Effect of Active Prolonged Inspiration Technique on Intractable Hiccups in Hemodialysis Patients

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ABSTRACT

Background: Non-pharmacological interventions like the Active Prolonged Inspiration technique, which combines sustained inspiratory effort and hypercapnia induction, offer a potential solution. Intractable hiccups, a distressing symptom in hemodialysis patients, significantly impair quality of life by disrupting eating, sleeping, and daily activities. This study determined the efficacy of active prolonged inspiration technique in relieving hiccups and its physiological effects in hemodialysis patients. **Methods:** thirty two hemodialysis patients (19 men and 13 women) were suffering from intractable hiccups with their age ranged from (45-64) years old recruited from El Sahel Teaching Hospital were randomized into two groups: Group A (9 men &7 women) received active prolonged inspiration training (3 sessions/week for 12 weeks) alongside conventional physical therapy training, while Group B (10 men &6 women) received conventional physical therapy training. Hiccups severity was assessed using a 0–10 scale, and arterial blood gases (PCO_2, PO_2, pH) were measured pre- and post-intervention, the duration of the study: from October 2024 to February 2025 **Results:** Group A exhibited a 67% reduction in hiccup scores, alongside a significant increase in PCO_2 (16%) and decrease in PO_2 (11.5%), indicating hypercapnia. Group B showed no significant changes. Between-group comparisons revealed statistically significant differences in post-intervention hiccup scores and PCO_2 levels ($p=0.001$), favoring active prolonged inspiration technique. No significant changes in pH were observed in either group. **Conclusion:** The active prolonged inspiration technique effectively reduces hiccup severity in hemodialysis patients, likely through hypercapnia and reflex arc modulation. Its simplicity, safety, and non-pharmacological nature make it a promising intervention for improving patient quality of life. Further research is warranted to optimize protocols and explore long-term efficacy.

Keywords: active prolonged inspiration technique, intractable hiccups, hemodialysis, hypercapnia, non-pharmacological intervention.

INTRODUCTION

Hiccups, also known as singultus, are involuntary contractions of the diaphragm muscle followed by laryngeal closure. They arise from a state of hyper excitability in the reflex arc, involving three main components: firstly, the afferent limb, responsible for receiving signals from either the central nervous system or irritated peripheral nerves, secondly, central brain processing; and thirdly, the efferent limb, where the brain sends signals through nerves to the diaphragm and respiratory muscles, triggering the characteristic hiccup response. Neurotransmitters such as dopamine (D) and gamma-aminobutyric acid (GABA) are implicated in this phenomenon (1).

Hiccups are a nearly universal phenomenon experienced by humans, even as early as in utero (2). They are also occasionally referred to by the medical term singultus from a Latin term meaning "sobbing" (3). The classic "hic" sound is created when the sudden inspiration is interrupted by the closing glottis.

Chronic kidney disease (CKD) is characterized by persisting renal damage and /or loss of renal function. The condition is associated with high morbidity and mortality throughout the continuum from early disease to advanced stages that require renal replacement therapy. Although much progress has been made in prevention, detection and treatment, CKD remains a major public health problem. Its global prevalence is estimated at 5–10 % and primarily because of cardiovascular morbidity and mortality, the global burden of CKD-associated diseases is alarmingly high (4).

The effects of chronic kidney disease are not limited only to the kidney but also involve other body systems, such as the respiratory system (5). When a person has end stage renal disease, the body becomes unable to keep homeostasis of the metabolic function as a result of loss of kidney function; therefore, renal replacement therapy is essential. Among the available renal replacement therapies, hemodialysis is the most commonly used (6, 7). While hemodialysis replaces kidney function to some extent, chronic hemodialysis has been reported as a catabolic process because of the negative protein and energy balance that leads to myopathy and loss of muscle mass (8).

When CKD develops into end-stage renal disease (ESRD), patients must receive hemodialysis (HD), peritoneal dialysis, or kidney transplantation to sustain life. Because 87.7% of ESRD patients choose HD as renal replacement therapy, we primarily focus on diaphragmatic dysfunction in HD patients in the present study. The clinical symptoms of diaphragm dysfunction mainly consist of unexplained dyspnoea (especially in the supine position), fatigue, and hiccups, all of which are prevalent in HD patients (9).

