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Research Article

The prescribing pattern of dopamine and dobutamine in congestive heart failure patients in a tertiary care teaching hospital

Vasa Sivasankar[1], Sankaralingam Ramalakshmi[*2], Tentu Harika[1], Meleveedu Ramesh[3,] Kaliamurthy Kousalya[2]

[1] Pharm D, Faculty of Pharmacy, Sri Ramachandra University, Porur, India
[2]Lecturers, Department of Pharmacy Practice, Faculty of Pharmacy, Sri Ramachandra University, Porur, Chennai, India
[3]Professor of Medicine, Department of Cardiology, Sri Ramachandra Medical Centre, Chennai, India

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ABSTRACT

Heart failure is a complex syndrome that is associated with profound disease morbidity and mortality and has an adverse impact on the quality of life. The objective of the study was to evaluate the safety and efficacy of Dobutamine & Dopamine inotropes in severe congestive heart failure patients. This prospective study was carried out in patients with left ventricular ejection fraction below 35% requiring hospitalization and on intravenous inotropic therapy for a period of 3 months. The data on patient demographics, etiology, clinical presentation, hemodynamic parameters, physical examination, laboratory parameters, route of administration of the inotropic drug, adverse events and length of the stay were recorded in the data collection form. The collected data were statistically analyzed using SPSS 16.0 version software. The study population comprised of 25 patients among these, 19 were on dobutamine, 3 were on dopamine and 3 were on combination therapy. There was significant improvement in the creatinine clearance after the therapy. Most commonly found adverse events was hypokalemia (28 %) followed by hyperkalemia (16 %), phlebitis (16 %), atrial fibrillation (8 %), hypovolemia & hyponatremia (4 %), pricking & redness at IV site (4 %). Sudden bradycardia was observed in one patient and death occurred in one patient. Majority of patients were administered medications through external jugular vein (EJV) (n=14; 56%). The most commonly prescribed inotrope was dobutamine and there was an improvement in the kidney function after inotropic therapy. The patients who received inotropes through peripheral IV lines were susceptible to phlebitis.

Key words: Heart failure, Dobutamine, dopamine, phlebitis.

INTRODUCTION

Cardiovascular diseases are leading cause of death in developing countries [1]. Heart failure is a complex syndrome which is associated with profound disease morbidity and mortality and has an adverse impact on the quality of life [2]. Most of the evidences on treatment are for heart failure due to left ventricular systolic dysfunction (LVSD) [3]. The Heart disease has emerged as the number one killer in both urban and rural areas of the country [4]. The incidence and prevalence estimates of heart failure (HF) are unreliable in India because of the lack of surveillance systems, to adequately capture these data [5]. Patients with heart failure (HF) have 6-9 times higher mortality rates over a five year period compared to those without the disease.

Heart failure is caused by structural or functional abnormalities of the heart. It may be due to LVSD which is associated with a reduced left ventricular ejection fraction or heart failure with a preserved ejection fraction (HFPEF). The beta-agonists such as dobutamine and dopamine are widely used to improve hemodynamics, in acutely decompensated chronic heart failure patients [6]. Dopamine has significant inotropic activity for the use in patients with advanced low-output cardiac failure because of its selective effect on promoting blood flow to

Corresponding Author Address:** Ramalakshmi S, Lecturer, Department of Pharmacy Practice, Faculty of Pharmacy, Sri Ramachandra University, Porur, Chennai-116, India: **E- Mail: sramalakshmi@rediffmail.com

renal and splanchnic beds via stimulation of non-adrenergic vasodilator receptors in these areas. The possible mechanisms of dopamine-induced elevation of left ventricular filling pressure, particularly at higher doses, are many and include increased preload and afterload due to excessive α-receptor mediated vasoconstriction, excessive tachycardia, and/or myocardial ischemia in patients with severe coronary artery disease. In addition, in patients with chronic heart failure, the inotropic response to dopamine may be diminished by prior myocardial catecholamine depletion or by "down regulation" of myocardial β-receptors secondary to prolonged compensatory sympathetic stimulation. In such patients the high doses of dopamine required to obtain an adequate inotropic effect which may be associated with excessive and undesirable α-receptor stimulation [7].

The sympathomimetic amines remain one of the primary forms of therapy because of their potent inotropic effect, yet none of those currently available for clinical use is wholly satisfactory [8]. Dobutamine is used commonly for cardiac decompensation. However, its safety has been currently questioned. Dobutamine, a sympathomimetic drug, in the presence of beta-blockers, might have a decreased effect. In this situation, dobutamine might not be the ideal choice for the treatment of patients with heart failure [9].
Although the current therapies for CHF are associated with favourable hemodynamic and symptomatic effects but, they also cause arrhythmias, tachycardia and may increase the myocardial oxygen demand which is associated with the risk of ischemia, and mortality [10].These agents should be used only as a temporary treatment because they are associated with increased long-term mortality. Therefore, these agents should not be administered except in true emergency situations. With this background, this study was carried out to evaluate the safety and efficacy of Dobutamine & Dopamine inotropes in severe congestive heart failure patients in our set up.

