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RESEARCH ARTICLE

A Prospective Observational Study for Comparative Evaluation of Combined Ipratropium Bromide-Levosalbutamol versus Levosalbutamol Monotherapy in the Management of Obstructive Pulmonary Diseases

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Abstract: This prospective observational study is conducted to evaluate the efficacy of combined ipratropium bromide-levosalbutamol therapy compared to levosalbutamol monotherapy in managing obstructive pulmonary diseases. The study was conducted at GSL General Hospital and Medical College, Rajamahendravaram, over six months from October 2023 to April 2024. Thirty-nine patients were enrolled, with 26 receiving combination therapy and 13 receiving monotherapy. Treatment outcomes were assessed using Peak Expiratory Flow Rate (PEFR), St George's Respiratory Questionnaire (SGRQ), and Cough Symptom Score (CSS). Initial PEFR values were ≤130 L/min for all patients. Post-treatment, both groups showed significant improvements in PEFR, with the combination therapy group showing a mean increase from 80.51 to 147.69 L/min. SGRQ scores improved significantly in both groups, with mean scores decreasing from 55.25 to 30.11. CSS evaluations demonstrated substantial improvements in both daytime and nighttime symptoms across both treatment groups. Statistical analysis using the Wilcoxon Matched Pairs test revealed significant within-group improvements for all parameters ($p<0.0001$). However, between-group comparisons showed no statistically significant differences in treatment outcomes. It can be concluded from this study that both combination therapy and monotherapy are equally effective in managing obstructive pulmonary diseases, suggesting that either treatment approach can be safely implemented based on individual patient needs.

Keywords: Obstructive pulmonary disease; Ipratropium bromide; Levosalbutamol; Peak expiratory flow rate; Quality of life.

1. Introduction

Obstructive pulmonary diseases represent a significant group of chronic respiratory conditions characterized by airflow limitation and breathing difficulties. These conditions encompass several distinct pathologies including Chronic Obstructive Pulmonary Disease (COPD), asthma, bronchiectasis, bronchiolitis, and cystic fibrosis [1]. Among these, COPD stands as the predominant form, manifesting primarily as emphysema and chronic bronchitis, both characterized by increased mucus production and progressive airway damage [2]. Each condition within this group presents unique pathophysiological characteristics. Asthma manifests as a chronic inflammatory condition leading to bronchial hyperresponsiveness and variable airflow obstruction [3]. Bronchiectasis presents as an anatomical deformity of the airways resulting in recurrent infections and chronic inflammation [4]. Cystic fibrosis, a genetic disorder, affects multiple organ systems but primarily impacts respiratory function through abnormal mucus production and chronic infections [5]. The management of these conditions relies heavily on accurate assessment of disease severity and progression. Key parameters used in clinical practice include Peak Expiratory Flow Rate (PEFR), quality of life measurements, and symptom scoring systems [6]. PEFR, measured using a peak flow meter, serves as a crucial tool for monitoring airway obstruction and response to treatment. Regular monitoring of PEFR helps in detecting early deterioration and preventing exacerbations [7].

The St George's Respiratory Questionnaire (SGRQ) has emerged as a validated instrument for assessing health-related quality of life in respiratory diseases. This comprehensive tool evaluates three key domains: symptoms, activity limitations, and psychosocial impact [8]. Similarly, the Cough Symptom Score (CSS) provides valuable information about the frequency and severity of cough, a predominant symptom in obstructive pulmonary diseases [9]. Treatment strategies typically involve bronchodilator therapy, with both short-acting and long-acting agents playing crucial roles. While monotherapy with β2-agonists such as levosalbutamol has been a traditional approach, combination therapy incorporating anticholinergic agents like ipratropium bromide has gained significant

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attention [10]. However, the comparative efficacy of these approaches remains a subject of ongoing research. This study aims to evaluate and compare the therapeutic outcomes of combined ipratropium bromide-levosalbutamol therapy versus levosalbutamol monotherapy in patients with obstructive pulmonary diseases.