Intractable hiccups (lasting more than one month) require medical attention. Intractable hiccups, although rare, can significantly impair a patient's quality of life. The etiology of intractable hiccups is diverse, but they are often associated with

serious underlying medical conditions, such as severe renal dysfunction and uremia (10).

Intractable hiccups can lead to complications such as exhaustion, feeding difficulties, disrupted sleep patterns, and significant impairment in a patient's quality of life. Although potentially idiopathic or drug-induced in certain cases, intractable hiccups necessitate medical attention as they are frequently linked to serious underlying medical conditions, including brain tumors, strokes, severe gastrointestinal diseases, and toxic-metabolic states, including severe renal dysfunction and/or uremia (10).

MATERIALS AND METHODS

This study was conducted in Elsahel hospital between October 2024 and February 2025 after the acceptance of faculty of physical therapy research ethical committee No:P.T.REC /012/005642. to determine the effect of active prolonged inspiration (HAPI) technique on relieving hiccup in hemodialysis Patients Pre and post treatment , Randomized Control Trial.

Sample Size calculation:

The sample size was calculated using the G*Power software (version 3.0.10). 32 individuals (including both men and women), ranging in age from 45 to 64, were included in the study and individuals were assigned into 2 groups. **Group (A)** 16 patients trained with intradialytic aerobic exercises and HAPI technique**. group(B**) 16 patients maintained on intradialytic aerobic exercises and hemodialysis for 12 weeks.

Inclusion criteria:

The study included patients aged between 45 and 64 years, encompassing both 19 men and 13 women. They were on hemodialysis while also suffering from persistent or recurrent hiccups. They were medically and psychologically stable, with no significant comorbidities that could interfere with the study. Additionally, they had been regularly receiving their physician-prescribed pharmacotherapy. They signed consent form prior to participation, ensuring voluntary participation and adherence to ethical research standards.

Exclusion criteria (11): Patients with chronic respiratory diseases, including bronchial asthma, were excluded from the study. Additionally, those who refused to participate or declined to sign the informed consent form were not enrolled.

Arterial blood gases (ABG).

ABG was drawn before and after the treatment period from the arm free of fistula before the hemodialysis session. Blood gas parameters including pH, PCO2, PO2 **(12).**

Hiccups Assessment Instrument (HAI)

Was devised to measure hiccup severity. Patients were asked to rate the severity of their hiccups on a 0–10 numerical scale, ranging from 0 for ‘‘no hiccups’’ to 10 for ‘‘worst hiccups.’’ Patients were informed that a rating of 1–3 would be considered ‘‘mild’’ hiccups, that is, nagging, annoying, but interfering little with Activities of Daily Living (ADL); 4–6 would be considered ‘‘moderate’’ hiccups, that is, interfering significantly with ADL;

and 7–10 would be ‘‘severe’’ hiccups, that is, disabling and unable to perform ADL **(13).**

Procedure

Group (A), Each patient was educated on the performance of the active prolonged inspiration technique 3 sets , each set contain 3 repetitions , 3 sessions weekly for 12 weeks . These sessions were performed intra-dialytic (after 1h from the beginning of the dialysis session**).**

Hiccup relief using Active Prolonged Inspiration technique.

Each patient was educated on the performance of the active prolonged inspiration technique. They were be instructed to inspire maximally then, once at peak inspiration, to continue to attempt to inhale for a total of 30 seconds. After 30 seconds, patients slowly exhale, and then resume normal respiration. When performing this technique, the patient contracts the diaphragm maximally, providing constant stimulus to the phrenic nerve. This is in contrast to classic breath-holding which allows the diaphragm to relax against a closed glottis **(14).**

It is important to maintain an open glottis because this ensures continuous inspiratory effort during the performance of the technique. A closed glottis creates conditions for the Valsalva maneuver or simple breath-holding if the technique is performed incorrectly. If patients were observed performing the technique incorrectly, they would be coached on correct performance. Following additional coaching, each patient would be able to successfully complete the technique **(14) .**

Group (B) conventional physical therapy.