MATERIALS AND METHODS

This prospective observational study was carried out in intensive care unit in the department of cardiology, Sri Ramachandra Medical centre for a period of 6 months which involved the data collection for 3 months. Patients of either sex, who were having Left ventricular ejection fraction below 35% requiring hospitalization and intravenous inotropic therapy were included in the study. Patients with severe hypotension not responding to intravenous fluids, mechanical ventilation, severe renal impairment (<30ml/min) or creatinine > 2.5 mg/dl, hepatic impairment, mechanical obstruction affecting ventricular filling and/ or out flow, hypokalemia not responding to potassium replacement therapy, acute myocardial infarction, severe or uncontrolled arrhythmias, acute myocarditis, congenital heart disease, primary pulmonary hypertension, pregnant or breastfeeding females, cancer, any systemic disease that can affect interpretation of the results, or significant hemodynamic instability requiring mechanical support were excluded from the study. With the approval of institutional ethics committee the data on patient demographics, aetiology, clinical presentation, hemodynamic parameters, physical examination, laboratory parameters, route of administration of the inotropes, adverse events were recorded in the data collection form. The patients were followed until discharged and the length of hospital stay was recorded.

The collected data were statistically analyzed using SPSS 16.0 version software. The results were represented as frequency, percentages; mean and standard deviation where ever applicable. The comparison of lab parameters and hemodynamic parameters for pre and post treatment was carried out by applying paired t test and a p value <0.05 was considered statistically significant.

RESULTS

The study population comprised of 25 patients with the mean age of 62.64 ± 11.84. The patient demography is summarized in table 1. Among the study population, 19 (76%) of the patients were on dobutamine, 3 (12%) patients were on dopamine and 3 (12%) patients were with combination of both. The comparison of the hemodynamic parameters for pre and post treatment of these patients showed in Table 2, shows no statistical significance.

Similarly, the comparison of the hemodynamic parameters for pre and post treatment for these patients showed in Table 3 which shows a significant improvement in serum creatinine levels (p value= 0.027). The route of administration of the inotropes among the study population was through external jugular vein (EJV) in 14 patients, femoral site in 4 patients, internal jugular vein (IJV) in 1, metacarpal site in 4, cephalic vein in 3, and brachial site in 1 patient. The changes in the route of administration during drug treatment were observed in 6 patients. Among these 4 patients were changed from EJV to femoral site, 1 patient from cephalic vein to EJV and 1 patient from metacarpal to EJV. The most commonly prescribed drug was digoxin in 22 patients followed by Clopidogrel in 19, Aspirin in 19, Spironolactone in

19, Torsemide in 18, Furosemide in 16, Atorvastatin in 15, Trimetazidine in 16, Metoprolol in 10, Ramipril in 8, Enoxaparin in 8, Acenocoumarin in 6, Nitroglycerin in 5, Bisoprolol in 3 and unfractionated Heparin in 2 patients.

The predominant adverse events which were observed was hypokalemia (28%) followed by hyperkalemia (16 %), phlebitis (16 %), atrial fibrillation (8 %), hypovolemia & hyponatremia (4 %), pricking & redness at IV site (4 %). Sudden bradycardia was observed in one patient and death occurred in one patient. The mean length of hospital stay of patients treated with dobutamine was 6.21 ± 2.32 days, dopamine was 5.66 ± 3.21 and combination of dobutamine and dopamine was 5.33 ± 2.08 days.

DISCUSSION

Chronic heart failure is the common health problem especially among elderly. In our study, the mean age of severe heart failure was the mean age of 62.64 ± 11.84yrs whereas a study conducted by Adamopoulos C et al. [11] the mean age was 72±13 years which might be attributed to the ethnic difference among the western population when compared to our population. The mean LVEF among our study population was 26.16 ± 5.38%. About 60% of the patients were with <30% of LVEF which was similar to a study conducted by Patrik Lynga et al. [12] which reported 57% of the patients with left ventricular ejection fraction (LVEF) of < 30%. In our study population, 48 % of the patients received dobutamine at dose of 2.5-7.5mcg/kg/min with a mean rate of infusion of 1.26 ± 0.68 ml/min. The doses at 2.5 – 20mcg/kg/min up to 40mcg/kg/min are titrated to desired response for cardiac decompensation. About 24 % of the patients received dopamine at a dose of 2.5-20 mcg/kg/min with a rate of infusion of 1.1 ± 0.54 ml/min. The doses at 5 – 15mcg/kg/min of dopamine will increase renal blood flow, heart rate, cardiac contractility and cardiac output. In majority of the patients the inotropes were administered through external jugular vein (EJV) (n=14; 56%), as these drugs should be administered into large vein to prevent the possibility of extravasations. The extravasation occurs due to alpha 1 agonist action which leads to intense local vasoconstriction. Peripheral extravasation of these medications into the surrounding connective tissue can lead to excessive local vasoconstriction with subsequent skin necrosis. Hence these should be administered via a central line.

