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Review Article

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Nitroglycerin in Suboptimal Versus the Remaining Doses in Hypertensive Crises Regards Propylene Glycol; Efficacy and Safety (Nitroglycerin on Trace Study); Retrospective Observational Study

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Abstract

Background: Hypertensive crises represent the most immediate danger to those afflicted and the most dramatic proof of the lifesaving potential of antihypertensive therapy. It is one of the most serious presentations in the emergency department for hypertensive patients. Hypertensive crises are largely preventable and often result from inadequate management of hypertension or poor adherence to therapy.

Method of study and patients: My study was an observational retrospective for 1043 cases. The study was conducted in both Ras El-Bar Central Hospital and Fraskour Central Hospital; in the Intensive Care Units. The author reported the 1043 cases of hypertensive crises over nearly 48-months, started from July 10, 2015, and, ended on Jul 10, 2019. Different doses within the normal range of i.v nitroglycerin was given. Both adverse effects (safety) and anti-hypertensive responses (efficacy) were recorded.

Results: Range of age in group I was 24-90 years and in group II was 24-88 years but with insignificant P-value (0.472). There is predominant female sex but with insignificant P-value (0.286). Predominant side effects in group II vs. group I with P-value (<0.001) was significant in group I vs. group II. There is no significant difference in response for both groups after nitroglycerine i.v infusion with P-value (0.735).

Conclusions: The author concluded that nitroglycerine is effective and safe in the treatment of hypertensive emergencies with the lowest vs. the remaining other nitroglycerin infusion doses. Regards the drug efficacy, no significant difference between the lowest and remaining other nitroglycerin infusion doses in treating hypertensive crises. Using the lowest nitroglycerin infusion dose in treating hypertensive crises safer, economically saver, and less anxious regards the serious adverse effects. Propylene glycol may be the suggested inducing agent for the side effects and its severity with increasing nitroglycerin infusion doses.

Keywords: Efficacy and safety; Hypertension crises; Lower versus remaining doses; Propylene glycol; Nitroglycerin on trace study; Nitroglycerin

Abbreviations

ACS	:	Acute coronary syndromes
AMI	:	Acute myocardial infarction
BP	:	Blood pressure
cGMP	:	cyclic GMP
DBP	:	Diastolic blood pressure

ECG	:	Electrocardiogram
ESH	:	European Society of Hypertension
ESO	:	European Stroke Organization
Euro-STAT	:	European registry for studying the Treatment of Acute hypertension
EUSI	:	European Stroke Initiative
FMD	:	Flow-mediated dilation
IUPAC	:	International Union of Pure and Applied Chemistry
LV	:	Left ventricular
LOAEL	:	The lowest-observed-adverse-effect level
MEG	:	Methyl ethyl glycol
NOAEL	:	The no-observed-adverse-effect-level
NO	:	Nitrous oxide
PCWP	:	Pulmonary capillary wedge pressure
PG	:	Propylene glycol
SBP	:	Systolic blood pressure
USA	:	United States of America
VMAC trial	:	Vasodilatation in the Management of Acute Congestive Heart Failure trial

Introduction

Hypertensive crises

Importance: Hypertension is an extremely common clinical problem. Approximately 1% of these patients will develop hypertensive crises at some point in their lifetime [1]. Hypertensive crises represent the most immediate danger to those afflicted and the most dramatic proof of the lifesaving potential of antihypertensive therapy [2]. It is one of the most serious presentations in the emergency department for hypertensive patients. Hypertensive crises are largely preventable and often result from inadequate management of hypertension or poor adherence to therapy [3]. Patients with hypertensive crises may require an immediate reduction in elevated blood pressure to prevent and arrest progressive end-organ damage [1]. A hypertensive crisis is a present when markedly elevated blood pressure is accompanied by progressive or impending acute target organ damage or death [3,4]. Prompt recognition, based primarily on physical signs and symptoms is essential. Appropriately aggressive therapy will often result in a satisfactory outcome [4,5]. Antihypertensive drugs that will be lowered aggressively of markedly elevated blood pressure within minutes to hours has changed the concepts of definition and therapy of hypertensive emergencies and urgencies [6,7]. Prompt treatment of hypertensive emergencies is only required to prevent target organ damage and death [8,9]. Blood pressure control in a hypertensive emergency should be attained as expeditiously as possible with a short-acting titratable intravenous antihypertensive medication to prevent ongoing and potentially permanent end-organ damage [10,11]. The admission to an intensive care unit with a closely supervised inpatient setting for an immediate BP reduction with titratable intravenous antihypertensive drugs is mandatory to arrest progressive organ damage. Therapeutic protocols and target BP in the single patient should be based on the clinical presentation and a prompt diagnostic workup [11,5]. Rapid triage is necessary to differentiate those who can safely be sent home and those need hospitalization for more serious problems [12]. On the other hand, overzealous or uncontrolled reduction in blood pressure may result in coma, stroke, myocardial infarction, acute renal failure, or death [13].