Intradialytic conventional physical therapy

Aerobic exercise of range of motion (ROM) UL and LL was done for a 15 minutes period, during the first 2 hours of the dialysis session (based on the patients’ capacity) and no exercise was prescribed during the second half of the session **(15)**.

The prescribed exercises included rotating the wrist as follows: 20 rounds per minute (RPM) clockwise, 20 RPM counter-clockwise, 20 times full flexion and extension of the wrist, 20 times full flexion and extension of the elbow joint, 20 RPM of rotating the ankles clockwise, 20 RPM of rotating the ankles counter-clockwise, 20 times full flexion and extension of the ankles **(15).**

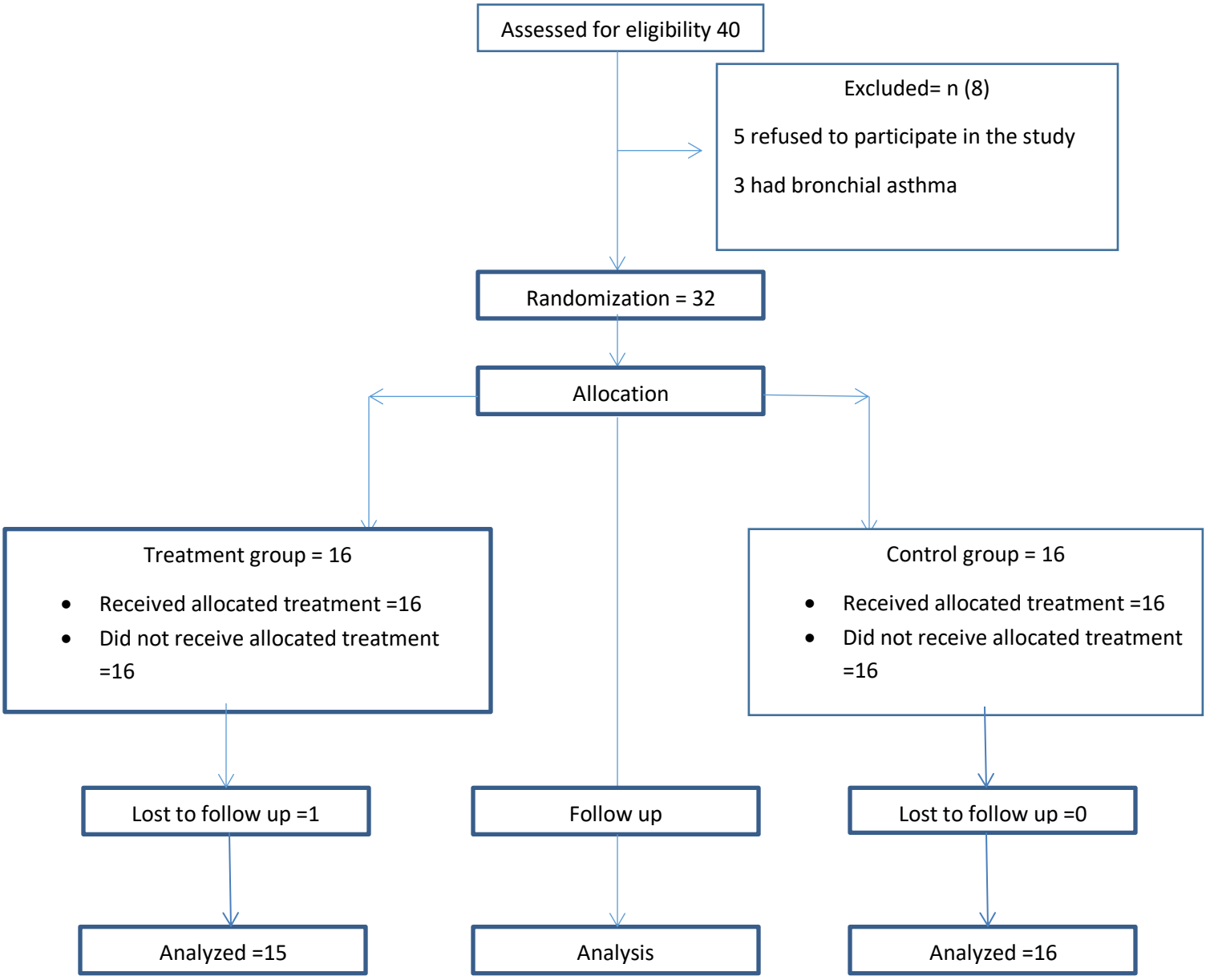

Figure (1) Randomization follow chart

Data analysis and statistical design

Data were expressed as mean± SD. Unpaired t-test was used to compare between subjects Characteristics of the two groups. Shapiro-Wilk test was used for testing normality of data distribution. MANOVA was performed to compare within and between groups' effects for measured variables (PCo2, PO2, HAI and PH). Statistical package for the social sciences computer program (version 20 for Windows; SPSS Inc., Chicago, Illinois,

USA) was used for data analysis. P less than or equal to 0.05 was considered significant.

Results

Demographic data of subjects:

A total of thirty two haemodialysis patients participated in this study; they were assigned into 2 equal groups; group (A), consisted of 16 patients trained with active prolonged inspiration technique for 3 sessions weekly for 12 weeks in addition to their medical treatment and heamodialysis (one patient was died after 10 weeks of beginning of treatment) and group (B), control group, consisted 16 patients maintained on their medical treatment and heamodialysis. As shown in table (1) and (figures 1); the mean