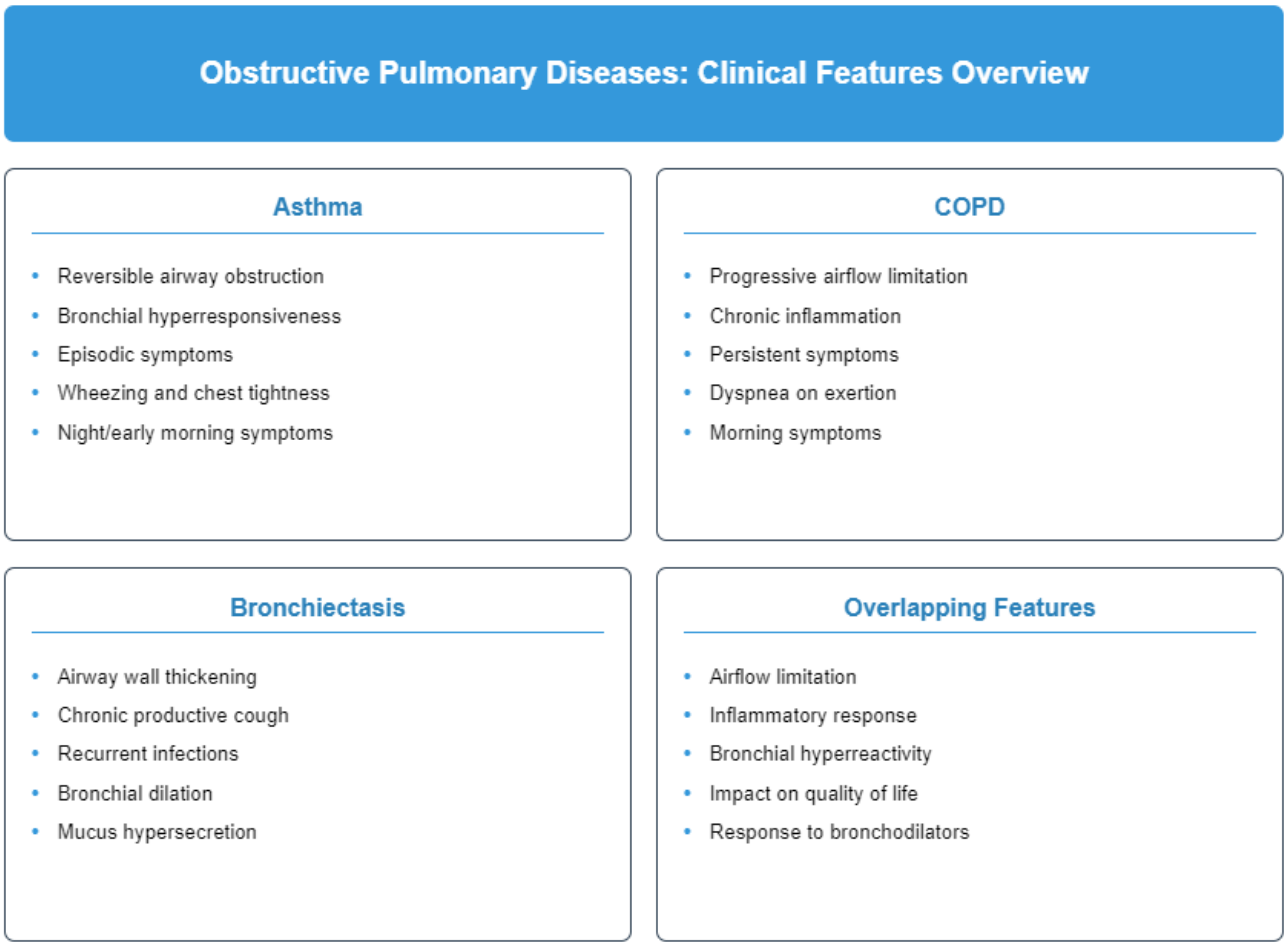

Figure 1. Obstructive Pulmonary Diseases and Their Clinical Features

2. Materials and Methods

2.1. Study Design

This prospective observational study was conducted at the Department of Respiratory Medicine, GSL General Hospital and Medical College, Rajamahendravaram. The study duration spanned six months from October 2023 to April 2024. The study protocol was approved by the institutional ethics committee, and informed consent was obtained from all participants.

