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The Clinical Impacts of Dopamine / Propranolol Combination Versus Norepinephrine As A Vasopressor In Critically Ill Septic During Norepinephrine Shortage

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Abstract

Objective: Septic shock is a state of extreme physiologic stress necessitating vasopressor administration. Norepinephrine is the vasopressor of choice for septic shock, while Dopamine is suggested as an alternative vasopressor in selected cases. Patients with septic shock treated during shortage of Norepinephrine, had higher mortality rates. We aim to evaluate the clinical effectiveness of Dopamine/Propranolol combination as an alternative for the management of septic shock during Norepinephrine shortages, and to gauge the percentage changes in each of: systolic blood pressure (%ΔSBP), mean arterial pressure (% ΔMAP), heart rate (%ΔHR), shock index and modified shock index (%ΔSI and %ΔmSI), risk of tachyarrhythmia, intensive care unit (ICU) and overall hospital length of stay (LOS), and 28-day ICU mortality.

Methods: A retrospective analysis was conducted in our institution between April 2017 and Sep 2018. Discharged or dead patients who failed to complete a minimum of 1 week after hospital admission were excluded. Patients' continuous variables were analyzed using Independent Samples and One-Sample T-test while categorical data were expressed as numbers with percentages by using Chi Square test.

Results: Dopamine/Propranolol combination demonstrated significant increases in the Means±SDs of: SBP_{avg} (101.87±10.00mmHg vs. 94.33±9.17mmHg); DBP_{avg} (60.12±7.32mmHg vs. 55.67±7.01 mmHg); and MAP_{avg} (71.31±11.69mmHg vs. 66.53±10.84 mmHg). And a significant reduction in HR_{avg} (95.13±8.7bpm vs. 107.31±9.35bpm); SI_{avg} (1.39±0.38 bpm/mmHg vs. 1.68±0.47 bpm/mmHg); and mSI_{avg} (1.39±0.38 bpm/mmHg vs. 1.68±0.47 bpm/mmHg) compared to Norepinephrine.

Conclusion: Our analysis suggests Dopamine/Propranolol combination as an appropriate alternative for the management of septic shock during Norepinephrine shortages.

Keywords: Critically-ill patients, Dopamine/Propranolol combination, Norepinephrine shortage, Mortality, Septic shock.

Introduction

Septic shock is a life-threatening condition characterized by a constellation of metabolic, cellular, and circulatory derangements with detrimental effects on homeostasis, hence being associated with an elevated risk of mortality.[1] The persistent hypotension indicating septic shock necessitates the use of vasopressors: clinical guidelines recommend Norepinephrine to restore mean arterial pressure (MAP) in patients with refractory hypotension despite volume resuscitation.[2,3] (*i.e.* failure of approximately 4 L≤ of resuscitation crystalloid solution to maintain MAP ≥65 mmHg or if evidence of volume overload is present).[4]

Norepinephrine, the first-line vasopressor in septic shock, has been shown to be both safer and more effective than Dopamine in restoring MAP in patients with septic shock.[2,5,6] Due to Dopamine's propensity to precipitate tachyarrhythmias, it is merely an alternative agent to be used in selected cases with low risk of tachyarrhythmias and absolute or relative bradycardia. [6, 7] This can be explained by the vasoactive agents' pharmacology: Norepinephrine has higher affinity to α-adrenergic receptors than β-adrenergic receptors. Producing clinically significant increments in MAP while producing little changes with respect to heart rate and cardiac output.[8] On the other hand, Dopamine has a higher affinity to β-adrenergic than α-adrenergic receptors, hence the higher risk for tachyarrhythmias.[3] This study challenges the Dopamine/Propranolol combination as an alternative to Norepinephrine during Norepinephrine shortages by gauging the percentage changes in each of: the systolic blood pressure (%ΔSBP); mean arterial pressure (%ΔMAP); heart rate (%ΔHR); septic shock and modified septic shock (%ΔSI and %ΔmSI); the risk of tachyarrhythmia; ICU and overall hospital length of stay (LOS); and 28-day ICU mortality.

