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EFFICACY AND SAFETY OF ACETAZOLAMIDE IN CONGESTIVE HEART FAILURE

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ABSTRACT: This experiment evaluated the efficacy and safety of acetazolamide in the treatment of congestive heart failure (CHF). The treatment outcomes were derived from an examination of clinical characteristics including gender distribution, weight fluctuations, comorbidities, symptoms, cardiac function, and quality of life. The study had 70 people aged between 21 and 85, with a little higher proportion of women (53%) compared to men (47%). Relative to the control group, the experimental group exhibited weight loss, improved respiration, and a reduction in symptoms such as coughing, pleural effusion, pedal edema, and crepitations. Furthermore, acetazolamide medication significantly enhanced the Minnesota Living with Heart Failure Questionnaire (MLHFQ), left ventricular ejection fraction (LVEF), and outcome measures including death, rehospitalization, partial decongestion, and effective decongestion. No significant adverse medication reactions were documented. Further research including bigger cohorts and extended follow-up periods is necessary, as the findings cannot be generalized due to the restricted sample size and brief study duration.

Keywords: *Acetazolamide, Congestive Heart Failure (CHF), comorbidities, cardiac function, MLHFQ (Minnesota Living with Heart Failure Questionnaire).*

1. INTRODUCTION

Congestive heart failure (CHF) is a significant global health concern. Fluid retention and internal congestion are manifestations of this condition, which is attributable to heart failure. Despite advancements in treatment strategies, managing congestive heart failure remains tough; therefore, innovative therapeutic approaches are necessary. Acetazolamide, a carbonic anhydrase inhibitor previously utilized for glaucoma and altitude sickness, has emerged as a viable adjunctive therapy for congestive heart failure (CHF) due to its diuretic effects and ability to enhance renal salt excretion. To thoroughly assess the efficacy of acetazolamide in managing CHF, numerous clinical factors must be meticulously analyzed.

This research aims to evaluate several clinical parameters to deliver a thorough assessment of acetazolamide's effect on congestive heart failure treatment. The study examines not only demographic factors such as gender and age distribution but also critical clinical variables including weight fluctuations, comorbidities, symptoms, cardiac function, and quality of life. This comprehensive methodology facilitates a detailed assessment of acetazolamide's treatment potential concerning several elements of CHF pathogenesis.

Managing fluid overload is crucial in the treatment of congestive heart failure, as it exacerbates symptoms and accelerates disease progression. Acetazolamide efficiently decreases fluid retention in congestive heart failure (CHF) via modifying renal tubular function and enhancing salt excretion. Comprehending its impact on cardiac function,

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symptomatology, and weight fluctuations is essential for delineating its treatment profile and informing therapeutic decision-making.

Comorbidities, including diabetes mellitus (DM) and hypertension (HTN), frequently occur in individuals with congestive heart failure (CHF), exacerbating the condition and complicating treatment [10]. The potential role of acetazolamide in enhancing overall clinical outcomes and reducing condition complexity can be elucidated by analyzing its impact on comorbidity profiles. The patients' perceptions of their health and functional ability influence their quality of life, rendering it a crucial objective in the treatment of congestive heart failure. The Minnesota Living Heart Failure Questionnaire (MLHFQ) can be utilized to assess the quality of life in patients with congestive heart failure (CHF). Data facilitates a deeper comprehension of treatments that exceed typical practices in the field.

This study assesses the efficacy of acetazolamide in treating congestive heart failure (CHF) by utilizing various clinical indicators based on previously established criteria. This study's findings suggest the potential for enhanced patient outcomes and increased treatment efficiency for CHF.

The major objective of this research is to evaluate the efficacy and safety of acetazolamide in the treatment of congestive heart failure. This study is to assess the efficacy of a combination therapy utilizing acetazolamide and loop diuretics in enhancing decongestion rates in individuals with congestive heart failure. The objective is to mitigate physical symptoms such as dyspnea and pedal edema, along with test metrics like left ventricular ejection fraction. We aim to improve the likelihood of effective decompensation and avert rehospitalization. Furthermore, we will assess heart function via the six-minute walk test and enhance NYHA functional class and quality of life as evaluated by the MLHFQ questionnaire.

2. MATERIALS AND METHODS

During a six-month period, we executed a prospective interventional trial in the cardiology departments of a multispecialty hospital in Hyderabad. Seventy participants diagnosed with congestive heart failure (CHF) participated in the trial.

Informed Consent

All subjects provided their informed consent prior to the commencement of the trial.

Ethical Approval

The Institutional Review Board (IRB) at Deccan College of Medical Sciences in Hyderabad, Telangana, granted approval for this study on February 22, 2023, under Approval No. 2023/39/009.