value of patients age of groups A and B were (56.06±7.8) and (55.38±7.09) years respectively, the mean value of patients weight were (80.63±9.93) and (81.44±8.02) kg respectively, the mean value of patients height were (167.31±8.49) and (166.5±7.93) cm respectively and the mean value of patients BMI were (28.6±4.19) and (29.5±2.57) kg/m^2 respectively. There were no significant difference between the mean value of patients' age, weight, height and BMI of both groups (p> 0.05).

Table (1): Demographic data of subjects of both groups

Demographic data	Group A (n=15)	Group B (n=16)	t-value	p-value
Age (years)	56.06±7.8	55.38±7.09	0.405	0.688
Weight (kg)	80.63±9.93	81.44±8.02	-0.194	0.848
Height (cm)	167.31±8.49	166.5±7.93	-0.012	0.991
BMI (kg/m^2)	28.6±4.19	29.5±2.57	-0.483	0.633
Sex men women	N (%) 7 (47%) 8 (53 %)	N (%) 9 (56%) 7 (44%)	χ^2= 0.285	0.724

Data was expressed as mean ± standard deviation, p- value: significance

I- Arterial blood gases:

I. a- PCo_2

Within group comparison

Group A: The mean values ± SD of PCo_2 pre and post study of group A were 31.93 ± 3.69 and 37.07 ± 2.31 mm Hg respectively. There was a statistical significant increase of PCo_2 post study as compared to pre study by 16% (p = 0.001).

Group B: The mean values ± SD of PCo_2 pre and post study of group B were 33.81 ± 3.9 and 32.31 ± 1.35 mm Hg respectively. There was no statistical significant difference of PCo_2 of group B between pre and post study (p = 0.057), It was decreased post study by 4% (Table 3, figure 2).

Between groups comparison

There was no statistical significant difference in the mean values of PCo_2 pre study between both groups (p= 0.180), while there was statistical significant difference post study between both groups (p= 0.001) in favor to group A (Table 3).

Table (2): Mean ±SD of Arterial blood gases pre and post study of both groups.