Material and Methods

This was a single-center observational retrospective study conducted in the departments of King Hussein Medical Center (KHMC) at Royal Medical Services (RMS) in Jordan. This study was approved by our Institutional Review Board (IRB), and a requirement for consent was waived owing to its retrospective design. This study included a 188 septic critically ill patients. Flow chart of our studied patients' selection and data collection process is fully illustrated in Figure 1.

An Independent and One Sample T-tests were conducted to analyze the continuous variables and to express them as Means±SDs in the overall studied cohort, septic mechanically ventilated critically ill patients who were on DOP/PROP vasopressors (Group I), and in septic mechanically ventilated critically ill patients who were on NE vasopressor (Group II), while the effect size was expressed as Mean differences±SEMs between Group I and Group II. Chi Square test was conducted to analyze the ordinal variables and to express them as number of participants (percentage) across overall and individual tested groups. Statistical analyses were performed using IBM SPSS ver. 25 (IBM Corp., Armonk, NY, USA) and P-values ≤0.05 were considered statistically significant.

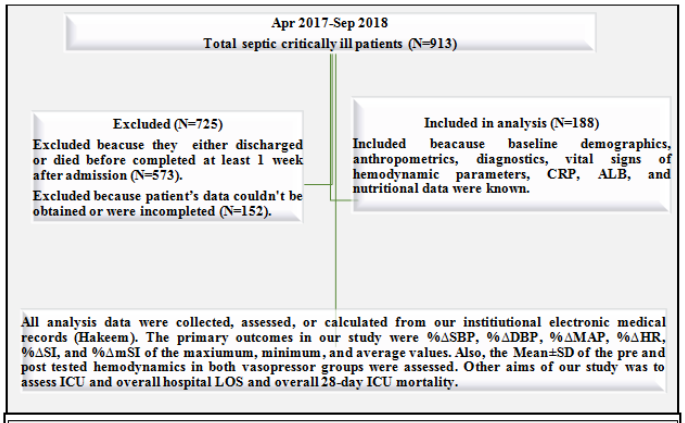

Fig 1. Flow chart of septic critically ill patient's selection and data collection process.

Apr: April.	CRP: C-reactive protein.	mSI: Modified shock index.
Sep: September.	LOS: Length of stay	ALB: Albumin.
%Δ: Percentage changes.	SI: Shock index	SBP: Systolic blood pressure.
DBP: Diastolic blood pressure.	MAP: Mean arterial pressure.	HR: Heart rate.

Results

The mean age of our 188 studied hyperglycemic critically ill patients was 58.94±10.37 years in which 131 patients (69.7%) of the eligible sample were male and 57 patients (30.3%) were female. The overall 28-day ICU mortality was 40.4% (76 patients) in overall studied cohort, 41.9% (36 participants) in Group I, and 39.2% (40 participants). The ICU and overall hospital LOS were 12.76±4.95 days and 17.07±6.98 days with an insignificant Mean differences±SEM of -0.02±0.73 days and -0.05±1.03 days, respectively. The Mean±SD of body weight (BW), body mass index (BMI), c-reactive protein (CRP), CRP to ALB ratio (CRP:ALB), total calorie input (TCI), protein density input (PD), total fluid input, vasopressor infusion rate, corrected calcium systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), corrected calcium (cCa^{+2}), magnesium level (Mg^{+2}), potassium level (K^{+}), maximum, minimum, and average blood glucose levels (BG_{min}, BG_{max}, and BG_{avg}), and total insulin dose were insignificant different between the two groups.