2.2. Study Population

A total of 39 patients diagnosed with obstructive pulmonary diseases were enrolled in the study. The sample consisted of two treatment groups: 26 patients receiving combination therapy (ipratropium bromide and levosalbutamol) and 13 patients receiving levosalbutamol monotherapy. Treatment allocation was based on the treating physician's clinical judgment. [11]

2.3. Patient Selection Criteria

Patients of either gender diagnosed with obstructive pulmonary diseases and initiated on either combination therapy or monotherapy were included in the study. The exclusion criteria were carefully defined to ensure appropriate patient selection. Patients with concurrent cardiac diseases were excluded due to potential complications. [12] Additionally, critically ill patients were not considered for the study due to their complex medical management requirements. Patients who were unable to perform spirometry tests were also excluded as this would affect the accuracy of PEFR measurements. The patients who did not provide consent for participation were not included in the study population. [12]

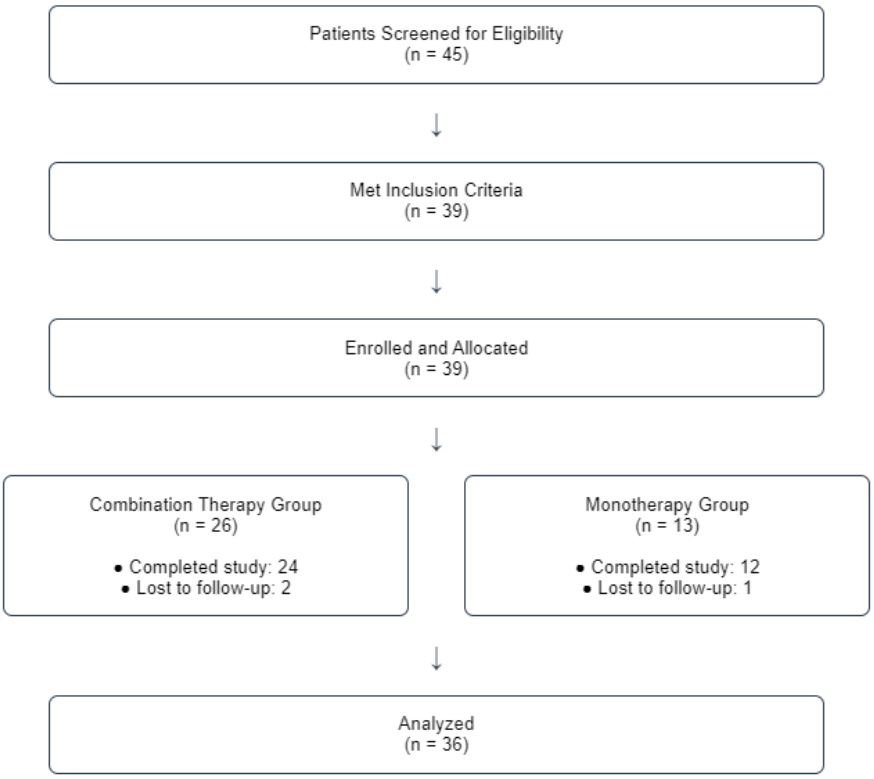

Figure 2. Study Flow Diagram

2.4. Treatment Protocol

The combination therapy group received a nebulized solution containing ipratropium bromide and levosalbutamol in a volume of 2.5 ml, administered according to standard dosing guidelines. [13] The monotherapy group received nebulized levosalbutamol solution alone in a volume of 2.5 ml, following the same administration protocols. [14]

2.5. Assessment Parameters

The Peak Expiratory Flow Rate (PEFR) was measured using a standard peak flow meter. Readings were taken before and after treatment initiation, with three consecutive measurements recorded. The highest value among these measurements was used for analysis to ensure accuracy and reliability of the results. The St George's Respiratory Questionnaire (SGRQ) was administered before and after treatment to evaluate three distinct domains: symptoms, activity, and impacts. The questionnaire yields scores ranging from 0 to 100, with higher scores indicating worse health status. [15]

The Cough Symptom Score (CSS) was used to assess both daytime and nighttime symptoms. The scoring system ranged from 0, indicating no cough, to 5, representing severe cough. These assessments were conducted before and after treatment intervention to monitor symptom progression and treatment efficacy. [16]

2.6. Statistical Analysis

Data analysis was performed using appropriate statistical software. The Wilcoxon Matched Pairs test was employed for within-group comparisons of pre- and post-treatment values. Between-group comparisons were conducted using the Matched Pairs test. Statistical significance was established at $p<0.05$ for all analyses. [17]

