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ORIGINAL ARTICLE

Low dose dopamine in prevention of GFR deterioration in acute decompensated heart failure with preserved ejection fraction.

Mahmoud ShawkyAbd El-Moneum[1], Ali Elshaier[2], Eman Elkeshk[1], Ahmed Bendary[1]

[1]Department of Cardiology,Benha University Hospital, Benha City, Egypt 2.Department of Cardiology,Alzaytoon Hospital, Cairo, Egypt.

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Abstract

Background: Low dose dopamine use in acute decompensated heart failure (ADHF) still lacks evidence. Our objective was to establish the value of low dose dopamine in ADHF patients withpreserved ejection fraction in prevention of glomerular filtration rate (GFR) deterioration, duration of hospital stay, 6 months cardiovascular (CV) mortality & re-hospitalization.

Methods: One hundred ADHF patients with preserved ejection fraction admitted to Benha&Alzaytoon cardiology departments were randomized into 2 groups, each composed of 50patients: group A received conventional ADHF treatment + low dose dopamine &group Breceived only conventional ADHF treatment. Patients of both groups were observed for duration of hospital stay, GFR changes, 6 months cardiovascular (CV) mortality & re-hospitalization.

Results: Low dose dopamine in "group A" failed to prevent deterioration of GFR assessed by delta GFR from admission to discharge (-9.20 ml /min± 12.76 for group A versus -5.42 ml/min ± 8.30 for group B, p value =0.083). It caused significant shortening in duration of hospital stay (3.9 days ± 1.41 for group A versus 4.76 days ± 1.33 for group B, p value =0.02). Low dose dopamine affected daily urinary output (UOP). It caused highly significant increase in UOP(2072 ml urine/day ± 404.08 for group A versus 1689.78 ml urine/day ± 193.02 for group B, p value<0.001). It also caused highly significant body weight loss assessed by weight loss from admission to discharge (-1.374 kg weight loss ± 0.46 in group A versus -0.872 kg weight loss ± 0.41 in group B , p value<0.001). It failed to achieve significant change regarding 6 months endpoints (8 re-hospitalizations & 2 CV deaths in group A versus 9 re-hospitalizations &1 CV death in group B, p value =1).

Conclusion: Low dose dopamine has no significant effect on reno-protection, morbidity & mortality of ADHF with preserved ejection fraction but it adds diuretic, decongestive effect&shortens the duration of hospital stay without increased risk of worsening renal functions.

Keywords: Acute decompensated heart failure heart failure. Low dose dopamine.Preserved ejection fraction.Worsening renal functions.

Introduction

ADHF, alongside worsening renal functions, is a core internal medicine problem. Its management depends on internists, clinical cardiologists and nephrologists for the vast majority of patients[1]. To prevent GFR deterioration in ADHF with preserved ejection fraction, a comprehensive review of therapeutic options and shared decision-making are critical.

Improvements in coordinated HF medical management by internists, cardiologists, and nephrologists will likely lead to fewer events of GFR deterioration, less hospitalizations & CV mortality from ADHF admissions[2]. One of these therapeutic options islow dose dopamine which was the interest of previous studies, as well as our study, to assess its value in prevention of worsening renal functions in ADHF with preserved ejection fraction[3].Our objective was toestablish the value of low dose dopamine in patients of ADHF with preserved ejection fraction in prevention of GFR deterioration, duration of hospital stay, 6 months CV mortality & re- hospitalization.

Patients and methods

This study was conductedover 1 year period from

September 2019 to September 2020 and was performed inBenha&Alzaytoon cardiology departments on one hundred (100) patientsofADHF with preserved ejection fraction(EF≥50%). The patients were randomized into 2 groups each composed of 50 patients:group A received conventional ADHF treatment+ low dose dopamine &group B received only conventional ADHF treatment. Patients of both groups were observed for duration of hospital stay, GFR changes, 6 months cardiovascular (CV) mortality & re-hospitalization.The protocol was approved by Benha hospital ethics committee.

