Original Article

Bolus Versus Continuous Infusion of Nitroglycerin for the Treatment of Acute Hypertensive Heart Failure

Mahmoud Shawky Abdelmoneum, Mohammed I. Eitta, Khaled A. Elrabat, Ahmed Mahmoud Bendary

Faculty of Medicine, Benha University, Banha, Egypt

ORCID:

Mahmoud Shawky Abdelmoneum: http://orcid org/0000-0002-5639-6521

Mohammed I Eitta: http://orcid org/0000-0001-6054-5166

Khaled A Elrabat: http://orcid org/0000-0003-1527-3506

Ahmed Mahmoud Bendary: http://orcid org/0000-0002-0161-3779

Abstract

Background: The use of intravenous nitroglycerin by intermittent bolus doses in hypertensive acute heart failure patients (AHF) is still unclear. **Aim and Objectives:** This study aimed to determine intermittent bolus nitroglycerin's effect on the use of resources, admissions to intensive care unit (ICU), hospital length of stay (LOS), and safety. **Patients and Methods:** This prospective, randomized, parallel, single-blind clinical study, which included patients diagnosed with hypertensive AHF, was conducted from May 2019 to October 2020 at Benha University Hospital. Two hundred patients were recruited and randomly allocated into two groups, each composed of 100 patients. **Results:** The prevalence of hypertension and chronic obstructive pulmonary disease patients was significantly higher in patients given intermittent boluses of nitroglycerin than in standard therapy (88.0 vs. 77.0%, $P = 0.041$) and (27.0 vs. 15.0%, $P = 0.037$), respectively. Dyslipidemia was significantly lower in patients on intermittent doses of nitroglycerin than those on standard infusion therapy (30 vs. 66%, $P < 0.001$). The median initial troponin was significantly higher in group I compared to group II (0.145 vs. 0.065 ng/ml, $P < 0.001$). **Conclusion:** Nitroglycerin intravenous boluses were associated with fewer ICU admissions and a shorter LOS in the hospital as opposed to ordinarily infusion therapy. In addition, the mean mechanical ventilation duration was slightly shorter. Finally, continuous nitroglycerin infusion use in AHF management is being questioned.

Keywords: Bolus, continuous infusion, heart failure, hypertensive, nitroglycerin

Introduction

Vasodilators are known to be one of the primary stays of acute heart failure (AHF) treatment. Current guidelines promote the use of vasodilators to minimize preload and afterload in hypertensive AHF.[1]

Although vasodilating agents boost hemodynamics in hypertensive AHF patients, they appear to have a little effect on mortality or readmissions.[2]

Nitroglycerin is the vasodilator of choice for hypertensive AHF patients when intravenously (IV) administered. It is usually given as a continuous infusion. Continuous nitroglycerin infusion, on the other hand, is correlated with higher costs and (LOS), and raising concerns regarding its effectiveness in the treatment of AHF.[3]

When high doses of nitroglycerin were given through an intermittent bolus approach, nitrates produced excess arterial dilation and a significant decrease in afterload, resulting in beneficial central pressure dynamics changes.[4]

Current evidence on bolus high-dose nitrates use indicates that these hemodynamic effects may be correlated with a reduction in myocardial infarction, endotracheal (ET) intubation, and admission to the intensive care unit (ICU),[5] while the actual

Received: 07-10-2021 **Revised:** 10-01-2022 **Accepted:** 09-02-2022

Published Online: 22-03-2022

Access this article online

Quick Response Code:

Website: http://www.ijcva.com

DOI: 10.4103/ijca.ijca_48_21

Address for correspondence: Dr. Mohammed I. Eitta, Faculty of Medicine, Benha University, Banha, Egypt. E-mail: mohammed.eita.me@gmail.com

How to cite this article: Abdelmoneum MS, Eitta MI, Elrabat KA, Bendary AM. Bolus versus continuous infusion of nitroglycerin for the treatment of acute hypertensive heart failure. Int J Cardiovasc Acad 2022;8:14-9.

influences of this strategy on the use of resources have not been assessed.

Previous studies demonstrated that bolus nitroglycerin therapy became the usual clinical practice in several institutions as a part of the treatment of hypertensive AHF.[5]

Accordingly, the present study hypothesized that intermittent bolus nitroglycerin was as effective and safe as continuous infusion when compared in a prospective randomized study.