The Means±SDs of SBP_{max}, $\%\Delta SBP_{max}$, SBP_{min}, $\%\Delta SBP_{min}$, SBP_{avg},$\%\Delta SBP_{avg}$, DBP_{max} $\%\Delta DBP_{max}$, DBP_{min}, $\%\Delta DBP_{min}$, DBP_{avg}, $\%\Delta DBP_{avg}$, MAP_{max}, $\%\Delta MAP_{max}$, MAP_{min}, $\%\Delta MAP_{min}$, MAP_{avg}, and $\%\Delta MAP_{avg}$ were significantly higher in septic critically ill patients who received DOP/PROP (Group I) than in septic critically patients who received NE (Group II) (109.67±10.98 mmHg vs 101.19±10.03 mmHg), (25.24%±2.38% vs 15.23%±2.54%), (96.69±8.61 mmHg vs 90.21±7.88 mmHg), (43.68%±3.22% vs 33.64%±3.54%), (101.87±10.00 mmHg vs 94.33±9.17 mmHg), (34.58%±3.38% vs 24.33%±3.71%), (67.27±6.12 mmHg vs 62.23±5.68 mmHg), (33.08%±3.69% vs23.03%±4.07%), (58.88±6.71 mmHg vs 62.23±5.68 mmHg), (52.63%±4.21% vs 42.54%±4.93%), (60.12±7.32 mmHg vs 55.67±7.01 mmHg), (36.54%±7.14% vs 26.34%±8.21%), (85.44±9.66 mmHg vs 79.69±8.84 mmHg), (43.59%±3.33% vs 33.57%±3.56%), (63.97±12.62 mmHg vs 60.34±11.62 mmHg), (61.92%±4.50% vs 51.92%±4.79%), (71.31±11.69 mmHg vs 66.53±10.84 mmHg), and (39.55%±7.38% vs 29.91%±7.77%) with significant Mean differences±SEMs of +8.49±1.53 mmHg, +10.02%±0.36%, +6.48±1.20 mmHg, +10.04%±0.49%, +7.54±1.39 mmHg, +10.25%±0.52%, +5.04±0.86 mmHg, +10.05%±0.57%, +3.85±0.94 mmHg, +10.09%±0.68%, +4.45±1.05 mmHg, +10.21%±1.13%, +5.75±1.35 mmHg, +10.02%±0.51%, 3.62±1.77 mmHg, 9.99%±0.68%, 4.78±1.65 mmHg, and 9.63%±1.11%, respectively.

In contrast, the Means±SDs of HR_{max}, $\%\Delta HR_{max}$, HR_{min}, $\%\Delta HR_{min}$, HR_{avg}, $\%\Delta HR_{avg}$, SI_{max}, $\%\Delta SI_{max}$, SI_{min}, $\%\Delta SI_{min}$, SI_{avg}, $\%\Delta SI_{avg}$, mSI_{max}, $\%\Delta mSI_{max}$, mSI_{min}, $\%\Delta mSI_{min}$, mSI_{avg}, and $\%\Delta mSI_{avg}$ were significantly higher in septic critically patients who were administered NE (Group II) than in septic critically ill patients who were administered DOP/PROP (Group I) (114.37±10.39 bpm vs 100.72±9.47 bpm), (-6.47%±1.69% vs -17.95%±1.55%), (91.86±6.32 bpm vs 81.47±5.88 bpm), (-1.40%±1.71% vs -12.87%±1.57%), (107.31±9.35 bpm vs 95.13±8.7 bpm), (-0.44%±3.35% vs -11.96%±3.09%), (1.29±0.23 bpm/mmHg vs 1.06±0.19 bpm/mmHg), (-14.44%±7.29% vs -29.99%±5.92%), (0.92±0.16 bpm/mmHg vs 0.76±0.13 bpm/mmHg), (-35.99%±7.29% vs -47.73%±5.98%), (1.16±0.22 bpm/mmHg vs 0.95±0.19 bpm/mmHg), (-7.46%±10.07% vs -24.14%±8.22%), (1.99±0.56 bpm/mmHg vs 1.66±0.48 bpm/mmHg), (-15.72%±14.92% vs -30.17%±12.49%), (1.18±0.22 bpm/mmHg vs 0.97±0.19 bpm/mmHg), (-18.51%±10.21% vs -32.71%±8.53%), (1.68±0.47 bpm/mmHg vs 1.39±0.38 bpm/mmHg), and (-9.47%±16.13% vs -25.15%±13.21%) with significant

Mean differences±SEMs of -13.65±1.46 bpm, -11.48%±0.24%, -10.39±0.89 bpm, -11.47%±0.24%, -12.19±1.33 bpm, -11.52%±0.47%, -0.23±0.03 bpm/mmHg, -15.56%±0.98%, -0.17±0.02 bpm/mmHg, -11.74%±0.99%, -0.21±0.03 bpm/mmHg, -16.69%±1.36%, -0.34±0.08 bpm/mmHg, -14.44%±2.03%, -0.20±0.03 bpm/mmHg, -14.20%±1.39%, -0.29±0.06 bpm/mmHg, and -15.69%±2.18%. Demographics, anthropometrics, haemodynamic, nutritional indices, and other follow-up comparison lab parameters of the study's septic mechanically ventilated critically ill patients are fully summarised in **Table 1-3**.