Patients were excluded if they met one of the following criteria: Patient refusal, Patient <18 years of age, Estimated GFR <15 milliliters/min/1.73m^2 , Known ejection fraction by noninvasive testing of < 50% within 12 months of admission to the hospital, Pregnancy , nursing mothers or positive pregnancy test in a female of childbearing period, Hemoglobin <8 g/dl, Systolic BP <90 mmHg on admission, Haemo-dynamically significant arrhythmias including ventricular tachycardia or defibrillator shock within 4 weeks, Acute coronary syndrome(ACS) within 4 weeks, Cardiac diagnoses in addition to or other than HFpEF: **I**. Active myocarditis **II**.Hypertrophic obstructive cardiomyopathy **III**.Severevalvular disease **IV**.Complex congenital heart disease **V**. Constrictive pericarditis **VI**. Severe pulmonary hypertension (RVSP ≥ 60), not secondary to HFPEF, Clinical evidence of digoxin toxicity, Non-cardiac pulmonary edema, History of temporary or permanent renal replacement therapy or ultrafiltration, Sepsis, Use of IViodinated contrast material/dye in last 72 hours or planned during hospitalization, Terminal illness (other than HF) with expected survival of less than 1 year& History of renal artery stenosis> 50%. All participants included in our study have been subjected to:

- Informed written consent.
- **Complete history taking:** including past history of hypertension, diabetes mellitus; its onset and duration, dyslipidemia, ischemic heart disease (IHD), premature coronary artery disease, peripheral vascular disease, chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), smoking habit&family history.
- **Physical examination:** on admission ,throughout the admission & on discharge including:
  1) General examination e.g. body weight, height, heart rate, blood pressure, other vital signs&urine volume in the bag.
  2) Local examination of heart e.g. heart sounds,lower limb edema and lung base auscultation.
- **Laboratory investigations:** complete blood count (CBC), creatinine, blood urea nitrogen (BUN)**, Na^+& K^+**.
  GFR defined as rate of blood flow through kidney per minute & measured by creatinine clearance which was calculated using Cockcroft Gault equation [4]

Creatinine Clearance Value in ml/min =

(140-age)x(weight in kg) / (72 X Serum creatinine)

Multiply by 0.85 if female

ECG: 12 lead ECG was performed for all patients on daily basis to detect anyabnormalitiese.g.: ischemic changes &arrhythmia.

- **Echocardiography**was done to all patients by GE 6S-RS (Sector)Probemedical System toestimate EF using m-mode method regularly &simpson's method if m-mode is insufficient (geographic distortion of LV cavity or paradoxical segment motion ,regional wall motion abnormality)[5]

Statistical analysis

Statistical analysis was done by SPSS v25 (IBM Inc., Chicago, IL, USA). Normality of data was checked with Shapiro-Wilks test and histograms and all quantitative variables were normallydistributed. Quantitative variables were presented as mean and standard deviation (SD) and compared between the two groups utilizing Student's t- test. Quantitative variables were presented as frequency and percentage (%) and were analyzed utilizing the Chi-square test or Fisher's exact test when appropriate. P

value < 0.05 was considered significant& P value < 0.001 was considered statistically highly significant[6].

RESULTS

Demographic features of studied patients

There was insignificant difference between the 2 groups regarding age & sex (P value=0.436&0.834).[table (1)]

Table 1: Demographic features of studied patients

Group A (n = 50)			Group B (n = 50)	P value
Age (years)	Mean ± SD	61.88 ± 8.21	63.1 ± 7.35	0.436
Sex	Male	18 (36%)	17 (34%)	0.834
	Female	32 (64%)	33 (66%)	

Risk factors& patient characteristics of studied patients

Comorbidities & patient characteristics were studied in both groups & showed no significant difference regarding[diabetes mellitus, hypertension, smoking, obesity, dyslipidemia, and past history (PH) of ischemic heart disease (IHD)] (P value = 0.914, 1, 0.308, 0.543, 0.662& 0.053 respectively).
[table (2)]

Table 2: Risk factors of studied patients

Group A (n = 50)			Group B (n = 50)	P value
Risk factors	Diabetes mellitus	17 (34%)	20 (40%)	0.914
	Hypertension	40 (80%)	40 (80%)	1
	Smoking	11 (22%)	12 (24%)	0.308
	Obesity	12 (24%)	14 (28%)	0.543
	Dyslipidemia	14 (28%)	13 (26%)	0.662
	PH of IHD	8 (16%)	10 (20%)	0.053

Admission clinical data

The admission clinical data showed insignificant difference between the 2 groupsregardingNa^+ ,K^+,creatinine, GFR& body weight. (P = 0.742, 0.574, 0.648, 0.461 and 0.233, 0.128 & 0.640 respectively)[table (3)]