Epidemiology: Hypertensive crises is a common issue in the emergency department [14]**.** Worldwide, hypertension may affect as many as 1 billion people and be responsible for approximately 7.1 million deaths per year. It is estimated that approximately 1% of patients with hypertension will, at some point, develop a hypertensive crisis [15].

Definition and Classification: An acute elevations in blood pressure that are associated with end-organ damage are called hypertensive crises [1]. Hypertensive crises with blood pressure > 180/120 mmHg are common issues in the emergency department [14]. If sudden elevation in systolic (SBP) and/or diastolic blood pressure (DBP) that are associated with acute end-organ damage (cardiovascular, cerebrovascular, or renal) is defined as a hypertensive crisis or emergency. In contrast, acute elevation in SBP and/or DBP not associated with evidence of end-organ damage is defined as a hypertensive urgency [8]. The severity of hypertensive crises is determined by the presence of target organ damage rather than the level of blood pressure [16].

Presentations and Differentiation: Differentiation between hypertensive emergencies and urgencies is related more to the presence of acute organ involvement than to BP elevation, per se. Hypertensive urgencies can be treated outside the intensive care unit with oral antihypertensive medications for 24-48 hours [11]. Hypertensive urgencies is including: severe uncomplicated essential hypertension, severe uncomplicated secondary hypertension, postoperative hypertension, hypertension associated with severe epistaxis, drug-induced hypertension, rebound hypertension, hypertensive encephalopathy, cerebral infarction, cerebral hemorrhage, advanced retinopathy, acute coronary syndromes, acute heart failure, aortic dissection, acute renal failure, and an eclampsia but hypertensive emergency is including: hypertensive encephalopathy, hypertension associated with acute cerebrovascular disease, hypertension associated with pulmonary edema, hypertension associated with acute coronary syndromes, hypertension associated with dissecting aortic aneurysm, pheochromocytoma, hypertension associated with acute renal failure, an eclampsia, micro-angiopathic anemia and severe hypertensive crises related to anxiety, panic attacks, or pain [11].

Target for Blood Pressure: Current guidelines suggest pharmacological intervention if systolic BP exceeds 180 mm Hg [17]. There is strong evidence to support treating hypertensive persons aged 60 years or older to a BP goal of less than 150/90 mmHg and hypertensive persons 30 through 59 years of age to a diastolic goal of less than 90 mmHg; however, there is insufficient

evidence in hypertensive [1]. Blood pressure treatment in the acute stage of stroke: The ESO recommends a reduction to < 140 mmHg systolic within one hour, according to recommendations of the ESH and the EUSI but not more than 20%. However, the absolute level of blood pressure may not be as important as the rate of increase [18,19].

Protocol: The best clinical setting in which to achieve this blood pressure control is in the intensive care unit, with the use of titratable intravenous hypotensive agents [1,3,15]. Complete evaluations in patients who present with a hypertensive crisis to effectively reverse, intervene, and correct the underlying trigger, as well as improve long-term outcomes after the episode [5]. The blood pressure must be quickly lowered to a target range of at least < 180 mmHg. In the case of intracerebral hemorrhage, blood pressure reduction appears to be beneficial [20]. Ensuring adequate follow-up after treatment of very elevated blood pressure is a critical step that is often mishandled [3].