Study Population

All individuals were required to be aged between 21 and 80 and possess both a clinical and echocardiographic diagnosis for inclusion. Participants were excluded if they had chronic renal disease, a hemoglobin level below 7 g/dL, or an estimated glomerular filtration rate (eGFR) below 20 mL/min/1.73 m^2.

Study Procedure

We prospectively recruited 70 patients with congestive heart failure. Inpatient and outpatient cardiology services were utilized to evaluate the study's participants, aged between 21 and 80. The standard treatment for the experimental group comprises beta-blockers, aldosterone antagonists, ACE inhibitors/angiotensin receptor blockers, loop diuretics, and a daily dosage

of 250 mg of oral acetazolamide. The comparative group had only traditional medical care as an option.

Statistical Analysis

We employed suitable parametric and non-parametric tests for the statistical analysis based on the data distribution. Continuous data were expressed as median (interquartile range) or mean ± standard deviation, whereas categorical variables were reported as percentages and frequencies. The alpha level was established at $p < 0.05$. The study was conducted utilizing Prism and Microsoft Excel.

3. RESULTS

Clinical Outcomes

Weight changes

The mean weight change for the control group was 1.114, while for the test group it was 7.171, indicating a substantial disparity. This demonstrates that the experimental group had superior weight loss during the trial. Welch's correction for the unpaired t-test indicated a highly significant difference ($p < 0.001$).

The results suggest that acetazolamide is beneficial in helping patients with congestive heart failure lose weight, better manage their fluids, and increase their urine output, with a mean difference of 6.057 and a narrow 95% confidence range (-6.989 to -5.126). Due to its effects on fluid equilibrium and weight reduction, acetazolamide has the potential to enhance clinical outcomes and quality of life for patients with congestive heart failure.

Table 1: Statistical analysis indicating that acetazolamide influences weight swings; abstract.

Unpaired t test with Welch's correction	Result
P value	<0.001
Significantly different (P < 0.05)	Yes
One- or two-tailed P value	Two-tailed
Welch-corrected t, df	t=13.10, df =44.75
Mean of column A	7.171
Mean of column B	1.114
Difference between means (B - A) ± SEM	-6.057 ± 0.4625
95% confidence interval	-6.989 to -5.126

Shortness of Breath (SOB)

Patients having shortness of breath (SOB) symptoms before, one month after, and three months after therapy are listed in Table 2 for both the test and control groups. The data are classified into five categories: I, II, III, IV, and nil. The absence or severity of shortness of breath is denoted by each grade.

Grades	Test						Control					
	Pre Treatment	%	1 month	%	3 months	%	Pre Treatment	%	1 month	%	3 months	%
I	0	0	9	25.7	4	11.4	0	0	5	14.28	3	8.57
II	4	11.42	18	51.4	4	11.42	4	11.42	11	31.42	13	37.1
III	15	42.8	2	5.71	0	0	14	40	16	45.71	13	37.1
IV	16	45.7	0	0	0	0	17	48.57	0	0	2	5.71
Nil	0	0	6	17.1	27	77.14	0	0	3	8.57	4	11.42

Table 2: Effect of Acetazolamide on Shortness of Breath (SOB)

Both the experimental and control groups revealed substantial changes in the evaluation of shortness of breath (SOB) symptoms during the three-month follow-up period. The intensity of shortness of breath in the test group dropped dramatically, especially in groups III and IV,

where many participants did not experience any symptoms by the end of the research period. This indicates that the therapy that was provided to the control group improved clinical outcomes and reduced shortness of breath.

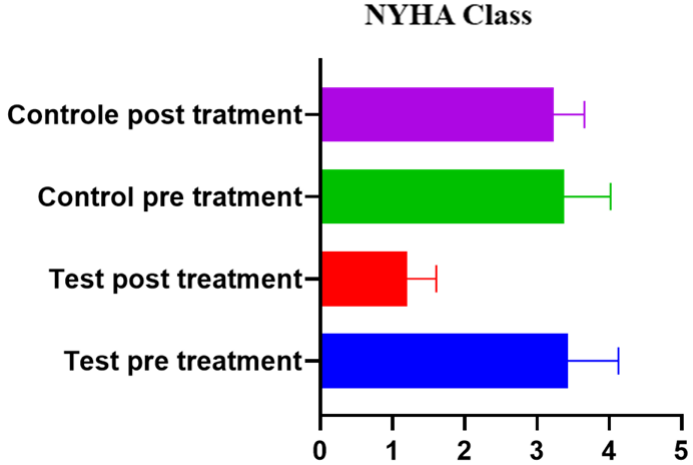
Conversely, the SOB of the control group exhibited significant fluctuations over time; nonetheless, they saw a lesser reduction in symptom severity. The prevalence of moderate to severe dyspnea in persons categorized as II and III rose after one month and remained at three months. It shows that the intervention utilized in the study group had a stronger impact in lowering breathlessness compared to the standard treatment. These data reveal that compared to normal treatment alone, the treatment considerably increased the test group's shortness of breath.