Arterial blood gases	Group A Mean ±SD	Group B Mean ±SD	MD (95% CI)	P-value	η^2
PCo_2 (mm Hg)					
Pre study	31.93 ± 3.69	33.81 ± 3.9	-1.88 (-4.67, 0.92)	0.180	0.061
Post study	37.07 ± 2.31	32.31 ± 1.35	4.75 (2.17, 7.34)	0.001*	0.328
MD (95% CI)	-5.14 (-6.73,-3.53)	1.5 (-0.05, 3.05)			
% of change	⇧ 16%	⇩ 4%			
P-value	0.001*	0.057			
PO_2 (mm Hg)					
Pre study	99.4 ± 6.21	95.38 ± 8.07	4.02 (-1.29, 9.34)	0.132	0.076
Post study	88 ± 4.84	97.63 ± 6.14	-9.62 (-13.7,-5.5)	0.001*	0.445
MD (95% CI)	11.4 (8.56, 14.24)	-2.25 (-5, 0.5)			
% of change	⇩ 11.5%	⇧ 2.4%			

P-value	0.001*	0.105			
PH					
Pre study	7.4 ± 0.07	7.39 ± 0.05	0.01 (-0.04, 0.05)	0.732	0.004
Post study	7.41 ± 0.05	7.41 ± 0.04	0.001 (-0.04,0.04)	0.939	0.001
MD (95% CI)	-0.01 (-0.04,0.01)	-0.02 (-0.05, 0.01)			
% of change	⬆ 0.13%	⇩ 0.27%			
P-value	0.268	0.117			

SD: standard deviation, CI: Confidence interval, p-value: level of significance, *: significant, η^2: partial eta square

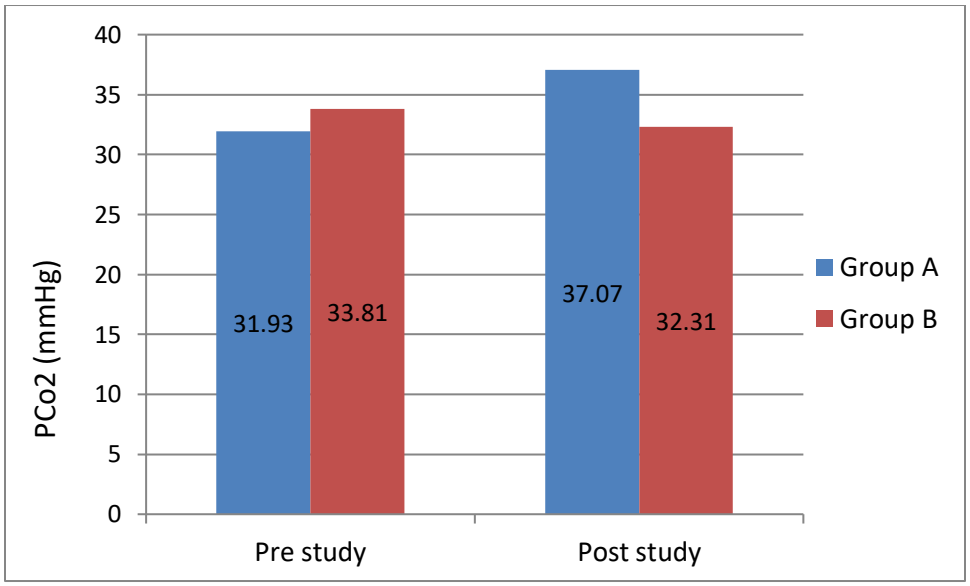

Figure (2): Mean values of PCo_2 pre and post study of both groups

I. b- PO_2

Within group comparison

Group A: The mean values ± SD of PO_2 pre and post study of group A were 99.4 ± 6.21 and 88 ± 4.84 respectively. There was a statistical significant decrease of PO_2 post study as compared to pre study by 11.5% (p = 0.001).

Group B: The mean values ± SD of PO_2 pre and post study of group B were 95.38 ± 8.07 and 97.63 ± 6.14 respectively. There was no statistical significant difference of PO_2 of group B between pre and post study (p = 0.105), It was increased post study by 2.4% (Table 2, figure 3).

Between groups comparison

There was no statistical significant difference in the mean values of PO_2 pre study between both groups (p= 0.132), while

there was statistical significant difference post study between both groups (p= 0.001) in favor to group A (Table 2).