Nitroglycerin

Pharmacology: Nitroglycerin is a potent venodilator and only at high doses affects arterial tone [15]. Once nitroglycerin is converted to nitric oxide, it activates guanylate cyclase and stimulates the production of cyclic GMP (cGMP). This produces smooth muscle relaxation, mainly in the venous system, and reduces myocardial preload [21]. Nitroglycerin reduces BP by reducing preload and cardiac output; this increases the severity of the hyperadrenergic state characteristic of acute postoperative hypertension [22]. Since a hypertensive crisis is usually accompanied by left ventricular failure, pulmonary edema, angina pectoris, or infarction, nitroglycerin has been definitively shown positively to influence these conditions, and preference should be given to nitroglycerin in the treatment of hypertensive crises [23]. Nitroglycerin may be advantageous in patients with significant coronary artery disease and the preferred in acute coronary syndrome [24,25] with or without hypertension, acute heart failure [25], cocaine toxicity/ pheochromocytoma [26], perioperative hypertension [27], volume overload, and pulmonary edema [28]. Endothelium-independent dilator response can be tested by low-dose sublingual n nitroglycerin [29]. Sodium nitroprusside and nitroglycerin are usually used to assess endothelium-independent vasodilation [30].

Administration: Intravenous nitroglycerin, however, is usually a better method to administer nitroglycerin because the dose can be rapidly adjusted upward or downward depending on the clinical and hemodynamic response [31].

For the treatment of hypertension, the initial dose of nitroglycerin is 5 µg/min by i.v infusion. The dose may be increased in increments of 5 µg/min every 3-5 minutes to a maximum rate of 20 µg/min. If the BP response is inadequate at 20 µg/min, the dose may be increased by 10 µg/min every 3-5 minutes, up to a maximum rate of 200 µg/min. When a partial response is achieved, dosing increments are made more carefully. Drug onset is within 2-5 minutes, and the duration of action is 5-10 minutes, with a half-life of 1-3 minutes [21]. Nitroglycerin should be infused at an initial rate of 5 mcg/min (or even 2.5 mcg/min in patients with borderline hypotension with eventual rates of 1000 mcg/ min in some patients. There are risks of tolerance induction and subsequent rebound. Given that even 10 mcg/min nitroglycerin induces some degree of tolerance within 24 hours, [32] a maximal infusion rate of 16 mcg/min is recommended in most cases [33].

Presentations and nitroglycerin: Intravenous nitroglycerin is often chosen for patients with myocardial ischemia since it dilates coronary vessels and decreases myocardial wall tension and oxygen consumption [34]. Myocardial ischemia or myocardial infarction may be associated with hypertension, which usually results from a preexisting high BP exacerbated by pain and agitation. In this setting, intravenous nitrates are useful in reducing systemic vascular resistance, as well as left ventricular preload, and in improving coronary perfusion [35]. Administration of low-dose nitroglycerin (≈ 60 µg/min) as an adjunct to other i.v antihypertensive therapy may be beneficial for patients with hypertensive emergencies associated with acute coronary syndromes or acute pulmonary edema [15,21]. Aortic dissection is the most dramatic and rapidly fatal complication associated with hypertensive emergencies. Acute BP reduction is essential to reduce shear forces on the damaged aorta. Treatment aims is to decrease systolic BP as rapidly as possible down to 100-110 mmHg and simultaneously control tachycardia resulting from the sympathetic activation [35].

The acute cardiogenic pulmonary edema necessitates rapid and specific interventions, including ventilation and reduction of left ventricular preload and afterload. The first-line treatment of this condition is based on intravenous administration of nitrates and loop diuretics. If this approach is not effective, vasodilators, such as urapidil, nicardipine, or sodium nitroprusside, are also indicated [11]. In acute pulmonary edema from various causes, including AMI, nitroglycerin can be strikingly effective, with some risk of precipitous falls in BP and of tachycardia or bradycardia. Nitroglycerin can relieve dyspnea within 15 to 20 minutes, with a fall of LV filling pressure and a rise in cardiac output [36]. Administration of low-dose nitroglycerin (≈ 60 µg/min) as an adjunct to other i.v. antihypertensive therapy may be beneficial for patients with hypertensive emergencies associated with acute coronary syndromes or acute pulmonary edema [20].

It is essential to control arterial blood pressure (BP) in both hemorrhagic and ischemic stroke patients to decrease morbidity following an acute event and decrease the long-term risk of stroke recurrence [37]. BP elevations commonly accompany ischemic stroke in previously hypertensive and in normotensive subjects. Stroke-related hypertension has been hypothesized to result from lesions in cerebral areas causing an impaired neurogenic control of the cardiovascular system [11]. Nitroglycerin is one of the commonly used drugs for the management of postoperative surgical hypertension [38]. But nitroprusside is often considered a drug of choice in hypertensive emergencies these settings [39]. Local application of vasodilators, such as nitroglycerine, may be useful to prevent or revert spasms of renal arteries, and the energy delivered is lower than that used for cardiac electrophysiological procedures [40].