Table 3: Admission clinical data

Group A (n = 50)			Group B (n = 50)	P value
Baseline serum sodium (mg/dl)	Mean ± SD	136.68 ± 4.03	137.04 ± 3.82	0.648
Baseline serum potassium (mg/dl)	Mean ± SD	4.06 ± 0.62	4.16 ± 0.70	0.461
Baseline serum creatinine (mg/dl)	Mean ± SD	1.728 ± 0.66	1.88 ± 0.63	0.233
Baseline GFR (ml/min/1.73m2 BSA)	Mean ± SD	56.37 ± 23.11	50.00 ± 18.09	0.128
Baseline weight (Kg)	Mean ± SD	87.49 ± 14.66	88.87 ± 14.60	0.640

Discharge clinical data

Discharge data were compared between 2 groups. There was also no significant difference between the 2 groups as regards Na+, k+, creatinine,GFR & body weight (P = 0.175, 0.339, 0.772, 0.395 and 0.522 respectively). [table (4)]

Table 4: Discharge clinical data:

		Group A (n = 50)	Group B (n = 50)	P value
Discharge serum sodium (mg/dl)	Mean ± SD	140.12 ± 1.76	139.6 ± 2.04	0.175
Discharge serum potassium (mg/dl)	Mean ± SD	4.41 ± 0.83	4.34 ± 0.33	0.339
Discharge serum creatinine (mg/dl)	Mean ± SD	1.98 ± 0.53	2.01 ± 0.51	0.772
Discharge GFR (ml/min/1.73m2 BSA)	Mean ± SD	47.17 ± 15.65	44.58 ± 14.68	0.395
Discharge weight (Kg)	Mean ± SD	86.12 ± 14.63	87.99 ± 14.6	0.522

Doses of medications

Dosing of regular medications of ADHF during intensive care stayshowed no significant difference between both groups as regards total Furosemide, Spironolactone and Enalapril doses (P = 0.317, 0.827 and 0.548 respectively). [table (5)]

Table 5: Doses of medications

Group A (n = 50)			Group B (n = 50)	P value
Total Furosemide IV dose (mg/day)	Mean ± SD	178 ± 15.25	174.8 ± 16.57	0.317
Total spironolactone dose (mg/day)	Mean ± SD	27.6 ± 18.36	26.8 ± 18.23	0.827
Total Enalapril dose (mg/day)	Mean ± SD	17.2 ± 4.86	16.6 ± 5.09	0.548

Short term clinical outcome

- GFR deterioration:Low dose dopamine failed to prevent GFR deterioration calculated by(GFR on discharge –GFR on admission) (P = 0.083).
- Duration of hospital stay: Low dose dopamine caused significant shorteningin duration of hospital stay(3.9 days ± 1.41 for group A versus 4.76 days ± 1.33 for group B, p value =0.02).
- weight loss: low dose dopamine achieved highly significant body weight loss calculated by (weight on discharge- weight on admission)(P value<0.001).
- Urinary outputs:Low dose dopamine affected daily UOP. It caused highly significant increase in UOP (2072 ml urine/day ± 404.08 for group A versus 1689.78 ml urine/day ± 193.02 for group B, pvalue<0.001). [table (6)]

Table 6: short term clinical outcome

		Group A (n = 50)	Group B (n = 50)	P value
Duration of hospital stay (days)	Mean ± SD	3.9 ± 1.41	4.76 ± 1.33	0.02*
Delta GFR (ml/min/1.73m2 BSA)	Mean ± SD	-9.20 ± 12.76	-5.42 ± 8.30	0.083
Weight loss (Kg)	Mean ± SD	-1.374 ± 0.46	-0.872 ± 0.41	<0.001**
Average urine output during admission (ml/day)	Mean ± SD	2072 ± 404.08	1689.78 ± 193.02	<0.001**

*significant **highly significant

6months endpoints

Low dose dopamine failed to achieve improvement regarding 6 months follow –up endpoints: re-hospitalization & mortality (P value = 0.79, 1 respectively). [table (7)]

Table 7: 6 months endpoints:

	Group A (n = 50)	Group B (n = 50)	P value
Re-hospitalization	8 (16%)	9 (18%)	0.79
Mortality	2 (4%)	1 (2%)	1

Discussion

Heart failure with preserved ejection fraction (HFPEF) is less understood &less researched issue in comparison to heart failure with reduced ejection fraction (HFREF)7.This was a randomized clinical study that aimed primarily to establish the value of low dose dopamine in ADHF patients with preserved ejection fraction in prevention of GFR deterioration, duration of hospital stay, 6 months CV mortality& re-hospitalization.

