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Original article:

Inotrope use in critically ill patients: Prevalence and effects on mortality

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Abstract:

Clinical Profile of critically ill patients needing inotropes in medical intensive care unit (MICU) of a tertiary care centre revealed that out of 399 patients admitted during study period, 54 (13.53%) needed inotropes. These 54 patients were suffering from septic shock (n=29), CVT/ GBS/ Infective meningitis (n=8), Acute febrile illness(n=6), fulminant hepatic failure(n=4), malaria(n=4), pulmonary thromboembolism(n=2), and dengue(n=1). The inotropes used included noradrenaline in 45 (83.33%), dopamine in 42 (77.78%) and dobutamine in 5 (9.26%) patients. Of critically ill patients requiring inotropes, 8 (12.96%) needed inotropes for 24 hours, 21(38.89%) needed inotropes for 48 hours and 25(46.30%) needed inotropes for>48 hours duration. There was no association amongst different type of inotropes used and outcome of patients.(p=0.336) Out of 54 needing inotropes, 11(20.37%) survived and 43 (79.62%) expired while out of 345 patients not needing inotropes, 221 (64.05%) survived and 124 (35.94%) expired. Need of inotropes was associated with significantly increased risk of death.

Key Words: inotropes; intensive care unit; adverse effects; mortality

INTRODUCTION

Inotropic drugs enhance myocardial contractility independent of changes in heart rate. Inotropic drugs increase heart rate and some of them have direct or indirect vasodilator properties,thereby, improving systolic performance. Inotropes are often used in MICU to stabilize patients with acute heart failure. [1] Inotropes are indicated in patients with acute systolic heart failure showing signs or symtoms of end organ dysfunction. [2]

Sepsis is often a contributory factor for mortality in critically ill patients. An elevated cardiac index along with decreased systemic vascular resistance leads to hypotension and hypo perfusion of vital organs in the early stages of septic shock. To reverse the hemodynamic and metabolic abnormalities of hyper dynamic septic shock, vasoconstrictors are the main stray of treatment.[3] For several cardiovascular syndromes, the therapeutic cornerstone for the management are inotropic and vasopressor agents. These agents have

excitatory and inhibitory actions on the heart and vascular smooth muscles along with important metabolic, pre-synaptic autonomic nervous system and central nervous system effects. In patients with life-threatening clinical conditions these agents by increasing cardiac output or vascular tone facilitate clinical recovery.[4]

Dopamine, dobutamine and norepine-phrine used alone or in combination are the inotropes commonly used in MICU. Dopamine acts on dopaminergic and adrenergic receptors to elicit clinical effects. The dopaminergic D_1 postsynaptic receptors are concentrated in the coronary, mesenteric, renal, and cerebral beds and D_2 pre-synaptic receptors in the vasculature and renal tissues. Dopamine promotes vasodilation and increased blood flow to these tissues.[4] Dobutamine, a potent inotrope with weaker chronotropic activity, at lower doses has a net vascular effect of mild vasodilation. Doses up to 15 microgram / kg/ min increase cardiac contractility without greatly affecting peripheral resistance due to the counterbalancing effects of α1-mediated vasoconstriction and β2-mediated vasodilation. At higher infusion rates there is progressive vasoconstriction. Despite its mild chronotropic effects at low to medium doses, dobutamine significantly increases myocardial oxygen consumpation. [4] Noradrenaline prim-arily increases systolic, diastolic, and pulse pressure and has a minimal net impact on cardiac output. It is a powerful vasoconstrictor with less potent direct inotropic properties due to its potent α1-adrenergic receptor agonist with modest β agonist activity.[4]

Inotropic drugs have side effects which include myocardial ischemia, and in some cases hypotension.[1] Apart from cardiovascular, metabolic and dermatological side effects, sympathomimetic amines can cause central nervous system stimulation, tremors, restlessness, and even confusion and psychosis. These effects are dose related and disappear on stopping the drugs.[5] High rates of psychiatric morbidity in MICU survivors was has been reported. A strong association between anxiety and inotropes was observed. Use of benzodiazepines was correlated with depression.[6]

There is a paucity of Indian studies in this area due to which the present study was undertaken to study the prevalence and clinical profile of the patients needing inotropes in (MICU). We also compared the type, duration, effects, complications and outcome of various inotropes used.