Adverse effect: The main side effects are headache and hypotension, both of which respond to decrease or cessation of the infusion [41]. Severe hypotension and reflex tachycardia have been reported in volume-depleted patients within minutes of initiating nitroglycerin infusion [22]**.** Headache is the most common adverse

effect, and methemoglobinemia is a rare complication of prolonged nitroglycerin therapy [21]. Methemoglobin is formed during the administration of all organic nitrates, but its mean concentration in patients receiving nitroglycerin for 48 hours or longer averaged only 1.5%, with no clinical symptoms [42]. Rebound is the abrupt increase in anginal frequency during accidental nitrate withdrawal (e.g., displacement of an intravenous infusion) or during nitrate-free periods [43]. The underlying mechanisms of a rebound are unopposed vasoconstriction (angiotensin II, catecholamines, and endothelin) during nitrate withdrawal with attenuation of net vasodilator effect of NO [44]. Tolerance to the hemodynamic effects of nitroglycerin may limit its clinical usefulness [21].

Contraindication: Nitrates should not be administered to patients with a systolic BP of less than 90 mm Hg, patients with right ventricular infarction, or those who received sildenafil (or it's equivalent) in the last 24 hours [45].

Comparison nitroglycerin with sodium nitroprusside and nifedipine: Although sodium nitroprusside is a rapid-acting and potent antihypertensive agents, it may be associated with significant toxicity [1]. Sodium nitroprusside is an extremely toxic drug and its use in the treatment of hypertensive emergencies should be avoided [15]. Furthermore, the short-acting calcium channel blocker nifedipine is associated with significant morbidity and should be avoided [9].

Propylene Glycol

Structure and properties: Propylene glycol, also called propane-1,2-diol, is a synthetic organic compound with the chemical formula $C_3H_8O_2$ [46]. The excipient of nitroglycerin solutions is propylene glycol. High concentration solutions of nitroglycerin contain propylene glycol. Intravenous administration of an excipient has been seen in some people, particularly with large dosages [47].

Propylene glycol toxicity: Propylene glycol toxicity may include: hypotension, bradycardia, QRS and T-wave abnormalities on the ECG, arrhythmia, cardiac arrest, serum hyper osmolality, lactic acidosis, and hemolysis [48]**.** Serious toxicity generally occurs at plasma concentrations over 4 g/L, which requires extremely high intake over a relatively short period, or when used as a vehicle for drugs or vitamins given intravenously or orally [49].

Symptomatology is dose-dependent, ranging from drowsiness to stupor, deep unconsciousness, and coma. Other signs include hyper osmolality of serum, lactic acidosis, and hypoglycemia [50,51]. Rapid intravenous injection of preparations of drugs containing propylene glycol as a solvent (in significant amounts) may cause unconsciousness, arrhythmias and even cardiac arrest [50,51]. PG is not acutely toxic to aquatic organisms except at very high concentrations. Repeated exposures of rats to propylene glycol (PG) did not result in side effects at levels up to 10% in water (estimated at about 10 g/kg bw/day) or 5% in feed (dosage reported as 2.5 g/kg bw/day) for periods up to 2 years. However, in cats, two studies of at least 90 days' duration show that a species-specific effect of increased Heinz bodies was observed (NOAEL=80 mg/kg bw/day; LOAEL=443 mg/kg bw/day), with other hematological effects (decrease in number of erythrocytes and erythrocyte survival) reported at higher doses (6-12% in diet, or 3.7-10.1 g/cat/day) [51].

Method of study and patients

My study was an observational retrospective for 1043 cases. The study was conducted in both Ras El-Bar Central Hospital and Fraskour Central Hospital; in the Intensive Care Units. The author reported the 1043 cases of hypertensive crises over nearly 48-months, started from July 10, 2015, and, ended on Jul 10, 2019. **(Table 1)** Different doses within the normal range of i.v nitroglycerin was given. Both adverse effects (safety) and anti-hypertensive responses (efficacy) were recorded. The cases were selected in the Emergency Department then admitted to the Critical Care Unit.