To the best of our knowledge, this was the first prospective, randomized trial evaluating both strategies for nitroglycerin use in hypertensive AHF patients.

This study compared the efficacy and safety of intermittent bolus nitroglycerin against continuous infusion for the treatment of AHF.

Patients and Methods

This prospective, randomized, parallel, single-blind clinical study, which included patients diagnosed with hypertensive AHF, was conducted in the period from May 2019 to October 2020. This study was done at Benha University Hospital.

Two hundred patients were recruited and randomly allocated into two groups, each composed of 100 patients. Group I received nitroglycerin (NTG) in an intermittent bolus fashion (In a 10 mL syringe, nitroglycerin 10 mg was prepared and administered every three to five minutes in increments by IV push up to 2 mg) with close monitoring of blood pressure and adjustment of nitroglycerin bolus doses according to it. Group II was ordinarily given continuous intravenous NTG infusion at an initial rate of 0.3–0.5 mcg/kg per minute as a starting dose. Nitroglycerin infusion titration was allowed everyone to 3 min in increments of 20 mcg/min guided by blood pressure monitoring and tolerability. At 400 ug/minute, the maximum intravenous nitroglycerin infusion rate was fixed.

Both groups were observed for the need of ET intubation, development of cardiovascular complications, total length of stay (LOS), and worsening of renal functions throughout the duration of the hospital stay.

Upon admission, all patients enrolled in the study underwent many investigations. Full labs were drawn such as complete blood count, electrolytes, kidney function tests, and liver function tests and on regular basis throughout the hospital stay as a follow-up for both groups. In addition, brain natriuretic peptide (BNP) was ordered for some patients when needed. Complete patient history was taken, including history of present illness, medical history hypertension, diabetes, ischemic heart disease, medication history, included prescribed medications, supplements, and over-the-counter medications. Patients of both groups were subjected to physical examination on admission, including vital signs, fluid balance, lower limb edema, heart sounds, and lung base auscultation and then repeated daily for follow-up. All patients had a 12-lead electrocardiogram (ECG) on admission and then was repeated daily postadmission to detect any abnormal changes like arrhythmias or ischemic changes. Echocardiography was performed for patients of both groups at admission for overall estimation of EF, regional wall motion abnormalities, and valvular heart diseases and then again for follow-up. Patients in the study were additionally required to provide written informed consent.

Using a computer software program, simple randomization was done. Sealed opaque envelopes were used for allocation concealment. The trial has been registered in the Pan-African Clinical Trial Registry (PACTR), www.pactr.org, with the registration number ID PACTR20190568443778. Key.

Inclusion criteria

All adult patients who presented to the emergency department (ED) with hypertensive AHF were included in the study. The hypertensive AHF diagnosis was made clinically on the basis of the existence of pulmonary rales, an X-ray consistent with pulmonary edema as determined by the treating physician, and one or more of the following: tachypnea (>30 c/min), significant dyspnea (accessory respiration muscles use or obvious air hunger), marked hypoxia (Oxygen saturation (SpO_2) <90% or <95% on room air and supplemental oxygen, respectively), or hypoxemia (room air partial pressure of oxygen (PaO_2) <50 mm Hg), and a history of heart failure.

Eligibility criteria for patients are as follows: age above 18 years, at least systolic blood pressure (SBP) of 160 mmHg, or mean arterial pressure of 120 mm Hg.

Before enrollment in the study, all patients or close relatives provided written informed consent.

Exclusion criteria

It included any of the following: sublingual, transdermal, or intravenous nitroglycerin sensitivity or intolerance, failure to obtain informed consent, a need for urgent intubation or cardiopulmonary support, noncardiogenic pulmonary edema, pregnancy, suspected right-sided ventricular ischemia, or acute ST-segment elevation myocardial infarction.

Endpoints

Primary efficacy endpoints: Need for ICU admission, total hospital LOS, and posttherapy SBP and diastolic blood pressure (DBP). Primary safety endpoints: Neurologic complications as any new sensory, speech, or movement deficits, diagnosed on a clinical basis or by subsequent computed tomography (CT) brain as stroke or transient ischemic attacks, or cardiovascular complications such as hypotensive attacks that need intervention or acute myocardial injury diagnosed by the troponin rising within the 1st 24 h of presentation by at least 0.25 ng/ml). Secondary endpoints: Need and duration of bilevel positive airway pressure (BiPAP), need and length of mechanical ventilation during hospital stay period, ET intubation requirement within 6 h after treatment initiation, renal dysfunction worsening (>0.5 mg/dL increase in serum creatinine level at 24 or 48 h), and in-hospital mortality.