MATERIAL AND METHODS

Study design& Sample

This prospective, observational, hospital based study was carried out in the MICU of a tertiary care hospital attached to a medical college over a period of six months. The study protocol was approved by the Institutional ethical committee. From the patients admitted to MICU during the study period subjects for the study were selected based on following criteria.

Inclusion criteria:

1. Consecutive patients needing inotropic support in MICU.
2. Age >12 years

Exclusion criteria:

1. Patients / relatives refused to give informed consent.

Study procedure:

After obtaining written informed consent from patient or his legally acceptable representative, all those who fulfilled inclusion & exclusion criteria were included in the study and observed during their period of stay in the MICU. Detailed history and findings on clinical examination were recorded in a specially designed proforma for the study. All the investigations, procedures and intervention done on the patient, various complications and outcomes were also entered in the proforma.

End points:

1. Transfer out of MICU
2. Discharge
3. Death

Statistical methods:

Descriptive statistics (Mean, Standard Deviation, Range, and Percentage) was used for analysis of data. For comparison of continuous data the students 't' test was used while for frequency data the chi-square test was used.

RESULTS

Total number of patients admitted in MICU during the study period was 399 out of which 54 (13.53%) patients needed inotropes while 345 (86.46%) patients did not need inotropes. Out of the 54 critically ill patients needing inotropes, 37 (68.52%) were female and 17 (31.48%) were male. Therefore the critically ill patients needing inotropes in MICU were predominantly female. Out of total number of patients (n=54) needing inotropes, 29 were of septic shock, 8 of CVT/ GBS/ Infective meningitis, 6 of Acute febrile illness, 4 of fulminant hepatic failure, 4 of malaria, 2 of pulmonary thromboembolism, 1 of dengue (Fig 3). The clinical outcome of use of different inotropes is also given in Table 1. Chi square test of association between intropes used and outcome of patient chi square test: (chi-square = 4.56; df = 4; probability = 0.336 > 0.05 p value) proved that there was no association amongst different type of inotropes used and outcome of patients. (Table 1)

Duration of use of various inotropes are given in Table 2 respectively. Pre-morbid conditions in critically ill patients needing inotropes in MICU is given in Table 3. Outcome in critically ill patients needing inotropes in MICU is shown in Table 4.

Fig 1 :Number of critically ill patients in MICU needing inotropes

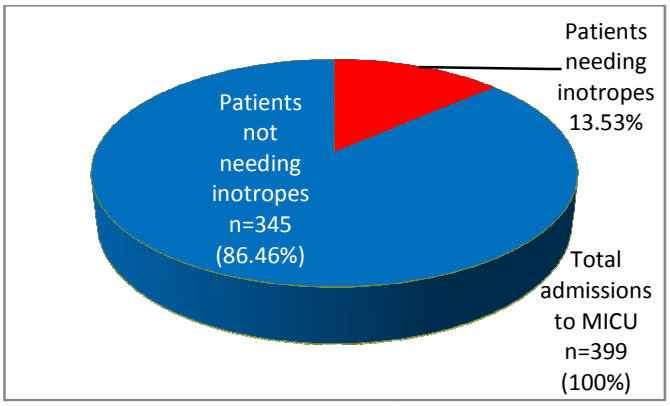

Fig.2. Gender distribution in critically ill patientswho required inotropes in MICU