Discussion

This retrospective study of 188 septic, mechanically ventilated patients establishes the clinical efficacy of Dopamine/Propranolol combination as an alternative to Norepinephrine in patients with septic shock during Norepinephrine shortages. Dopamine, the predominantly β_1-adrenergic agonist at lower doses, when combined with the non-selective β-blocker Propranolol demonstrated significant increases in the Means±SDs of: SBP_{avg} (101.87±10.00 mmHg vs. 94.33±9.17 mmHg); DBP_{avg} (60.12±7.32 mmHg vs. 55.67±7.01 mmHg); and MAP_{avg} (71.31±11.69 mmHg vs. 66.53±10.84 mmHg), respectively. And a significant reduction in HR_{avg} (95.13±8.7bpm vs. 107.31±9.35bpm); SI_{avg} (1.39±0.38 bpm/mmHg vs. 1.68±0.47 bpm/mmHg); and mSI_{avg} (1.39±0.38 bpm/mmHg vs. 1.68±0.47 bpm/mmHg) compared to Norepinephrine. Reducing the HR in patients with septic shock can reduce myocardial oxygen consumption and improve ventricular filling, and coronary perfusion, consequently improving the aforementioned hemodynamic parameters. [9] One of the first reports of Propranolol use in sepsis backdates to 1968 when Berk *et al* demonstrated Propranolol's role in reducing fluid requirements and improving survival in the animal model. [10] Since then several authors have investigated the role β-blockers in mitigating the detrimental effects of the hyper-adrenergic state in septic shock. [11,12,13] Most prominently, Morelli *et al*,[9] used Esmolol, a cardioselective β-blocker, titrated to maintain heart rate within a pre-determined range in patients with septic shock. Esmolol increased in stroke volume, maintained MAP and reduced Norepinephrine requirements and reduced overall 28-day mortality.

Furthermore, the concept of decatecholaminization has been proposed to partially or even completely replace catecholamine use in critically ill patients, with β-blockers considered for that use.[11,13] However Norepinephrine remains the mainstay treatment for septic shock and its shortages engender significant increases in mortality in patients with septic shock requiring the life-saving drug.[14] To combat the unfavorable effects of Dopamine on the septic heart during Norepinephrine shortages, we used Propranolol, in conjunction with Dopamine to manage patients septic shock. The findings of this study must be seen in light of some limitations including: its retrospective design and use of single-center data. Nonetheless, our center is an experienced and high-volume unit, so our data may be useful in other centers. A larger, multisite, and prospective study is required to investigate the role of Propranolol in improving the hemodynamic parameters of patients with septic shock and to compare regarding cardioselectivity.

Table 1. Demographics, anthropometrics, nutritional indices, and other comparison lab parameters of our studied septic patients.

Table 1. Demographics, anthropometrics, nutritional indices, and other comparison lab parameters of our studied septic patients.