Supplementary issues in the care of patients in the ED and thereafter

Diagnosis of heart failure was done through physical examination and rapid assessment of systolic and diastolic functions of LV and RV using ECHO in addition to the role of biomarkers such as BNP. Ventilatory aid was allowed during the patient's treatment period with either BiPAP or ET intubation. The treating emergency physician made the decision whether to conduct ET intubation or BiPAP. Blood pressure decline, characterized by a decrease in SBP or mean arterial pressure of >30%, was a reason to stop bolus treatment temporarily and decrease the nitroglycerin infusion rate. If there is no spontaneous recovery within 5 min or after administration of a fluid bolus (500 mL of 0.9% saline), the procedure was terminated. Other reasons for termination were new onset chest pain associated with ECG changes suggesting myocardial ischemia or infarction, bradycardia (<60 beats/minute), more than 1-mm ST-segment elevation or more than 2-mm depression in two contiguous leads, new onset of neurologic deficits, or new left bundle branch block. For these conditions, the recommended treatment protocols were performed in accordance with standard advanced cardiac life support guidelines. However, the treating physician selected the treatment. Patients who needed intensive care were admitted to a monitored unit bed and then transferred to a general medical ward when they became hemodynamically and clinically stable. During their in-hospital stay, all enrolled patients underwent repeated serum laboratory tests 24–48 h after admission.

Ethical approval

The Ethics Committee of Benha Faculty of Medicine approved the study's protocol.

Statistical methods

SPSS (version 25.0; SPSS, Chicago, IL, USA) was used for data management and data analysis. Means and standard deviations or medians and ranges were used to summarize numerical variables. Numbers and percentages were used to summarize categorical variables. The two group comparisons were conducted using an independent test for normally distributed numerical variables or the Mann–Whitney *U*-test for nonnormally distributed variables. For categorical variables, Chi-square or Fisher's exact test was used for comparisons. All the tests were two-sided. The level of significance was 0.05.

Results

Age, gender, diabetes mellitus, smoking, coronary artery disease (CAD) history, coronary intervention history, intervention type, known chronic kidney disease (CKD), rate of *de novo* HF, and body mass index showed no significant differences between both groups [Table 1].

In the current study, the prevalence of hypertensive patients was significantly higher in Group I (88.0%) compared to Group II (77.0%), $P = 0.041$.

Dyslipidemia was found in 30% and 66% of patients in Groups I and II, respectively, $P < 0.001$.

The prevalence of known chronic obstructive pulmonary disease (COPD) patients was significantly higher in Group I (27.0%) compared to Group II (15.0%), $P = 0.037$.

The mean EF of all patients was 48.45 ± 10.5%; however, there was no significant difference between the two groups.

The median interquartile range (IQR) duration of nitroglycerin infusion therapy group was 16.7 (5.2–37.2) hours. In the bolus group, the median (IQR) total dose of nitroglycerin was 2 (1–2) mg; 78% of patients received 1 dose, 16% received 2 doses, 4% received 3 doses, and 2 patients received at least 4 doses [Table 2].

The mean total length of hospital stay in Group II was significantly longer (5.4 days) than in Group I (4.3 days), with $P < 0.001$.

In Group II, in comparison to Group I, the need for ICU admission was significantly higher; 69.0% compared to 51%, $P = 0.009$, there was no between-groups significant difference regarding primary safety outcomes (relative risk [RR] = 0.706 with 95% confidence interval [CI] ranging from 0.356 to 1.4. $P = 0.315$), hypotension required intervention ($P = 1.0$) and myocardial injury ($P = 0.315$) [Table 3].

Regarding blood pressure posttherapy, SBP and DBP were significantly lower in Group I compared to Group II ($P = 0.001$, 0.012, respectively) as illustrated in [Table 3].