Our results showed marked female gender predominance. Out of 100 HFPEF patients, 65 patients were females (64% in group A& 66% in group B). Mean age was 63.1 years&61.8years for group A & Brespectively. No significant difference was reported between the 2 groups regarding age &sex. Our results were in agreement with Faxen et al. who studied 378 HFPEF patients& reported that 215(57%) werefemales& mean age was 67&69years for the 2 groups7.Also, our results were in agreement with ROPA-DOP study conducted by Sharma et al. which reported that out of 90 HFPEF patients, 61 (68%) were females &mean age for patients was 66 years3.

Our results showed that the most attributable risk factor to HFPEF was hypertension while IHD was less attributable to HFPEF patients. Out of 100 ADHF patients with preserved ejection fraction, 80 (80%) were hypertensive, 37(37%) diabetic, 23(23%) smokers,26(26%) obese,27 (27%) dyslipidemic&only 18 (18%) ischemic .There were no significant differences between the 2 groups regarding hypertension , diabetes, smoking ,dyslipidemia, IHD(P value = 1, 0.914, 0.308, 0.543& 0.053 respectively).

Our results were in agreement with Edelmann et al who studied1294 HFPEF patients& reported that 1,014patients (78.4%) were hypertensive , 313 (24.2%) diabetic, 699 (54.0%) dyslipidemic, 486 (37.6%) obese&only 405 (31.3%) ischemic8.

Our results were in agreement withArizminidi et al.who studied168 HFPEF patients&reported that 150 (89.3%) were hypertensive,72 (42.9%) diabetic,54 (32.1%) smokers&42 (25%) were obese9.

Our results were in disagreement with Abebeet al.who studied164 HFPEFpatients&reported that only 56 (34.15%)were hypertensive, only 2 (1.22%) diabetic and 18 (10.9%)ischemic10.

Our results showed that low dose dopamine failed to prevent deterioration of GFR assessed by delta GFR from admission to discharge (-9.20 ml /min± 12.76 for group A versus -5.42 ml/min ± 8.30 for group B, p value =0.083). Low dose dopamine caused significant shortening in duration of hospital stay (3.9days ± 1.41 for group A versus 4.76 days ± 1.33 for group B, p value =0.02). Low dose dopamine affected daily urinary output (UOP). It caused highly significant increase in UOP (2072 ml urine/day ± 404.08 for group A versus 1689.78 ml urine/day ± 193.02 for group B, p value<0.001). It also caused highly significant body weight loss assessed by weight loss from admission to discharge (-1.374 kg weight loss ± 0.46 in group A versus -0.872 kg weight loss ± 0.41 in group B , p value<0.001). It failed to achieve significant change regarding 6 months endpoints (8 re-hospitalizations & 2 CV deaths in group A versus 9 re-hospitalizations &1 CV death in group B, p value =1).

Our results werein agreement with the ROPA-DOP study conducted by Sharma et al. whichreported that low dose dopamine failed to prevent deterioration of GFR assessed by delta GFR from admission to discharge (-8.23 ml /min± 12.76 for low dose dopamine versus -6.14 ml/min ± 8.30 for no dopamine , p value =0.071).Low dose dopamine failed to affect 1 year rehospitalization(20 rehospitalizationsfor low dose dopamine versus 23 rehospitalizationsfor no dopamine, p value=0.32). Low dose dopamine failed to affect 1 year mortality (7 CV deaths for low dose dopamine versus 8 CV deaths for no dopamine, p value=0.63).

Our results were in disagreement with the same study regarding duration of hospital stay, UOP & weight loss. In the former study ,low dose dopamine failed to shorten duration of hospital stay (5-10 days for low dose dopamine versus 4-10 days for no dopamine, p value=0.61) Low dose dopamine failed to achieve significant increase in UOP (2.5 L/day for low dose dopamine versus L/day for no dopamine, p value =0.68).It also failed to achieve significant weight loss (-4.32 kg for low dose dopamine versus -4.1 kg for no dopamine, p value= 0.27)3.

Conclusion

Low dose dopamine has no significant effect on reno-protection, morbidity & mortality of ADHF patient with preserved ejection fraction but it adds diuretic, decongestive effect&causes significant shortening in duration of hospital stay in ADHF patients with preserved ejection fraction without increased risk of worsening renal functions.

Limitations

Small sample size- Limited duration of the study

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