    - Helps manage blood pressure and blood sugar levels
    - Reduces fatigue and improves overall energy levels
    - Enhances quality of life and mental well-being
2. **Safety Considerations**
    - Importance of gradual progression and listening to your body
    - Recognizing symptoms that require stopping exercise (e.g., dizziness, chest pain, excessive fatigue)
    - Monitoring vital signs before and after exercise
    - The role of the healthcare team in ensuring a safe exercise program
3. **Encouragement for Long-Term Physical Activity**
    - Strategies to incorporate movement into daily life
    - Setting realistic and achievable fitness goals
    - The importance of consistency in maintaining physical health

This standardized education session will be delivered **before the intervention begins**, ensuring that all participants receive **equal guidance and motivation**, regardless of their assigned exercise group.

- **Monitoring and Coordination:** The doctor will monitor secondary outcome measures throughout the study. They will inform team members to obtain consent from the patients and initiate the intervention.

Nurse's Responsibilities:

- **Consent and Randomization:** The nurse will contact patients immediately after the doctor's initial consultation to obtain informed consent. They will perform the randomization by flipping a coin; however, the nurse and patient will remain blinded to the group assignment.
- **Patient Support and Secondary Outcomes:** The nurse will answer any further questions from patients and re-educate them if necessary. They will start taking secondary outcome measures according to the protocol and send the patient to the physical therapist.

Physical Therapist's Responsibilities:

- **Patient Reception and Primary Outcomes:** Upon receiving patients from the nurse, the physical therapist will address any additional questions and provide further education if needed. They will take primary outcome measures as specified in the protocol.
- **Treatment Administration:** The physical therapist will commence the physical therapy treatment according to the assigned group (intradialytic or pre-dialysis). For pre-dialytic patients, it is crucial to check and record vital signs both before and after the therapy session to ensure patient safety and monitor any immediate effects of the intervention.

- **Six-Minute Walk Test (6MWT):**

- **Preparation:** Ensure the treadmill is calibrated and set to a comfortable speed. Explain the test to the patient, emphasizing that they should walk at their own pace and that they can slow down or stop if needed.
- **Conducting the Test:** Start the timer for six minutes once the patient begins walking. Encourage the patient verbally but do not set a specific pace. Monitor the patient for any signs of distress or discomfort throughout the test.
- **Post-Test:** Record the total distance walked in six minutes. Allow the patient to rest and monitor their vital signs to ensure they recover well.

- **Five Times Sit to Stand Test (FTSST):**

- **Preparation:** Ensure a standard chair without armrests is available and supported against the wall. The patient should sit in the middle of the chair, back straight, feet flat on the floor, and arms crossed over their chest.
- **Conducting the Test:** Explain the test to the patient, instructing them to stand up fully and sit down five times as quickly as possible. Start the timer as soon as the patient begins the first stand.
- **Post-Test:** Stop the timer once the patient sits down after the fifth stand. Record the total time taken to complete the five repetitions. Monitor the patient for any signs of fatigue or discomfort.

This structured approach ensures that each team member understands their specific tasks and responsibilities, facilitating a coordinated and effective study process that prioritizes patient care and accurate data collection.

Interventions:

A- Intradialytic Physical Therapy Group:

1. **Frequency:** Physical therapy sessions are scheduled to coincide with dialysis treatments, typically two times a week for three months.

2. **Duration:** Each session for 30minutes of the dialysis treatment, this typically ranges from 3 to 4 hours. The physical therapy component within the session may vary based on patient tolerance and other factors.

3. **Exercise Program**

    - Warm-up (5 minutes): Begin with gentle cardiovascular warm-up activities such as cycling on a stationary bike at a comfortable pace.

    - Resistance Training (15-20 minutes): Perform resistance exercises using resistance bands or light dumbbells. Exercises may include:
        - Bicep curls: 2 sets of 10-15 repetitions
        - Tricep extensions: 2 sets of 10-15 repetitions
        - Leg presses: 2 sets of 10-15 repetitions
    - Cool-down and Relaxation (5 minutes): Conclude the session with gentle stretching and relaxation techniques to promote recovery and reduce muscle tension.
    - The limb connected to the device will not be exercised.

4. **Total Number of Sessions:** Over the intervention period (e.g., 3 months), participants attend physical therapy sessions two times a week, resulting in approximately 24 sessions.

B- Pre-Dialysis Physical Therapy Group:

1. **Frequency:** Physical therapy sessions are scheduled separately from dialysis treatments, allowing for greater flexibility. Sessions may be scheduled two times per week based on patient availability and preference.

2. **Duration:** Each session typically for 30 minutes, depending on the specific exercise program and patient tolerance.

3. **Exercise Program**

    - Warm-up (5 minutes): Begin with gentle cardiovascular warm-up activities such as cycling on a stationary bike at a comfortable pace.

- Resistance Training (20-25 minutes): Incorporate resistance exercises using various equipment or bodyweight. Example exercises may include:
    - Squats: 2 sets of 10-12 repetitions
    - Lunges: 2 sets of 10-12 repetitions per leg
    - Chest presses: 2 sets of 10-12 repetitions
- Flexibility and Stretching (10-15 minutes): Perform stretching exercises targeting major muscle groups to improve flexibility and range of motion. Hold each stretch for 15-30 seconds and repeat 2-3 times.
- Balance and Stability (10-15 minutes): Include balance exercises such as standing on one leg, heel raises, and balance board activities to improve stability and coordination.
- Cool-down and Relaxation (5 minutes): Conclude the session with gentle stretching and relaxation techniques to promote recovery and reduce muscle tension.