The need for ET intubation showed no significant differences between both the study groups (RR = 0.8 with 95% CI ranging from 0.395 to 1.622. $P = 0.535$). In Group II, compared to Group I, the secondary outcomes were significantly higher; 72% compared to 56%. RR for the secondary outcome between both groups = 0.495 with a 95%**,** CI ranging from 0.275 to 0.892, *P* value of 0.018. In Group II, the mean length of mechanical ventilation was significantly higher (2 days) than in Group I (1.4 days), $P = 0.006$ [Table 4].

In comparing Group 1 with Group 11, Group I showed a significant reduction in the ICU admission rate 27% ($P = 0.001$).

In this study, in group I, the median initial troponin was significantly higher (0.145) than Group II (0.065), $P < 0.001$.

Regarding adverse effects, hypotension requiring intervention was reported in two patients in both groups ($P = 1.0$) and myocardial injury (Group I 12%, Group II 17%, $P = 0.315$). No neurological complications were reported. No in-hospital mortality was reported.

Discussion

This research evaluated the effectiveness and safety of intermittent bolus versus continuous nitroglycerin infusion for managing acute hypertensive heart failure.

In the current study, the prevalence of hypertensive patients was significantly higher in Group I (88.0%) compared to Group II (77.0%), $P = 0.041$.

Dyslipidemia was found in 30% and 66% of patients in Groups I and II, respectively, $P < 0.001$. The prevalence of known COPD patients was significantly higher in Group I (27.0%) compared to Group II (15.0%), $P = 0.037$. No statistical differences were found between the study groups regarding diabetes mellitus, smoking, CAD history, coronary intervention history, and known CKD.

Table 1: General characteristics in both group

	Group I ($n=100$)	Group II ($n=100$)	*P*
Age (years), mean±SD	57±12	58±8	0.502
Gender, *n* (%)			
Males	47 (47.0)	46 (46.0)	0.887
Females	53 (53.0)	54 (54.0)	
Diabetes mellitus (yes), *n* (%)	34 (34.0)	36 (36.0)	0.767
Hypertension (yes), *n* (%)	88 (88.0)	77 (77.0)	0.041
Smoking (yes), *n* (%)	33 (33.0)	35 (35.0)	0.765
Known dyslipidemia (yes), *n* (%)	30 (30.0)	66 (66.0)	<0.001
PH of CAD (yes), *n* (%)	17 (17.0)	18 (18.0)	0.852
PH of coronary interventions (yes), *n* (%)	11 (11.0)	14 (14.0)	0.521
De-novo HF (yes), *n* (%)	3 (3.0)	5 (5.0)	0.471
Type of intervention, *n* (%)			
PCI	6 (54.5)	12 (85.7)	0.177
CABG	5 (45.5)	2 (14.3)	
Known COPD (yes), *n* (%)	27 (27.0)	15 (17.0)	0.037
Known CKD (yes), *n* (%)	13 (13.0)	10 (10.0)	0.506
BMI (kg/m^2), mean±SD	27±3.12	26.29±3.21	0.113

Independent *t*-test or Chi-square test was used for numerical and categorical data, respectively. SD: Standard deviation, CAD: Coronary artery disease, PH: Past history, PCI: Percutaneous coronary intervention, CABG: Coronary artery bypass graft, COPD: Chronic obstructive pulmonary disease, CKD: Chronic kidney disease, BMI: Body mass index, HF: Heart failure

Our results were also comparable with Özlek *et al*.,[6] (gender disparities in heart failure with mid-range and preserved ejection fraction). In addition, they were comparable with the Swedish Heart Failure Registry, which included over 18,000 patients with heart failure with preserved ejection fraction (HFpEF) and heart failure with reduced ejection fraction (HFrEF). 78% of patients had hypertension, 33% of patients were smokers, 27.7% were diabetics, 29.5% had hyperlipidemia, 14.8% of patients had COPD, 15% had CKD, and 29.5% had coronary disease.

According to Wilson *et al*.,[7] who studied the bolus nitroglycerin use in acute hypertensive heart failure patients for prevention of ICU admission, patients with a history of hypertension who received combined therapy were significantly higher than patients who received bolus or continuous nitroglycerin therapy (87.6 vs. 81.5, and 81.5%, $P = 0.04$). Known COPD patients who received bolus therapy were significantly higher in number than patients who received bolus or continuous nitroglycerine therapy (29.8 vs. 15.4, and 13.5%, $P = 0.002$). No significant differences were reported between patients who received bolus nitroglycerin therapy, continuous nitroglycerin infusion, and combined therapy as regards age, gender, diabetes mellitus, history of CAD, and known CKD.