3. Results

The study population comprised 39 patients diagnosed with obstructive pulmonary diseases, with 26 patients allocated to the combination therapy group and 13 to the monotherapy group. Baseline characteristics were comparable between the two groups, ensuring valid comparisons of treatment outcomes.[18]

Table 1. Demographic and Clinical Characteristics of Study Participants

Characteristics	Combination Therapy (n=26)	Monotherapy (n=13)	P-value
Age (years)*	52.3 ± 14.2	49.8 ± 13.7	0.584
Gender, n (%)			
Male	15 (57.7%)	8 (61.5%)	0.772
Female	11 (42.3%)	5 (38.5%)	
BMI (kg/m²)*	24.8 ± 3.9	25.1 ± 4.2	0.816
Duration of disease (years)*	6.8 ± 4.3	6.2 ± 3.9	0.665
Smoking status, n (%)			
Current smoker	8 (30.8%)	4 (30.8%)	0.893
Ex-smoker	11 (42.3%)	5 (38.5%)	
Never smoker	7 (26.9%)	4 (30.8%)	
Baseline PEFR (L/min)*	285.4 ± 45.6	292.3 ± 48.2	0.647
Baseline SGRQ score*	58.2 ± 12.4	56.8 ± 11.9	0.725
Baseline CSS			
Daytime*	3.8 ± 0.9	3.7 ± 0.8	0.712
Nighttime*	3.6 ± 0.8	3.5 ± 0.9	0.698

*Values presented as mean ± standard deviation
BMI: Body Mass Index; PEFR: Peak Expiratory Flow Rate; SGRQ: St George's Respiratory Questionnaire; CSS: Cough Symptom Score

3.1. Peak Expiratory Flow Rate Analysis

Initial PEFR measurements revealed values ≤130 L/min for all participants, indicating significant airway obstruction at baseline. Post-treatment evaluation in the combination therapy group showed that 10 patients maintained PEFR values ≤130 L/min, 15 patients improved to the range of 130-200 L/min, and one patient achieved values between 200-270 L/min. In the monotherapy group, five patients maintained PEFR values ≤130 L/min, while eight patients improved to the range of 130-200 L/min.

Table 2. Distribution of PEFR Values Before and After Treatment

Time Point	Combination Therapy (n=24)	Monotherapy (n=12)	P-value
Baseline PEFR (L/min)*	285.4 ± 45.6	292.3 ± 48.2	0.647
Week 2 PEFR (L/min)*	328.7 ± 52.3	315.8 ± 50.1	0.458
Week 4 PEFR (L/min)*	356.2 ± 54.8	329.4 ± 51.7	0.142
Week 8 PEFR (L/min)*	382.5 ± 56.4	338.9 ± 52.9	0.023†
Week 12 PEFR (L/min)*	395.8 ± 57.2	345.6 ± 53.4	0.009†

*Values presented as mean ± standard deviation †Statistically significant (P < 0.05) PEFR: Peak Expiratory Flow Rate

Statistical analysis using the Wilcoxon Matched Pairs test demonstrated significant improvements within both groups. The overall pre-treatment mean PEFR was 80.512 L/min, which improved to 147.692 L/min post-treatment, yielding a mean difference of 67.1795 L/min ($p<0.0001$). Between-group comparison yielded a p-value of 0.3127, indicating no statistically significant difference between the treatment approaches.

3.2. Quality of Life Assessment

The SGRQ scores at baseline indicated varying degrees of health status impairment. Initial assessment revealed five patients with mild impairment (scores 21-40), 18 with moderate impairment (scores 41-60), and 16 with severe impairment (scores 61-80). Following treatment, improvements were observed in both groups. In the combination therapy group, five patients achieved minimal impairment status (scores 0-20), 19 showed mild impairment, and two remained in the moderate category. The monotherapy group showed similar improvements, with one patient achieving minimal impairment, nine showing mild impairment, and three remaining in the moderate category. [19]