Among the study population, the mean serum creatinine level decreased from 1.56 ± 0.46 to 1.42 ± 0.47 mg/dl after the inotropic treatment which was statistically significant (P value = 0.027). Similarly a study conducted by Abdul Al-Hesayen et al. [13] demonstrated a significant reduction in efferent renal sympathetic activity in patients with heart failure with infusion of a positive inotropic agent dobutamine and a study conducted by Varriale P et al. [14] showed a significant improvement in renal function and urinary output; serum blood urea nitrogen 48.9 +/- 10.3 to 32.1 +/- 14.4 mg/dl ($p<0.05$); serum creatinine 1.97 +/- 0.24 to 1.49 +/- 0.39 mg/dl ($p<0.05$); creatinine clearance 35.6 +/- 11.6 to 48.8 +/- 12.3 ml/min ($p<0.05$); and indexed urinary output 0.56 +/- 0.16 to 2.02 +/- 0.72 ml/kg/h ($p<0.05$). Which can be explained by the fact that the dopamine stimulates the DA_1 and DA_2 receptors and cause vasodilation of the splanchnic and renal vasculature. While, dobutamine increases the stroke volume due to its positive inotropic action which is proportional to the increase in renal blood flow. The predominant adverse events which were observed among the study population were hypokalemia (28 %), hyperkalemia (16 %) and phlebitis (16 %).

Majority of the patients were prescribed with digoxin (n=22; 88%) as the concomitant drug. In a study conducted by Digitalis Investigation Group [15] there was a trend towards a decrease in the risk of death attributed to worsening heart failure (risk ratio, 0.88; 95 % confidence interval, 0.77 to 1.01; P=0.06) with the digoxin when compared to a placebo group. In patients with chronic left ventricular dysfunction, the hemodynamic effects will be improved in combination.

The mean length of hospital stay among the patients on dobutamine was 6.21 ± 2.32 days, dopamine was 5.66 ± 3.21days and with combination was 5.33 ± 2.08 days. In a study conducted by Mucio T O et al. [16] the length of hospitalization with dobutamine was 7.9 ± 4.8 with a range of 4 – 18 days. One of the limitations of this study was that, the sample size was less and hence a comparison of safety and efficacy could not be done between these inotropes.

CONCLUSION

From our study it can be concluded that the inotropes are mostly useful in treating systolic heart failure. Most commonly prescribed inotrope was dobutamine. There was an improvement in the kidney function after inotropic therapy and the patients who received inotropes through peripheral IV lines are susceptible to phlebitis. Inotropes reduces the length of hospital stay. Further studies are required to be carried out with follow up over a large group to draw further conclusion.

Table 1 BASELINE DEMOGRAPHICS OF THE STUDY POPULATION

Demographics	Frequency(n=25)	Percentage (%)
Age		
<40	1	4
41-50	3	12
51-60	8	32
>60	13	52
Sex		
Male	18	72
Female	7	28
LVEF (%)		
< 30	15	60
30 & above	10	40
History of drug allergies		
With allergy	2	8
Without allergy	23	92

Table 2 COMPARISON OF HEMODYNAMIC PARAMETERS BEFORE AND AFTER TREATMENT

PARAMETERS BEFORE AND AFTER INOTROPIC TREATMENT	MEAN ± SD	MEAN DIFFERENCE	95% CONFIDENCE INTERVAL OF THE DIFFERENCE		P VALUE
			LOWER	UPPER	
Heart Rate (beats/min)		-1.48	-7.02	4.06	0.587
Before	87.72 ± 13.38				
After	86.24 ± 12.22				
SBP (mmHg)		-5.12	-13.02	2.78	0.194
Before	111.12 ± 21.83				
After	106 ± 14.72				
DBP (mmHg)		-3.2	-7.61	1.21	0.148
Before	70.4 ± 12.4				
After	67.2 ± 8.9				
Mean BP (mmHg)		2.62	-4.04	9.29	0.425
Before	82.764 ± 13.3				
After	80.14 ± 10				

Table 3 COMPARISON OF LABORATORY PARAMETERS BEFORE AND AFTER TREATMENT

PARAMETERS BEFORE AND AFTER INOTROPIC TREATMENT	MEAN ± SD	MEAN DIFFERENCE	95% CONFIDENCE INTERVAL OF THE DIFFERENCE		P VALUE
			LOWER	UPPER	
BUN (mg/dl)		-2.6	-6.66	1.46	0.199
Before	26.72 ± 15.76				
After	24.12 ± 15.19				
Creatinine (mg/dl)		-0.14	-0.27	-0.01	0.027*
Before	1.56 ± 0.46				
After	1.42 ± 0.47				
Fluid Input (ml)		169.54	-90.64	429.73	0.191
Before	865.73 ± 408.01				
After	1035.27 ± 390.66				
Urine Output (ml)		259.6	-125.36	644.56	0.177
Before	1459 ± 832.87				
After	1718.6 ± 886.46				

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