Variable		Total (N=188)	Group I (N=86) DOP/PROP Mean±SD	Group II NE (N=102) Mean±SD	Group I vs Group II Mean diffeenc±SEM	P-Value
Age (Yrs)		58.94±10.37	58.8310.31	59.04±10.47	-0.21±1.52	0.889 (NS)
Gender	Female	57 (30.3%)	25 (29.1%)	32 (31.4%)		0.428 (NS)
	Male	131 (69.7%)	61 (70.9%)	70 (68.6%)		
BW (Kg)		74.05±10.23	73.34±9.69	74.65±10.68	-1.31±1.49	0.383 (NS)
BMI (Kg/m^2)		25.90±3.97	25.57±3.68	26.18±4.20	-0.61±0.58	0.294 (NS)
CRP (mg/dl)		13.19±4.27	12.97±3.99	13.38±4.51	-0.42±0.63	0.507 (NS)
ALB (g/dl)		2.37±0.18	2.38±0.17	2.37±0.18	0.02±0.03	0.548 (NS)
CRP:ALB (X:1)		5.72±2.45	5.59±2.25	5.84±2.62	-0.24±0.36	0.503 (NS)
H.ALB (g/day)		20.48±2.98	20.58±2.81	20.39±3.12	0.19±0.44	0.665 (NS)
TCI (Cal/day)		651.6±79.46	652.19±76.45	651.13±82.29	1.06±11.7	0.928 (NS)
TCI (Cal/kg/day)		9.49±0.70	9.53±0.68	9.47±0.72	0.06±0.10	0.546 (NS)
PD (g/100 Cal)		1.45±0.68	1.48±0.72	1.43±0.64	0.06±0.09	0.578 (NS)
∑Fluid Input (ml/day)		2709±422	2704±393	2714±446	-10.0±61.9	0.872 (NS)
Vasopressor Rate (ml/hr)		6.73±6.39	12.46±2.23	12.41±2.09	0.05±0.32	0.873 (NS)
NE rate (mcg/min)		12.43±2.15	0.00±0.00	12.41±2.09	-12.41±0.23	0.000 (S)
DOP rate (mcg/kg/min)		5.69±6.40	12.46±2.23	0.00±0.00	12.46±0.22	0.000 (S)
PROP rate (mg/hr)		0.11±0.13	0.25±0.04	0.00±0.00	0.25±0.00	0.000 (S)
cCa^{+2} (mg/dl)		8.05±0.29	8.07±0.22	8.02±0.33	0.05±0.04	0.216 (NS)
Mg^{+2} (mg/dl)		1.26±0.06	1.25±0.04	1.26±0.07	-0.009±0.01	0.252 (NS)
BG_{min} (mg/dl)		140.8±15.18	141.7±15.30	140.1±15.12	1.54±2.23	0.491 (NS)
BG_{max} (mg/dl)		236.7±21.66	235.8±19.73	237.3±23.23	-1.52±3.18	0.633 (NS)
BG_{avg} (mg/dl)		188.7±6.72	188.8±5.72	188.7±7.48	0.03±0.99	0.975 (NS)
∑ Insulin dose (IU/day)		99.88±48.19	99.4±46.0	100.3±50.18	-0.89±7.07	0.899 (NS)
$\%BG_{var}$		50.51%±16.7%	49.7%±16.53%	51.2%±16.97%	-1.49%±2.5%	0.545 (NS)
K^+ (mEq/l)		2.84±0.19	2.84±0.18	2.85±0.20	-0.01±0.03	0.841 (NS)
Pre-ICU LOS (day)		4.32±3.95	4.30±3.68	4.33±4.18	-0.03±0.58	0.957 (NS)
ICU LOS (day)		12.76±4.95	12.74±4.92	12.76±5.00	-0.02±0.73	0.977 (NS)
Hospital LOS (day)		17.07±6.98	17.05±6.99	17.10±7.00	-0.05±1.03	0.960 (NS)
Overall 28-day ICU Survival		112 (59.6%)	50 (58.1%)	62 (60.8%)		0.413 (NS)
Overall 28-day ICU Mortality		76 (40.4%)	36 (41.9%)	40 (39.2%)		

Data were presented as either Mean±SD and Mean difference±SEM by using One sample T-test and Independent T-test or as Number (Percentage) by using Chi square test.

Group I: Septic mechanically ventilated critically ill patients who were on DOP/PROP vasopressors.

Group II: Septic mechanically ventilated critically ill patients who were on NE vasopressors.

DOP/PROP: Dopamine 400 mg/Propranolol 2 mg in 100 ml 0.9% NaCl.

Yrs: Years.
S: Significant (P≤0.05).
NS: Non-Significant (P>0.05).
PD: Protein density.
IU: International unit.
LOS: Length of stay.
BW: Body weight.
BMI: Body mass index.
CRP: C-reactive protein.
ALB: Albumin.
Mg: Magnesium level.
H.ALB: Human Albumin 20%.
CRP:ALB: CRP to ALB ratio.
TCI: Total calories input.
BG: Blood glucose level.
ICU: Intensive care unit.
cCa: Corrected calcium level.
Min: Minimum.
Max: Maximum.
Avg: Average.
K" Potassium.
Cal: Kilocalorie.