Cardinal Function:

The results of the cardinal function test were compared between the control and experimental groups both before and after treatment, and also within each group. The Wilcoxon matched-pairs signed-rank test was utilized to ascertain statistical significance. Significant statistical alterations ($p < 0.001$) were seen between the test group's pre- and post-treatment results, demonstrating that the medicine enhanced cardiac function in a quantifiable manner. Conversely, no significant alteration was observed in the control group ($p = 0.1322$). The post-treatment scores of the two groups exhibited substantial differences ($p < 0.001$), indicating that the intervention produced superior functional improvement compared to standard therapy.

Distribution of NYHA Class:

Figure 1 illustrates the outcomes of the Wilcoxon matched-pairs signed-rank test, employed to compare the distribution of NYHA classes prior to and following treatment. The test group exhibited a statistically significant reduction in symptom severity post-therapy ($p < 0.0001$). Nonetheless, no significant alteration was observed in the control group ($p = 0.3833$). Post-therapy, there were discernible alterations in the groups relative to standard care, signifying that the intervention exerted a substantial influence on NYHA class.



Results indicating a substantial alteration from pre- to post-treatment imply that the treatment positively influenced the test group's NYHA classification. This indicates that the medication effectively alleviated heart failure symptoms and enhanced functional ability in these patients.

Left Ventricular Ejection Fraction (LVEF) — Data Analysis

We employed an unpaired t-test with Welch's correction to ascertain whether a significant difference in left ventricular ejection fraction (LVEF) existed between the test and control

groups (Figure 2). A statistically significant difference ($p < 0.001$) was noted in the mean change in LVEF among the groups, based on the data. The Welch-corrected t-value of 7.267 indicates a significant difference in improvements between the two groups.

The experimental group exhibited a superior average change in LVEF compared to the control group (0.2749). This suggests that patients receiving acetazolamide exhibited superior cardiac function relative to those undergoing conventional medical treatment. The test group exhibited a significant enhancement in left ventricular ejection fraction post-therapy, as evidenced by the negative mean difference ($B - A = -0.1680 \pm 0.02312$) and the 95% confidence interval (-0.2142 to -0.1218).

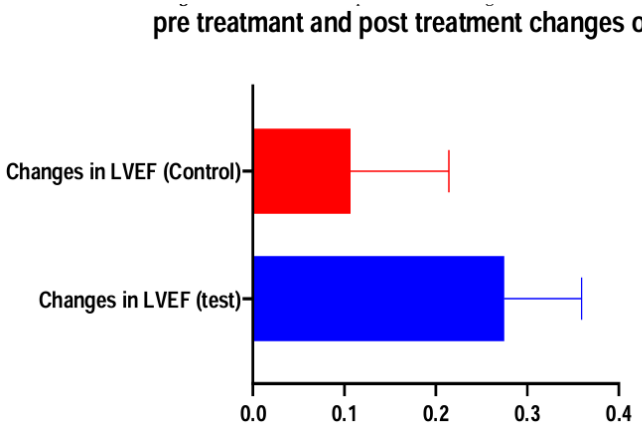


Figure 2: Pre-treatment and post-treatment changes in LVEF

The findings indicate that acetazolamide can enhance LVEF in individuals with congestive heart failure, representing a significant implication. These findings possess significant clinical ramifications, as they indicate that heart failure patients with elevated LVEF levels exhibit superior cardiac health and reduced mortality rates. Due to its beneficial effect on LVEF, acetazolamide presents a promising novel therapeutic option for heart failure management and the enhancement of long-term outcomes.

Minnesota Living With Heart Failure Questionnaire (MLHFQ) — Data Analysis

The MLHFQ scores of the test and control groups were compared pre- and post-treatment utilizing the Wilcoxon matched-pairs signed-rank test. The results indicated that the MLHFQ ratings of neither group were substantially different from one another prior to the commencement of treatment. Nonetheless, post-treatment, significant variations were evident. Figure 3 indicates a statistically significant disparity between the MLHFQ scores of the two groups, with the experimental group exhibiting markedly higher values.

Acetazolamide enhanced quality of life more significantly than conventional therapy alone, as indicated by the MLHFQ. Acetazolamide is effective in alleviating symptoms of heart failure and improving patient health, as indicated by the findings.