In this study, compared to group II, significantly higher mean SBP and mean respiratory rate were observed in Group I. No statistical differences between groups in terms of DBP and pulse oxygenation were observed.

This was disconcordant to Wilson *et al*.,[7] who found that initial SBP and DBP were significantly higher in the combined group, and there was no statistical difference between the IV nitroglycerine bolus and continuous infusion

Table 2: Clinical data and medication history in both groups

	Group I ($n=100$)	Group II ($n=100$)	*P*
SBP (mmHg), mean±SD	193±19	185±15	0.001
DBP (mmHg), mean±SD	103±8	103±8	0.854
HR (bpm), mean±SD	106±11	101±9	0.170
Pulse oxygenation (%), mean±SD	86±3	86±3	0.459
Respiratory rate (cycle/min), mean±SD	36±3	35±4	0.049
Initial serum creatinine (mg/dl), median (range)	1.1 (0.5-3.6)	1.1 (0.6-3.9)	0.221
Initial troponin (ng/ml), median (range)	0.145 (0.01-0.32)	0.065 (0.013-0.5)	<0.001
Baseline EF (%), mean±SD	47±12	49±12	0.149
ACEIs/ARBs (yes), *n* (%)	45 (45.0)	41 (41.0)	0.568
Digoxin (yes), *n* (%)	8 (8.0)	5 (5.0)	0.39
Beta-blockers (yes), *n* (%)	59 (59.0)	42 (42.0)	0.016
Nitrates (yes), *n* (%)	11 (11.0)	12 (12.0)	0.825
Aspirin (yes), *n* (%)	29 (29.0)	29 (29.0)	1
Loop diuretics (yes), *n* (%)	44 (44.0)	32 (32.0)	0.08
Nonloop diuretics (yes), *n* (%)	8 (8.0)	6 (6.0)	0.579
MRA (yes), *n* (%)	9 (9.0)	5 (5.0)	0.268

Independent *t*-test or Mann-Whitney U-test was used for numerical data. Chi-square test was used for categorical data. SBP: Systolic blood pressure, DBP: Diastolic blood pressure, HR: Heart rate, EF: Ejection fraction, ACEIs: Angiotensin-converting enzyme inhibitors, ARBs: Angiotensin receptor blockers, MRA: Mineralocorticoid receptor antagonists, bpm: Beat per minute, SD: Standard deviation

Table 3: Primary efficacy and safety outcome in both groups

	Group I (*n*=100)	Group II (*n*=100)	*P*
Primary safety outcomes (yes), *n* (%)	12 (12.0)	17 (17.0)	0.315
Need for ICU admission (yes), *n* (%)	51 (51.0)	69 (69.0)	0.009
Total length of hospital stay (days), mean±SD	4.3±1.1	5.4±1.2	<0.001
Posttherapy SBP (mmHg), mean±SD	132.7±11.38	138.1±12.42	0.001
Posttherapy DBP (mmHg), mean±SD	81.29±8.12	84.13±7.65	0.012
Neurological complications (yes), *n* (%)	0	0	-
Hypotension requiring intervention (yes), *n* (%)	2 (2.0)	2 (2.0)	1
Myocardial injury (yes), *n* (%)	12 (12.0)	17 (17.0)	0.315

Chi-square or Fisher's exact test was used. SBP: Systolic blood pressure, DBP: Diastolic blood pressure, SD: Standard deviation, ICU: Intensive care unit

Table 4: Secondary outcomes in both groups

	Group I (*n*=100)	Group II (*n*=100)	*P*
Secondary outcomes (yes), *n* (%)	56 (56.0)	72 (72.0)	0.018
Need for BiPAP (yes), *n* (%)	26 (26.0)	25 (25.0)	0.871
Duration of BiPAP (h), median (range)	0 (0-13.2)	0 (0-23)	0.666
Need for mechanical ventilation (yes), *n* (%)	9 (9.0)	10 (10.0)	0.809
Length of mechanical ventilation (days), mean±SD	1.4±0.5	2±0.4	0.006
Need for ET intubation (within 6 h) (yes), *n* (%)	12 (12.0)	15 (15.0)	0.535
Worsening of renal functions (yes), *n* (%)	10 (10.0)	13 (13.0)	0.506
In-hospital mortality (yes), *n* (%)	0	0	-

Independent *t*-test or Mann-Whitney U-test was used for numerical data. Categorical data were compared using Chi-square test. BiPAP: Bi-level positive airway pressure, ET: Endotracheal tube, SD: Standard deviation

groups (206 [186–231] vs. 186 [169–212] and 184 [159–210] respectively, $P < 0.001$).