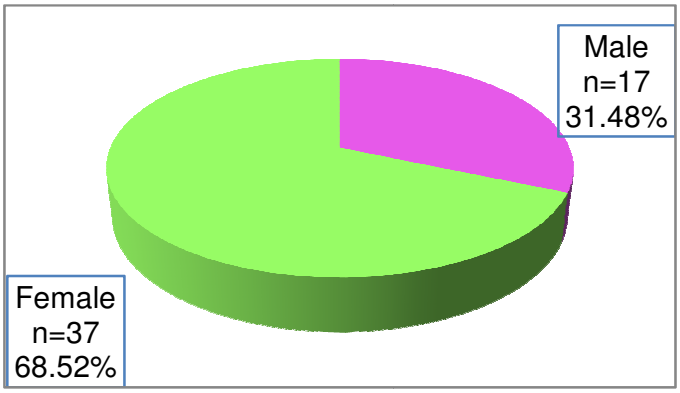

Fig.3. Profile of patients needing inotropes in Medical Intensive Care Unit (n=54)

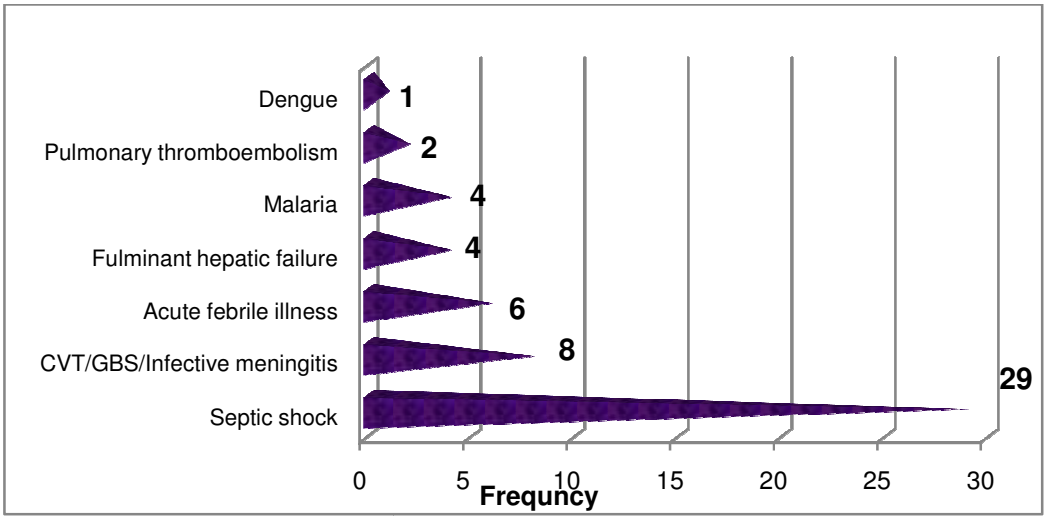

Table 1. Inotropes used in critically ill patients and their outcome in Medical Intensive Care Unit (n=54)

Inotrope	**Frequency(%)**	**Outcome***	**Frequency(%)**
noradrenaline	45 (83.33%)	Survived	6(11.11%)
		Expired	39(72.22%)
dopamine	42(77.78%)	Survived	8(14.81%)
		Expired	34(62.96%)
dopamine + noradrenaline	33(61.11%)	Survived	3(5.56%)
		Expired	30(55.56%)
dobutamine	5(9.26%)	Survived	2(3.70%)
		Expired	3(5.56%)
dobutamine + noradrenaline	3(5.56%)	Survived	0(0.00%)
		Expired	3(5.56%)

* chi-square = 4.56; df = 4; probability = 0.336 > 0.05

Table 2. Duration of use of different inotropes in critically ill patients in Medical Intensive Care Unit

Duration Of inotropes	**Frequency**	**Percentage**
24Hours	8	12.96%
48Hours	21	38.89%
> 48Hours	25	46.30%

Table 3. Pre-morbid conditions in patients needing inotropes in Medical Intensive Care Unit

Pre Morbid Conditions	**Frequency**	**Percentage**
Hypertension	9	16.67%
Diabetes Mellitus	11	20.37%
Ischemic Heart Disease	5	9.26%
Others*	5	9.26%

*Tuberculosis, chronic obstructive pulmonary disease, bronchial asthma, cerebrovascular accident, jaundice, peripheral vascular disease

Fig.4: Outcome in critically ill patients needing inotropes in Medical Intensive Care Unit (N=54)