The cases were divided into two groups:

- **Group I:** it included 652 patients (62.51%) of hypertensive crises. These cases were treated with nitroglycerine i.v infusion starting with 3.75 µg/min and gradually increased for each sub-group of patients until the dose of 67.5 µg/min
- **Group II:** it included 391 patients (37.49%) of hypertensive crises: These cases were treated with nitroglycerine i.v infusion starting with 75 µg/min and gradually increased for each sub-group of patients until the dose of 202.5 µg/min. Both response and side effects were observed for the first three hours' post-nitroglycerine i.v infusion **(Table 2)**.

Issue	Definition
Title	Nitroglycerin in suboptimal versus the remaining doses in hypertensive crises regards propylene glycol; efficacy and safety (Nitroglycerin on trace study)
Estimated Enrollment	1043 participants
Study Type	Observational
Observational Model	Case-only
Time	Retrospective
Study Start Date	10-Jul-15
Estimated Study Completion Date	10-Jul-19
Analytic method	Comparative using both Chi-Squared test and P-value

Table 1: showing remarks of the study method and data.

Eligibility criteria

Inclusion criteria: All cases with hypertensive emergency with evidence of end-organ damage - Patients from age 18 and up to 75years old.

Exclusion criteria

- Right ventricular infarction with inferior myocardial Infarction.
- Parkinsonism.
- Any other cases of hypertensive emergency but with evidence of orthostasis.
- Hypersensitivity to nitroglycerin.

The cases were selected depending on two criteria

- An elevation in SBP and/or DBP should be more than180/120.
- An associated presentation of the hypertensive patient should have evidence of the end-organ damage e.g. an accelerated or malignant hypertension, hypertensive encephalopathy, acute left ventricular failure, Pheochromocytoma crisis, drug-induced hypertension, possibly ischemic stroke. The acute aortic dissection, eclampsia and ischemic stroke may be missed in my study.

Each patient underwent to rapid complete history, clinical examination, and some workup

- **Immediate investigation:** e.g. ECG, chest x-ray, and brain CT scan (if a stroke or hypertensive encephalopathy).
- **Later investigation:** echocardiography, serum creatinine, blood urea, plasma sodium, serum potassium, and some special investigation for Pheochromocytoma.

Group	Nitroglycerin Concentration: (mg)/ Solvent(ml)	Maintenance dose by μg/min	Maintenance dose by drops/ min	No. of Patient for each Dose	Side effects
Group I	1.25mg/50 ml Solvent	3.75	3	68	-
	2.5mg/50 ml Solvent	7.5	3	68	-
	5mg/50 ml Solvent	15	3	67	Slight headache
	7.5mg/50 ml Solvent	22.5	3	67	Muscle twitches
	10mg/50 ml Solvent	30	3	66	Headache
	12.5mg/50 ml Solvent	37.5	3	66	Dizziness
	15mg/50 ml Solvent	45	3	64	Tachycardia
	17.5mg/50 ml Solvent	52.2	3	64	Flushing
	20mg/50 ml Solvent	60	3	62	Vomiting
	22.5mg/50 ml Solvent	67.5	3	60	Headache- Dizziness
Group II	25mg/50 ml Solvent	75	3	31	Headache- Dizziness
	27.5mg/50 ml Solvent	82.5	3	30	Headache- Dizziness
	30mg/50 ml Solvent	90	3	29	Headache- Dizziness
	32.5mg/50 ml Solvent	97.5	3	28	Headache- Dizziness
	35mg/50 ml Solvent	105	3	26	Mixed 3 Side Effects
	37.5mg/50 ml Solvent	112.5	3	25	Mixed 3 Side Effects
	40mg/50 ml Solvent	120	3	24	Mixed 4 Side Effects
	42.5mg/50 ml Solvent	127.5	3	23	Mixed 4 Side Effects
	45mg/50 ml Solvent	135	3	22	Mixed 4 Side Effects
	47.5mg/50 ml Solvent	142.5	3	21	Mixed 5 Side Effects
	50mg/50 ml Solvent	150	3	20	Mixed 5 Side Effects
	52.5mg/50 ml Solvent	157.5	3	19	Mixed ≥ 5 Side Effects
	55mg/50 ml Solvent	165	3	18	Mixed ≥ 5 Side Effects
	57.5mg/50 ml Solvent	172.5	3	17	Mixed ≥ 5 Side Effects
	60mg/50 ml Solvent	180	3	16	Mixed ≥ 5 Side Effects
	62.5mg/50 ml Solvent	187.5	3	15	Mixed ≥ 5 Side Effects

	65mg/50 ml Solvent	195	3	14	Mixed ≥ 5 Side Effects
	67.5mg/50 ml Solvent	202.5	3	13	Mixed ≥ 5 Side Effects

Table 2: Showing the maintenance doses for nitroglycerine by ug/min in both groups.