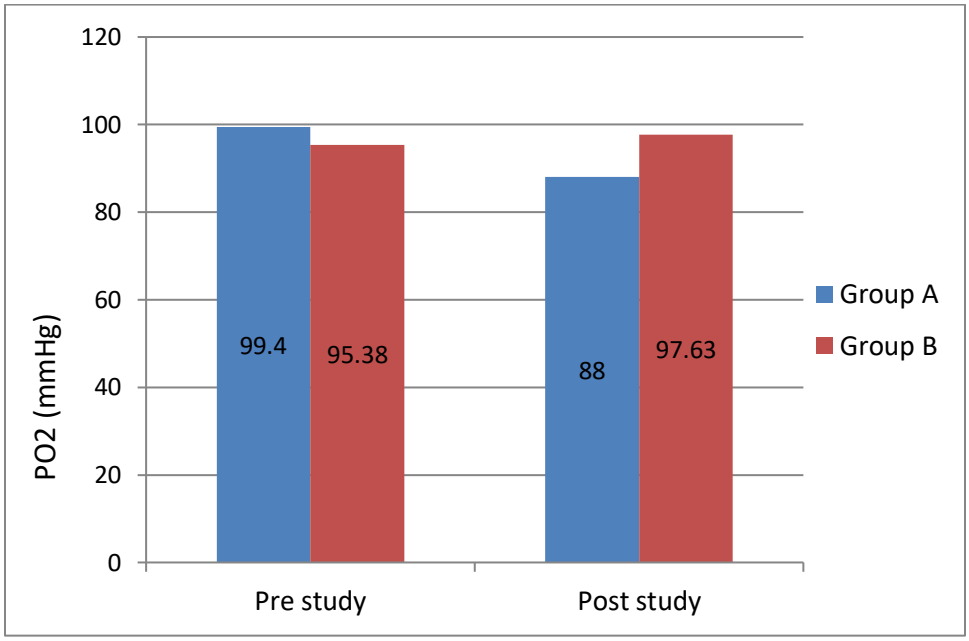

Figure (3): Mean values of PO_2 pre and post study of both groups

II- PH:

Within group comparison

Group A: The mean values ± SD of PH pre and post study of group A were 7.4 ± 0.07 and 7.41 ± 0.05 respectively. There was no statistical significant difference of PH of group A between pre and post study (p = 0.268), It was increased post study by 0.13%.

Group B: The mean values ± SD of PH pre and post study of group B were 7.39 ± 0.05 and 7.41 ± 0.04 respectively. There was no statistical significant difference of PH of group B between pre and post study (p = 0.057), It was increased post study by 0.27% (Table 2, figure 4).

Between groups comparison

There was no statistical significant difference in the mean values of PH pre study between both groups (p= 0.732), Also there was no statistical significant difference post study between both groups (p= 0.939) (Table 2).

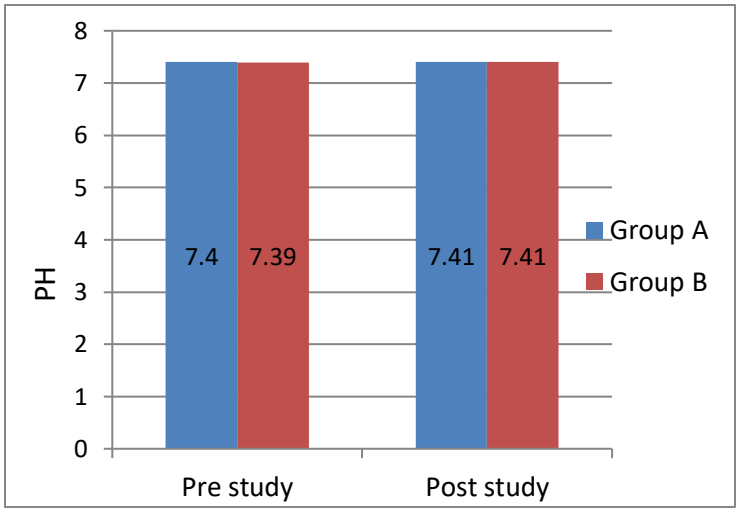

Figure (4): Mean values of PH pre and post study of both groups

III- Hiccups score:

Within group comparison

Group A: The mean values ± SD of Hiccups score pre and post study of group A were 5.27 ± 1.7 and 1.73 ± 1 respectively. There was a statistical significant decrease of Hiccups score post study as compared to pre study by 67% (p = 0.001).