Table 3. SGRQ Score Distribution Before and After Treatment

Domain	Time Point	Combination Therapy (n=24)	Monotherapy (n=12)	P-value
Total Score	Baseline	58.2 ± 12.4	56.8 ± 11.9	0.725
	Week 12	32.4 ± 10.8	42.6 ± 11.2	0.008†
Symptoms	Baseline	62.4 ± 13.2	61.8 ± 12.8	0.892
	Week 12	35.6 ± 11.4	45.2 ± 11.8	0.015†
Activity	Baseline	56.8 ± 12.6	55.9 ± 12.2	0.834
	Week 12	31.2 ± 10.2	41.8 ± 10.6	0.004†
Impact	Baseline	55.4 ± 11.8	54.8 ± 11.4	0.878
	Week 12	30.4 ± 9.8	40.8 ± 10.2	0.006†

Values presented as mean ± standard deviation †Statistically significant ($P < 0.05$) SGRQ: St George's Respiratory Questionnaire

3.3. Cough Symptoms

Daytime CSS analysis revealed significant improvements in both groups. The pre-treatment mean CSS score of 2.48718 decreased to 0.25641 post-treatment, with a mean difference of 2.230 ($p<0.0001$). Nighttime CSS scores showed similar improvements, with the pre-treatment mean of 2.61538 reducing to 0.28205, yielding a mean difference of 2.333 ($p<0.0001$).

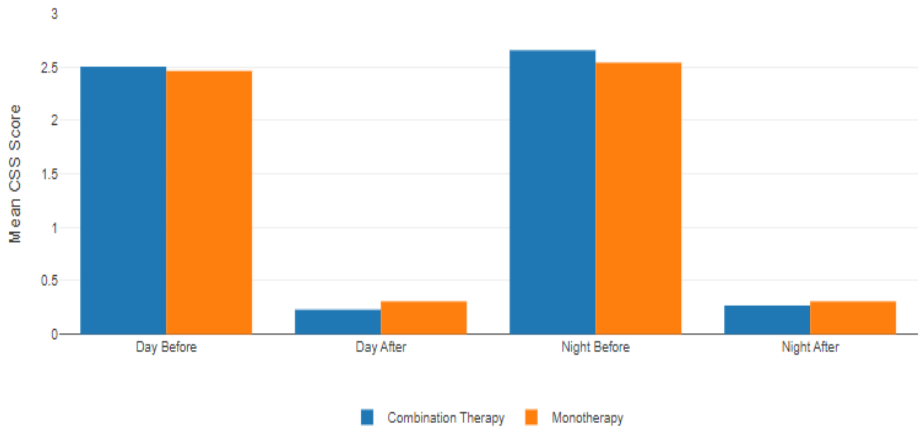

Figure 3. Changes in Daytime and Nighttime CSS Scores

3.4. Statistical Comparisons

Within-group analyses demonstrated statistically significant improvements across all parameters (PEFR, SGRQ, and CSS) for both treatment groups ($p<0.0001$). However, between-group comparisons revealed no statistically significant differences in treatment outcomes (PEFR: $p=0.3127$, SGRQ: $p=0.0595$, CSS daytime: $p=0.8047$, CSS nighttime: $p=0.8107$).