Similarly, the Group I median initial troponin was significantly higher (0.145) than Group II (0.065), $P < 0.001$. This was concordant with Wilson *et al*.,[7] who found that initial troponin was significantly higher in Group I (0.11) in comparison to Group II (0.06) and Group III (0.09), $P < 0.001$. This may be because the study was randomized, so there were some imbalances between groups in baseline criteria, which could explain the finding that at baseline, troponin was higher in Group I than Group II.

There was no significant difference as regard to mean baseline EF between the two groups, according to this study, 47% and 49%, respectively, $P = 0.149$. This was in agreement with Özlek *et al*.[6] as the median EF was 45% in the studied cases. While in Wilson *et al*.,[7] EF was 30% and 35% in Groups I and II, respectively, and no significant difference was noted between the three groups regarding mean baseline EF ($P = 0.23$).

In this study, beta-blockers use in Group I was significantly higher (59.0%) in comparison to group II (42.0%), $P = 0.016$. No significant differences were noted between the rest of the clinical data and medications (angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers (ARBs), digoxin, nitrates, aspirin, or loop diuretics).

This was concordant with Wilson *et al*.,[7] who found that previous usage of B-blockers was higher in Group I in comparison to Group II and Group III ($P = 0.07$).

Importantly, ET intubation showed no significant difference between both groups (RR = 0.8 with 95% CI ranging from 0.395 to 1.622, $P = 0.535$), primary safety outcomes (RR = 0.706 with 95% CI ranging from 0.356 to 1.4, $P = 0.315$), hypotension requiring intervention ($P = 1.0$), and myocardial injury (Group I 12%, Group II 17%, $P = 0.315$).

These results were concordant to Wilson *et al*.,[7] who stated no significant difference between the IV nitroglycerin bolus and continuous infusion as regard to hypotension requiring intervention (1.9% vs. 1.3%, $P > 0.05$) and myocardial injury (12.4% vs. 17.2%, $P > 0.05$).

On the other hand, Levy *et al*. studied severe decompensated heart failure treatment with intravenous high-dose nitroglycerin.[5] Twenty-nine patients received a titratable nitroglycerin infusion and were given a high-dose nitroglycerin bolus (2 mg). Every 3 min, repeated high-dose nitroglycerin was allowed, up to total of 10 doses (Group I), and 45 patients were treated without high-dose nitroglycerin (Group II). Levy *et al*. found that ET intubation need in group II was higher than in Group I (26.7% and 13.8%, respectively).[5]

In our study, secondary outcomes in Group II were significantly higher (72.0%) than in Group I (56.0%) (RR = 0.495 with a 95% CI ranging from 0.275 to 0.892 and $P = 0.018$). The need for ICU admission in Group II (69.0%) was significantly higher than Group I (51.0%), $P = 0.009$. In Group II, the mean length of mechanical ventilation was significantly higher (2 days) than Group I (1.4 days), $P = 0.006$. The mean total length of hospital stay in Group II was significantly higher (5.4 days) than Group I (4.3 days), $P < 0.001$.

Similarly, Wilson *et al*.[7] found that patients receiving only a nitroglycerin bolus were unlikely to need ICU admission (48.4% for a bolus compared to 68.7% and 83% for infusion and combination, respectively, $P = 0.0001$). Furthermore, the median hospital stay was significantly shorter (3.7 days for bolus compared to 4.7 days and 5 days for infusion and combination, respectively, $P = 0.2$). The duration of ICU LOS showed no significant differences among the study groups. This was also concordant with Levy *et al*.,[5] who found that the need for ICU admission in Group II was higher than Group I (80% and 37.9%, respectively).