Group B: The mean values ± SD of Hiccups score pre and post study of group B were 5.38 ± 2.78 and 5.69 ± 2.5 respectively. There was no statistical significant difference of Hiccups score of group B between pre and post study (p = 0.335), It was increased post study by 6% (Table 3, figure 5).

Between groups comparison

There was no statistical significant difference in the mean values of Hiccups score pre study between both groups (p= 0.898), while there was statistical significant difference post study between both groups (p= 0.001) in favor to group A (Table 3).

Table (3): Mean ±SD of Hiccups score pre and post study of both groups.

Hiccups score	Group A Mean ±SD	Group B Mean ±SD	MD (95% CI)	P-value	η^2
Pre study	5.27 ± 1.7	5.38 ± 2.78	-0.11 (-1.82, 1.6)	0.898	0.001
Post study	1.73 ± 1	5.69 ± 2.5	-3.95 (-5.46,-2.4)	0.001*	0.497
MD (95% CI)	3.53 (2.86, 4.2)	-0.31 (-0.97, 0.34)			
% of change	⇩ 67%	⇧ 6%			
P-value	0.001*	0.335			

SD: standard deviation, CI: Confidence interval, p-value: level of significance, *: significant, η^2: partial eta square

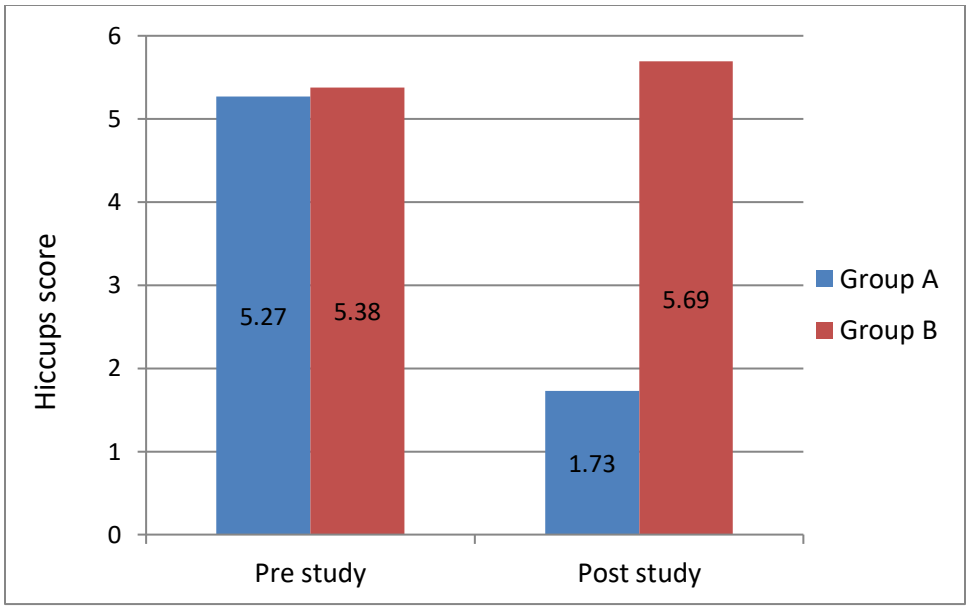

Figure (5): Mean values of Hiccups scorepre and post study of both groups

DISCUSSION

The primary outcome of this study, the significant reduction in hiccup scores by 67% in (Group A), strongly suggests that the active prolonged inspiration technique is an effective non-pharmacological intervention for relieving hiccups in the studied population of hemodialysis patients. This finding is clinically significant, as persistent hiccups can severely impact the quality of life in these patients, affecting nutrition, sleep, and overall well-being (16).