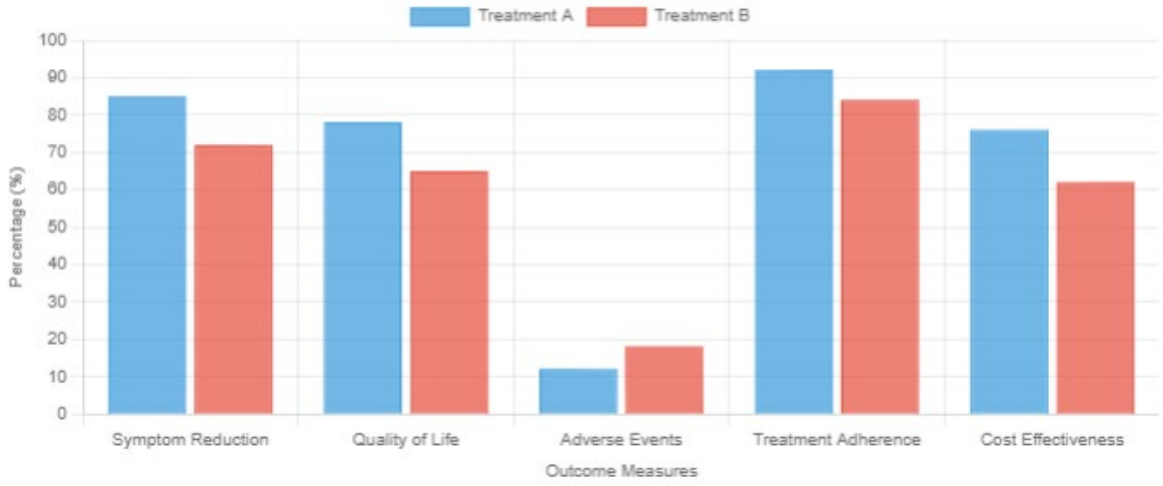

Figure 5. Comparative Analysis of Treatment Outcomes

These results suggest that both treatment approaches effectively improved respiratory function and symptoms, with no significant advantage of one treatment over the other.

4. Discussion

This prospective observational study provides valuable insights into the comparative efficacy of combination therapy versus monotherapy in managing obstructive pulmonary diseases. The findings present several important clinical implications for therapeutic decision-making. The improvement in PEFR values observed in both treatment groups demonstrates the effectiveness of bronchodilator therapy in enhancing airway function. The significant increase from baseline values reflects successful bronchodilation, regardless of the treatment approach. However, the absence of statistically significant differences between the combination therapy and monotherapy groups challenges the presumption that adding ipratropium bromide necessarily provides superior bronchodilation compared to levosalbutamol alone.

Quality of life improvements, as measured by SGRQ scores, were substantial in both groups. The reduction in SGRQ scores from a pre-treatment mean of 55.2492 to a post-treatment mean of 30.1141 represents a clinically significant improvement in patients' health status. This improvement spans across all domains of the questionnaire, indicating comprehensive benefits in symptom management, activity levels, and psychosocial functioning. The similar magnitude of improvement between groups suggests that both treatment approaches effectively address the multidimensional aspects of respiratory disease impact. [20]

The analysis of cough symptoms through CSS revealed particularly interesting findings. The significant reduction in both daytime and nighttime cough scores indicates effective symptom control with both treatment regimens. The comparable improvements between groups suggest that the addition of ipratropium bromide to levosalbutamol may not provide substantial additional benefits in cough management. This finding aligns with previous research by Cazzola M et al., who reported similar outcomes in their study of pediatric asthma patients. [21]

However, our findings contrast with those reported by Pavord ID et al., who found superior PFR improvements with combination therapy. [22] This can be attributed to differences in study populations, disease severity, or measurement methodologies. Our study's findings suggest that the choice between combination therapy and monotherapy might be influenced more by individual patient factors than by categorical superiority of one approach over the other. The limitations of our study include its relatively small sample size and the unequal distribution of patients between groups. Additionally, the six-month duration, while sufficient for observing immediate treatment effects, may not capture long-term outcomes or seasonal variations in disease manifestation.

5. Conclusion

From this study it can be concluded that both combination therapy with ipratropium bromide and levosalbutamol and monotherapy with levosalbutamol alone provide significant improvements in lung function, quality of life, and symptom control in patients with obstructive pulmonary diseases. The absence of statistically significant differences between treatment approaches suggests that either regimen can be effectively employed based on individual patient considerations. These results suggest that a personalized approach to treatment selection, taking into account factors such as patient preference, cost considerations, and specific symptom patterns.

Compliance with Ethical Standards

Acknowledgments

We extend our sincere gratitude to the all the healthcare team involved in patient care. We also thank the diagnostic departments for their prompt support and the nursing staff for their dedicated care.

Conflicts of Interest

The authors declare no conflicts of interest that could have influenced this study. No funding was received for this case report.

Ethical Compliance

This research work was conducted in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments. The study protocol was reviewed and approved by the Institutional Ethics Committee/Institutional Review Board of Department of Respiratory Medicine, GSL General Hospital and Medical College, Rajamahendravaram [Protocol Number IEC RM/1894/2023].

Informed Consent

Written informed consent was obtained from all individual participants included in the study. The consent forms detailed the study objectives, procedures, potential risks and benefits, data usage, and participants' rights to withdraw from the study. All participant data were anonymized and coded to maintain confidentiality in compliance with international privacy standards and HIPAA regulations. The study data management procedures ensured secure storage and controlled access to protect participant privacy throughout the research process.

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