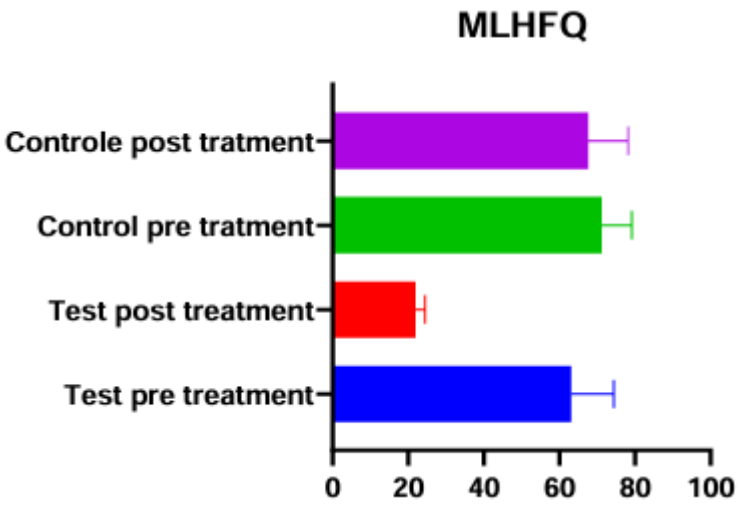


Figure 3: Bar diagram of MLHFQ scores

Endpoint Data Analysis

The endpoint data analysis categorized the test and control groups into four classifications: partial decongestion, mortality, rehospitalization, and effective decongestion (Figure 4). A statistically significant p-value below 0.001 signifies a substantial disparity in the distribution of these categories between the two groups. This indicates that the intervention—presumably acetazolamide—exerted a substantial effect on endpoint results relative to standard care.

The descriptive statistics provide insights into the distinctions and trends within each endpoint category throughout the study groups. The results indicate that the intervention effectively reduced traffic, mortality, and readmission rates for patients in the experimental group relative to the control group.

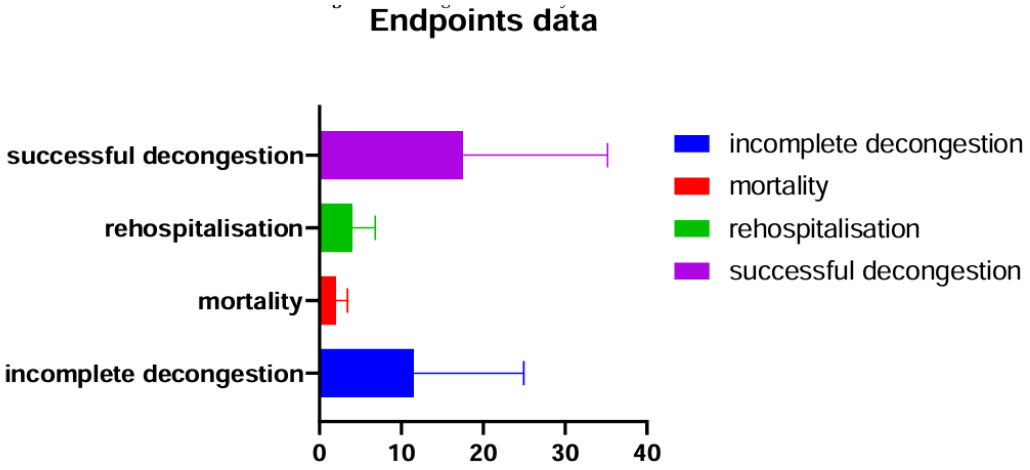


Figure 4: Bar diagram showing summary of clinical outcomes

4. CONCLUSION

Researchers discovered that acetazolamide significantly outperformed both placebo and the established course of care in individuals with congestive heart failure (CHF). The New York Heart Association (NYHA) functional class improved, and symptoms included dyspnea, crepitations, cough, pedal edema, and pleural effusion were eased, demonstrating that acetazolamide significantly facilitated weight reduction. Furthermore, endpoint outcomes such as hospitalization, mortality, decongestion, and effective decongestion were markedly improved by acetazolamide. The Minnesota Living with Heart Failure Questionnaire

(MLHFQ) not only enhances quality of life but also has the potential to diminish mortality and morbidity in individuals with congestive heart failure (CHF).

Although acetazolamide exerted a minor influence on serum electrolyte levels, its impact was not significant. This indicates that individuals with CHF can effectively control their condition. The findings indicate that acetazolamide enhances clinical outcomes, alleviates CHF symptoms, and augments cardiac function. This indicates that it is an effective alternative for managing CHF. Comprehensive assessment of its long-term safety and therapeutic advantages requires more investigation.

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