The lack of improvement and slight worsening in group (Group B) further underscores the positive effect attributable to the active prolonged inspiration intervention. This outcome directly challenges the study's null hypothesis, which posited no significant effect of the active prolonged inspiration technique. The results indicate that the null hypothesis can be rejected for the primary outcome of hiccup relief.

The effectiveness of the active prolonged inspiration technique observed in this study aligned with the findings reported by Stacey & Bassett (2024), who also documented immediate hiccup relief in patients using this method. The proposed dual mechanism of active prolonged inspiration interruption of the hiccup reflex arc through conscious, continuous activation of respiratory muscles (phrenic and vagal nerve stimulation) and the induction of transient hypercapnia – likely contributes to

its success (17). The sustained inspiratory effort aims to override the involuntary diaphragmatic spasms characteristic of hiccups, while the breath-holding component, even with an open glottis, promotes CO2 accumulation.

The significant increase in arterial PCO2 (16%) and the concurrent significant decrease in arterial PO2 (11.5%) in Group A post-intervention provide physiological evidence supporting the proposed mechanism involving hypercapnia.

The active prolonged inspiration technique, involving maximal inspiration and continued inspiratory effort for 30 seconds, effectively functions as a form of controlled breath-holding.

This prolonged period without effective ventilation would naturally lead to an accumulation of CO2 and a reduction in O2 in the arterial blood. While the current study measured arterial PCO2, the observed increase to a mean of 37.07 mmHg in Group A, from a baseline of 31.93 mmHg, indicates a clear shift towards a hypercapnic state during or immediately following the HAPI maneuver. It is plausible that PCO2 levels might peak even higher during the 30-second maneuver itself.

The lack of significant change in arterial pH in Group A, despite the rise in PCO2, is an interesting observation. A 16% increase in PCO2 would typically be expected to cause a slight decrease in pH due to respiratory acidosis. However, the mean pH remained stable (7.4 pre to 7.41 post). This could be due to several factors: the intermittent nature of the HAPI application (3 sessions weekly) might not be sufficient to cause a sustained systemic pH change detectable at the point of blood gas analysis, the body's buffering systems might have effectively compensated for the transient CO2 rise, or the timing of the blood gas measurement relative to the active prolonged inspiration maneuver might not have captured the peak acidosis.

The most clinically significant finding of this study was the substantial reduction in hiccup severity scores in the intervention group (from 5.27 ± 1.7 to 1.73 ± 1, representing a 67% decrease). This improvement moved patients from the "moderate" category (scores 4-6, defined as "interfering significantly with Activities of Daily Living") to the "mild" category (scores 1-3, defined as "nagging, annoying, but interfering little with Activities of Daily

Living"), indicating a meaningful clinical benefit.

The magnitude of this improvement exceeds that reported for many pharmacological interventions for hiccups. For instance, Steger et al. (2015) reviewed various pharmacological treatments for persistent hiccups and found variable response rates, with many medications showing only modest efficacy. The substantial improvement observed with the active prolonged inspiration technique suggests that this non-pharmacological approach may be particularly effective for hemodialysis patients suffering from hiccups.

The active prolonged inspiration technique, aims for a temporary increase in PaCO2 to break the hiccup cycle, which appears to have been achieved.

The control group (Group B) showed no significant changes in these blood gas parameters, reinforcing that the observed physiological shifts in Group A are attributable to the active prolonged inspiration intervention.

CONCLUSION

The findings of this study indicate that the Active Prolonged Inspiration technique is an effective non-pharmacological intervention for relieving hiccups in hemodialysis patients. The significant reduction in hiccup scores, accompanied by physiological changes indicative of transient hypercapnia, supports the proposed mechanisms of action involving both direct modulation of the hiccup reflex arc and alteration of blood gas parameters. The active prolonged inspiration technique offers a promising, safe, and accessible treatment option that can improve the quality of life for hemodialysis patients burdened by persistent hiccups.

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