4. **Total Number of Sessions:** Over the intervention period of 3 months, participants attend physical therapy sessions two times per week, resulting in approximately 24 sessions.

C- Patients of both groups will be informed to stop the exercise immediately if they felt any of the following symptoms

- Headache
- Palpitations
- Dizziness
- Anxiety
- Nausea
- Exhaustion

D- Blood samples will be collected by Nurse staff at baseline and once per month after dialysis and submit the results in secondary outcome measure.

Outcome Measures:

Primary Outcome Measure:
Physical Function:
Six-Minute Walk Test
Five Times Sit to Stand Test
Quality of Life (Kidney Disease Quality of Life questionnaire)

Secondary Outcome Measures:
Hemoglobin Levels
Electrolyte Levels (Sodium, Potassium, Calcium, Phosphorus)

Data Collection

Data collection will be in 3 stages of the study

1- Baseline Assessment:

Demographic data and baseline measurements of outcome variables will be collected before the intervention.

2- Re-assessments:
Assessments will be conducted at regular intervals every 4 weeks throughout 3 months.

3- Follow-up Assessments:
Final assessments will be conducted after 6 months.

Adverse Events Monitoring:
Any adverse events or complications related to physical therapy interventions will be monitored and documented.

Statistical Analysis:

Descriptive Statistics

- **Baseline Characteristics:** Summarize demographic and clinical characteristics of participants using means and standard deviations for continuous variables and frequencies and percentages for categorical variables.
- **Comparability:** Use t-tests for continuous variables and chi-square tests for categorical variables to compare baseline characteristics between the two groups to ensure comparability.

1. Primary Analysis

- **Intention-to-Treat (ITT) Analysis:** Analyze all participants in the groups to which they were randomized, regardless of adherence to the intervention.
- **Per-Protocol (PP) Analysis:** Analyze only those participants who completed the study as per the protocol to assess the true efficacy of the intervention.

Hemoglobin Levels and Electrolyte Levels

- **Model:** Use repeated measures ANOVA or linear mixed models to assess changes in hemoglobin and electrolyte levels over time between the two groups.

- **Fixed Effects:** Time, group (IDPT vs. PDPT), and interaction between time and group.
- **Random Effects:** Include a random intercept for participants to account for within-subject correlations.
- **Post-hoc Tests:** Conduct pairwise comparisons with Bonferroni correction if significant interactions are found.

2. Secondary Analysis

- **Quality of Life:** Use paired t-tests or Wilcoxon signed-rank tests to compare baseline and follow-up Quality of Life scores within each group. Use independent t-tests or Mann-Whitney U tests to compare changes between groups.

3. Subgroup Analysis

- **Predefined Subgroups:** Conduct subgroup analyses based on factors such as age, gender, baseline physical function, and dialysis modality.
- **Interaction Terms:** Include interaction terms in the models to assess whether the effect of the intervention differs across subgroups.

4. Handling Missing Data

- **Missing Data Mechanism:** Assess the pattern and mechanism of missing data (e.g., missing completely at random, missing at random, or missing not at random).
- **Imputation Methods:** Use multiple imputation or maximum likelihood estimation methods to handle missing data, ensuring the robustness of the results.

5. Sensitivity Analysis

- **Robustness Check:** Conduct sensitivity analyses to assess the robustness of the findings, such as excluding participants with major protocol deviations or using alternative statistical models.

6. Reporting Results

- **CONSORT Flow Diagram:** Include a CONSORT flow diagram to depict the flow of participants through each stage of the study.
- **Tables and Figures:** Present baseline characteristics, primary and secondary outcomes, and subgroup analyses in tables and figures for clarity.
- **Interpretation:** Interpret the results in the context of clinical significance, limitations of the study, and implications for practice.

Ethical Considerations:

This study will be conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and will adhere to all relevant regulations and guidelines for research involving human subjects.

Informed Consent

All participants will be provided with detailed information about the study purpose, procedures, risks, benefits, and their rights as research participants. Informed consent will be obtained from each participant before their enrollment in the study. Participants will have the opportunity to ask questions and clarify any concerns regarding their participation before providing consent.

Confidentiality

Confidentiality of participant information will be strictly maintained throughout the study. Participant data will be anonymized and stored securely to protect their privacy. Only authorized members of the research team will have access to identifiable participant information, and data will be used solely for research purposes.

Voluntary Participation

Participation in the study will be entirely voluntary, and participants will have the right to withdraw from the study at any time without consequences. Withdrawal from the study will not affect participants' access to standard medical care or other services.

Risk Assessment and Mitigation

Potential risks associated with participating in physical therapy interventions will be minimized through careful screening of participants, close monitoring during interventions, and adherence to established safety protocols. Participants will be informed about any potential risks or discomforts associated with the study procedures, and steps will be taken to mitigate these risks.

Beneficence and Non-Maleficence

The study aims to contribute to the advancement of knowledge in the field of renal rehabilitation and improve the quality of care for individuals undergoing dialysis. The welfare and well-being of participants will be prioritized throughout the study, and measures will be taken to ensure that any potential benefits outweigh risks.

Ethical Approval

Ethical approval for the study will be obtained from the Research Ethics Committee (REC) at MOH. The study will be conducted in compliance with the approved protocol, and any amendments to the protocol will be submitted for ethical review and approval.

Limitations:

Potential limitations of the study design include sample size limitations, participant adherence to interventions, and generalizability of findings.

Implications and Conclusion:

Findings from this study will provide valuable insights into the effectiveness of intradialytic versus pre-dialysis physical therapy interventions for individuals undergoing dialysis, with implications for optimizing rehabilitation strategies in this population.

References:

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