Table 2. Comparison baseline and follow-up hemodynamics of blood pressures in our studied septic patients.

Variable	Total (N=188)	Group I (N=86) DOP/PROP Mean±SD	Group II NE (N=102) Mean±SD	Group I vs Group II Mean diffeenc±SEM	P-Value
SBP_{max0} (mmHg)	87.68±8.04	87.55±8.15	87.78±7.99	-0.24±1.18	0.840 (NS)
SBP_{max1} (mmHg)	105.07±11.27	109.67±10.98	101.19±10.03	8.49±1.53	0.000 (S)
$\%\Delta SBP_{max01}$	19.81%±5.57%	25.24%±2.38%	15.23%±2.54%	10.02%±0.36%	0.000 (S)
SBP_{min0} (mmHg)	67.38±5.09	67.33±5.23	67.42±4.99	-0.09±0.75	0.898 (NS)
SBP_{min1} (mmHg)	93.17±8.81	96.69±8.61	90.21±7.88	6.48±1.20	0.000 (S)
$\%\Delta SBP_{min01}$	38.23%±6.05%	43.68%±3.22%	33.64%±3.54%	10.04%±0.49%	0.000 (S)
SBP_{avg0} (mmHg)	75.71±6.49	75.60±6.61	75.80±6.42	-0.19±0.95	0.834 (NS)
SBP_{avg1} (mmHg)	97.78±10.25	101.87±10.00	94.33±9.17	7.54±1.39	0.000 (S)
$\%\Delta SBP_{avg01}$	29.02%±6.23%	34.58%±3.38%	24.33%±3.71%	10.25%±0.52%	0.000 (S)
$\%SBP_{var0}$	26.65%±2.47%	26.58%±2.39%	26.71%±2.53%	-0.13%±0.36%	0.720 (NS)
$\%SBP_{var1}$	12.03%±2.83%	12.55%±2.65%	11.59%±2.91%	0.95%±0.41%	0.021 (NS)
DPB_{max0} (mmHg)	50.51±3.70	50.44±3.76	50.57±3.67	-0.13±0.54	0.816 (NS)
DPB_{max1} (mmHg)	64.53±6.39	67.27±6.12	62.23±5.68	5.04±0.86	0.000 (S)
$\%\Delta DBP_{max01}$	27.63%±6.35%	33.08%±3.69%	23.03%±4.07%	10.05%±0.57%	0.000 (S)
DBP_{min0} (mmHg)	38.52±3.59	38.50±3.72	38.54±3.51	-0.04±0.53	0.941 (NS)
DBP_{min1} (mmHg)	56.79±6.69	58.88±6.71	55.03±6.18	3.85±0.94	0.000 (S)
$\%\Delta DBP_{min01}$	47.16%±6.82%	52.63%±4.21%	42.54%±4.93%	10.09%±0.68%	0.000 (S)
DBP_{avg0} (mmHg)	43.92±3.71	43.91±3.82	43.93±3.63	-0.02±0.54	0.964 (NS)
DBP_{avg1} (mmHg)	57.70±7.47	60.12±7.32	55.67±7.01	4.45±1.05	0.000 (S)
$\%\Delta DBP_{avg01}$	31.01%±9.25%	36.54%±7.14%	26.34%±8.21%	10.21%±1.13%	0.000 (S)
$\%DBP_{var0}$	27.52%±3.46%	27.46%±3.41%	27.57%±3.51%	-0.12%±0.51%	0.821 (NS)
$\%DBP_{var1}$	13.87%±4.49%	14.30%±3.91%	13.51%±4.93%	0.79%±0.66%	0.228 (NS)
MAP_{max0} (mmHg)	59.56±6.04	59.44±6.17	59.67±5.96	-0.22±0.89	0.800 (NS)
MAP_{max1} (mmHg)	82.32±9.64	85.44±9.66	79.69±8.84	5.75±1.35	0.000 (S)
$\%\Delta MAP_{max01}$	38.16%±6.08%	43.59%±3.33%	33.57%±3.56%	10.02%±0.51%	0.000 (S)
MAP_{min0} (mmHg)	39.51±7.08	39.41±7.15	39.59±7.05	-0.19±1.04	0.854 (NS)
MAP_{min1} (mmHg)	62.00±12.19	63.97±12.62	60.34±11.62	3.62±1.77	0.042 (S)
$\%\Delta MAP_{min01}$	56.49%±6.82%	61.92%±4.50%	51.92%±4.79%	9.99%±0.68%	0.000 (S)
MAP_{avg0} (mmHg)	51.001±6.28	50.93±6.37	51.07±6.23	-0.14±0.92	0.881 (NS)
MAP_{avg1} (mmHg)	68.72±11.46	71.31±11.69	66.53±10.84	4.78±1.65	0.004 (S)
$\%\Delta MAP_{avg01}$	34.32%±8.97%	39.55%±7.38%	29.91%±7.77%	9.63%±1.11%	0.000 (S)
$\%MAP_{var0}$	40.09%±6.92%	40.18%±7.06%	40.01%±6.83%	0.16%±1.02%	0.874 (NS)
$\%MAP_{var1}$	30.97%±9.07%	31.49%±9.12%	30.54%±9.04%	0.95%±1.33%	0.475 (NS)