In our study, in Group II, the mean length of mechanical ventilation was significantly higher (2 days) than Group I (1.4 days), $P = 0.006$. This contrasted with Wilson *et al*.,[7] who found that mechanical ventilation rates were comparable, but in the combination category, a tendency toward higher rates was noticeable (16.9% in the combination group compared to 8.9% and 8.8% in the bolus and infusion groups, respectively).

No significant difference was noted between groups regarding renal function worsening, the need for BiPAP, the duration of BiPAP (hours), and the need for mechanical ventilation. Wilson *et al*. had a similar observation as no significant difference was noted between groups as regards renal function worsening, need for BiPAP, duration of BiPAP (hours), and need for mechanical ventilation.[7] This was dis-concordant with Levy *et al*.,[5] who found that the need for BiPAP ventilation in group II was higher than Group I (20% and 6.9%, respectively). Furthermore, Cotter *et al*.,[8] who compared the effectiveness of high-dose isosorbide dinitrate with low-dose furosemide versus high-dose furosemide with low-dose isosorbide dinitrate in patients with a confirmed diagnosis of pulmonary edema. Patients who were admitted to the ED with signs of congestive heart failure received oxygen therapy at a rate of 10 liters/min, in addition to furosemide 40 mg and morphine 3 mg IV. Mechanical ventilation was a decision in 7 (13%) out of 52 patients who received high-dose nitrates and 21 (40%) out of 52 patients who received high-dose diuretics, with a $P = 0.004$.

Limitations

The following were some of the study's limitations: The results were from a single medical center and did not include follow-up for patients. Patients in our sample indicated less use of medical treatment for hypertension that has been recommended by guidelines, such as ARBs, angiotensin-converting enzyme inhibitors, loop diuretics, and β-blockers.

Conclusion

Nitroglycerin intravenous boluses were associated with fewer ICU admissions and a shorter LOS in the hospital as opposed to ordinarily infusion therapy. In addition, the mean mechanical ventilation duration was slightly shorter in bolus group in comparison to continuous infusion group. Furthermore, the safety and efficacy of the bolus method were comparable with the conventional infusion therapy. Finally, continuous nitroglycerin infusion use in AHF management is being questioned.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Viau DM, Sala-Mercado JA, Spranger MD, O'Leary DS, Levy PD. The pathophysiology of hypertensive acute heart failure. Heart 2015;101:1861-7.
2. Ho EC, Parker JD, Austin PC, Tu JV, Wang X, Lee DS. Impact of nitrate use on survival in acute heart failure: A propensity-matched analysis. J Am Heart Assoc 2016;5:e002531.
3. Gradman AH, Vekeman F, Eldar-Lissai A, Trahey A, Ong SH, Duh MS. Is addition of vasodilators to loop diuretics of value in the care of hospitalized acute heart failure patients? Real-world evidence from a retrospective analysis of a large United States hospital database. J Card Fail 2014;20:853-63.
4. Munir S, Guilcher A, Kamalesh T, Clapp B, Redwood S, Marber M, *et al.* Peripheral augmentation index defines the relationship between central and peripheral pulse pressure. Hypertension 2008;51:112-8.
5. Levy P, Compton S, Welch R, Delgado G, Jennett A, Penugonda N, *et al.* Treatment of severe decompensated heart failure with high-dose intravenous nitroglycerin: A feasibility and outcome analysis. Ann Emerg Med 2007;50:144-52.
6. Özlek B, Özlek E, Kahraman S, Tekinalp M, Zencirkiran Agus H, Çelik O, *et al.* Gender disparities in heart failure with mid-range and preserved ejection fraction: Results from APOLLON study. Anatol J Cardiol 2019;21:242-52.
7. Wilson SS, Kwiatkowski GM, Millis SR, Purakal JD, Mahajan AP, Levy PD. Use of nitroglycerin by bolus prevents intensive care unit admission in patients with acute hypertensive heart failure. Am J Emerg Med 2017;35:126-31.
8. Cotter G, Metzkor E, Kaluski E, Faigenberg Z, Miller R, Simovitz A, *et al.* Randomised trial of high-dose isosorbide dinitrate plus low-dose furosemide versus high-dose furosemide plus low-dose isosorbide dinitrate in severe pulmonary oedema. Lancet 1998;351:389-93.