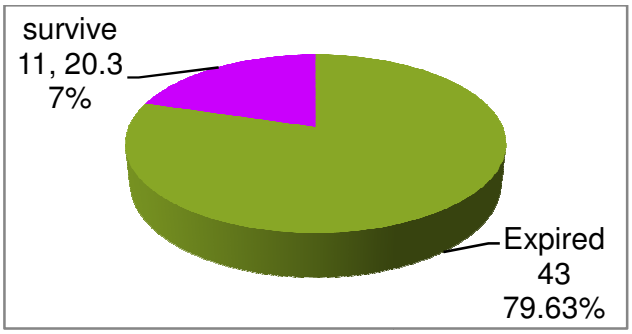

TABLE 4: Relation of outcome to need of Inotropes in critically ill patients

	Total Patients n (%)	Survived n (%)	Died n (%)
Inotropes needed	54 (13.53)	11 (20.37)	43 (79.62)
Inotropes not needed	345 (86.46)	221 (64.05)	124 (35.94)
Total	399 (100.00)	232 (58.14)	167 (41.85)

Chi square =36.6; df=1; P<0.0001

Out of total of 339 patients admitted in MICU during study period, 58.14% (n=232) survived and 41.85% (n=167) expired. Out of 54 patients needing inotropes 20.37% (n=11) survived and 79.62% (n=43) expired ,345 patients not needed inotropes 64.05% (n=221) survived and 35.94% (n=124) expired. Statistical analysis revealed that need of inotropes was significantly associated with increased risk of death.

DISCUSSION

The commonest inotrope used in the present study was noradrenaline followed by dopamine. This is in agreement with the observations of an earlier study that noradrenaline is the commonest vasopressor agent used in septic shock.[7]

A major observation in the study sample was that out of the 54 patients requiring inotropes 20.37% survived while 79.62% expired. As compared to this, out of 345 patients not requiring inotropes 64.05% survived while 35.94% expired. After applying chi-square test, a highly significant association was found between needing inotropes and mortality. This finding is in agreement with a retrospective observational study using data from the Acute Decompensated Heart Failure (ADHERE) national registry which reported that short-term vasodilator therapy was associated with significantly lower in-hospital mortality than inotropic treatment.[8] Similarly the OPTIME-CHF (Outcomes of a Prospective Trial of Intravenous Milrinone for

Exacerbations of Chronic HF) trial also showed that chronic heart failure patients on intravenous inotrope had increased morbidity associated with hypotension and new atrial arrhythmias. An extension of the trial also noted that patients with ischaemic heart failure on IV milrinone were not only hospitalized longer but also had an increased 60 day mortality. [9] In addition a retrospective cohort study of 1,326 cardiac surgery patients also concluded that postoperative inotrope exposure was independently associated with worse outcomes.[10] The results of the present study are also in accordance with another study which observed that inotropes following cardiopulmonary bypass are associated with higher 30-day mortality.[11] However, a recent meta-analysis reviewing previous 20 years literature including 177 randomized control trials involving 28,280 patients revealed no difference in mortality between the group receiving inotropes and the control group which is not in agreement with our findings. In settings of vasoplegic syndromes, sepsis and cardiac surgery the use of inotropes was associated with a reduction in mortality. Further analysis failed to identify any subgroup of patients with increased mortality associated with inotrope therapy. [12]

The present study did not find any association amongst different type of inotropes used in the study and outcome of patients. (Table 4). Previous observational study on inotrope administration in patients in septic shock noted that dopamine use was associated with increased mortality while norepinephrine did not show a trend towards higher mortality. [7] An Indian study also reported that norepinephrine was more useful in reversing the hemodynamic and metabolic abnormalities of septic shock compared to dopamine. [3] The large meta-analysis mentioned above also found that the only inotrope associated with improved survival was levosimendan which was not used in the present study. [12]

LIMITATIONS

Limitations of the study include small sample size and study carried out at a single centre.

CONCLUSION

In critically ill patients in medical intensive care unit the need of inotropes was associated with significantly increased risk of death.

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