Data were presented as either Mean±SD and Mean difference±SEM by using One sample T-test and Independent T-test or as Number (Percentage) by using Chi square test.

Group I: Septic mechanically ventilated critically ill patients who were on DOP/PROP vasopressors.

Group II: Septic mechanically ventilated critically ill patients who were on NE vasopressors.

DOP/PROP: Dopamine 400 mg/Propranolol 2 mg in 100 ml 0.9% NaCl.

SBP: Systolic blood pressure. 0: Baseline before vasopressors. Max: Maximum. %Δ:Percentage changes.

DBP: Diagnostic blood pressure. 1: After vasopressors. Min: Minimum. Avg: Average.

MAP: Mean arterial pressure. Var: Variation

Table 3. Comparison baseline and follow-up hemodynamics of HRs and shock indices in our studied septic patients.

Variable	Total (N=188)	Group I (N=86) DOP/PROP Mean±SD	Group II NE (N=102) Mean±SD	Group I vs Group II Mean diffeenc±SEM	P-Value
HR_{max0} (bpm)	122.45±11.07	122.71±11.34	122.23±10.89	0.48±1.63	0.766 (NS)
HR_{max1} (bpm)	108.13±12.07	100.72±9.47	114.37±10.39	-13.65±1.46	0.000 (S)
$\%\Delta HR_{max01}$	-11.72%±5.96%	-17.95%±1.55%	-6.47%±1.69%	-11.48%±0.24%	0.000 (S)
HR_{min0} (bpm)	93.28±6.24	93.42±6.38	93.16±6.16	0.26±0.92	0.775 (NS)
HR_{min1} (bpm)	87.11±8.02	81.47±5.88	91.86±6.32	-10.39±0.89	0.000 (S)
$\%\Delta HR_{min01}$	-6.65%±5.96%	-12.87%±1.57%	-1.40%±1.71%	-11.47%±0.24%	0.000 (S)
HR_{avg0} (bpm)	107.9±8.54	108.0±8.72	107.7±8.42	0.26±1.25	0.833 (NS)
HR_{avg1} (bpm)	101.74±10.89	95.13±8.7	107.31±9.35	-12.19±1.33	0.000 (S)
$\%\Delta HR_{avg01}$	-5.71%±6.59%	-11.96%±3.09%	-0.44%±3.35%	-11.52%±0.47%	0.000 (S)
$\%HR_{var0}$	26.83%±2.62%	26.86%±2.68%	26.81%±2.58%	0.05%±0.38%	0.889 (NS)
$\%HR_{var1}$	20.45%±2.49%	20.05%±2.49%	20.78%±2.45%	-0.73%±0.36%	0.045 (S)
SI_{max0} (bpm/mmHg)	1.49±0.15	1.49±0.15	1.49±0.15	0.003±0.02	0.868 (NS)
SI_{max1} (bpm/mmHg)	1.18±0.25	1.06±0.19	1.29±0.23	-0.23±0.03	0.000 (S)
$\%\Delta SI_{max01}$	-21.55%±10.25%	-29.99%±5.92%	-14.44%±7.29%	-15.56%±0.98%	0.000 (S)
SI_{min0} (bpm/mmHg)	1.01±0.06	1.01±0.07	1.01±0.06	0.002±0.01	0.850 (NS)
SI_{min1} (bpm/mmHg)	0.85±0.17	0.76±0.13	0.92±0.16	-0.17±0.02	0.000 (S)
$\%\Delta SI_{min01}$	-41.36%±8.91%	-47.73%±5.98%	-35.99%±7.29%	-11.74%±0.99%	0.000 (S)
SI_{avg0} (bpm/mmHg)	1.24±0.10	1.24±0.11	1.24±0.10	0.002±0.02	0.907 (NS)
SI_{avg1} (bpm/mmHg)	1.06±0.23	0.95±0.19	1.16±0.22	-0.21±0.03	0.000 (S)
$\%\Delta SI_{avg01}$	-15.09%±12.45%	-24.14%±8.22%	-7.46%±10.07%	-16.69%±1.36%	0.000 (S)
SI_{var0} (bpm/mmHg)	38.82%±4.14%	38.86%±4.28%	38.79%±4.03%	0.06%±0.61%	0.915 (NS)
SI_{var1} (bpm/mmHg)	31.44%±1.82%	31.55%±1.88%	31.35%±1.77%	0.20%±0.27%	0.448 (NS)
mSI_{max0} (bpm/mmHg)	2.33±0.27	2.34±0.28	2.33±0.26	0.006±0.04	0.884 (NS)
mSI_{max1} (bpm/mmHg)	1.84±0.55	1.66±0.48	1.99±0.56	-0.34±0.08	0.000 (S)
$\%\Delta mSI_{max01}$	-22.33%±15.59%	-30.17%±12.49%	-15.72%±14.92%	-14.44%±2.03%	0.000 (S)
mSI_{min0} (bpm/mmHg)	1.44±0.09	1.44±0.10	1.43±0.09	0.002±0.01	0.892 (NS)
mSI_{min1} (bpm/mmHg)	1.08±0.23	0.97±0.19	1.18±0.22	-0.20±0.03	0.000 (S)
$\%\Delta mSI_{min01}$	-25.01%±11.82%	-32.71%±8.53%	-18.51%±10.21%	-14.20%±1.39%	0.000 (S)
mSI_{avg0} (bpm/mmHg)	1.83±0.17	1.84±0.17	1.83±0.17	0.003±0.02	0.912 (NS)
mSI_{avg1} (bpm/mmHg)	1.55±0.45	1.39±0.38	1.68±0.47	-0.29±0.06	0.000 (S)
$\%\Delta mSI_{avg01}$	-16.64%±16.77%	-25.15%±13.21%	-9.47%±16.13%	-15.69%±2.18%	0.000 (S)
mSI_{var0} (bpm/mmHg)	48.64%±5.70%	48.69%±5.89%	48.59%±5.56%	0.09%±0.84%	0.909 (NS)
mSI_{var1} (bpm/mmHg)	47.25%±10.15%	47.47%±10.30%	47.07%±10.07%	0.40%±1.49%	0.788 (NS)

Data were presented as either Mean±SD and Mean difference±SEM by using One sample T-test and Independent T-test or as Number (Percentage) by using Chi square test.

Group I: Septic mechanically ventilated critically ill patients who were on DOP/PROP vasopressors.

Group II: Septic mechanically ventilated critically ill patients who were on NE vasopressors.

DOP/PROP: Dopamine 400 mg/Propranolol 2 mg in 100 ml 0.9% NaCl.

HR: Heart rate.

SI: Shock index (HR/SBP).

mSI: Modified shock index (HR/MAP).

0: Baseline before vasopressors.

1: After vasopressors.

%Δ:Percentage changes.

Max: Maximum.

Min: Minimum.

Avg: Average.

Var: Variation

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