Results

Variable	Group I	Group II
No.	No: 652 Percent (62.51%)	No: 391 Percent (37.49%)
Age	Range: 24-90 median: 66 mean:63.83	Range: 24-88 median: 65 mean:63.23
Sex		
M	287 (44 %)	187 (48 %)
F	365 (56 %)	204 (52 %)
1st Hour BP Reduction No.	576 (88.34%)	349 (89.25%)
2nd Hour BP Reduction No.	65 (9.969%)	34 (8.69%)
3rd Hour BP Reduction No.	11 (1.68%)	8 (2.04%)
Side Effects:		
Headache	22 (3.37%)	34 (10.99%)
Dizziness	11 (1.68%)	46 (11.76%)
Hypotension	14 (2.14%)	43 (10.99%)
Flushing	1 (0.15%)	5 (1.27%)
Vomiting	- (0 %)	7 (1.79%)
Rebound	23 (3.5 %)	15 (3.8 %)
Muscle twitches	3 (0.46%)	11 (2.81 %)
Reflex tachycardia	4 (0.61%)	17 (4.3 %)
Mixed Side Effects	8 (1.2%)	38 (9.7 %)
Hypertension Associate		
Angina	176 (26.9%)	114 (29.15%)
MI	14 (2.1%)	11 (2.8%)
CHF	59 (9.04%)	63 (16.1%)
APO	14 (2.1%)	29 (7.4%)
Stroke	21 (3.2%)	11 (2.8%)
Dizziness	93 (14.26%)	35 (8.95%)
Headache	147 (22.5%)	65 (16.6%)
Phyochromocytoma	19 (2.9%)	9 (2.3%)
Renal Hypertension	7 (1.07%)	4 (1.02%)
Dypsnea	47 (7.2 %)	21 (5.37%)
Agitation	15 (2.3%)	8 (2.046%)
Restlessness	40 (6.1%)	21 (5.37%)
BP after infusion : 90/70	14 (2.14%)	43 (10.9%)

100/70	4 (0.6%)	9 (0.02%)
110/70	155 (23.77%)	79 (20.2%)
120/80	100 (15.33%)	20 (5.1%)
120/70	111 (17.02%)	62 (15.8%)
130/70	71 (10.88%)	34 (8.6%)
130/80	61 (9.35%)	47 (12.02%)
140/60	1 (0.15 %)	12 (3.06%)
140/70	9 (1.38%)	22 (5.6%)
140/80	126 (19.3%)	63 (16.1%)
SBP	Range: 180-270 median: 210 mean: 215.67 SD19.9	Range: 190-270 median: 210 mean: 212.48 SD 20.8
DBP	Range: 120-160 median:140 mean: 139.6 SD 9.766	Range: 130-170 median:140 mean: 143.17 SD 12.36
PP	Range: 130-150 median:70 mean: 76.25 SD 20.75	Range: 20 -140 median:70 mean: 69.41 SD 23.03
MBP	Range: 140-190 median: 163.3 mean: 164.99 SD 10.06	Range: 150-203 median: 163 mean: 166.21 SD 11.36
Pulse	Range: 45-150 median:76 mean: 79.36 SD 15.41	Range: 40-145 median:86 mean: 81.42 SD 16.51
Note: APO: Acute pulmonary edema, **BP:** blood pressure, **CHF:** Congestive heart failure, **DBP:** Diastolic blood pressure, **HTN:** Hypertension, **MBP:** Mean blood pressure, **MI:** Myocardial infarction, **PP:** Pulse pressure, **SBP:** Systolic blood pressure.		

Table 3: Showing the percent's and numbers general collective data in both groups of the study.

Age: The range of age in group I was 24-90 and in group II was 24-88 **(Figure 1)** but with insignificant P-value (0.472) **(Table 1)**.

Group	Age				T-test	
	Range	Mean	±	SD	t	P-value
Group I	24 -90	63.833	±	13.074	0.719	0.472
Group II	24 -88	63.230	±	13.136		

Table 1: Age in group I vs. group II.

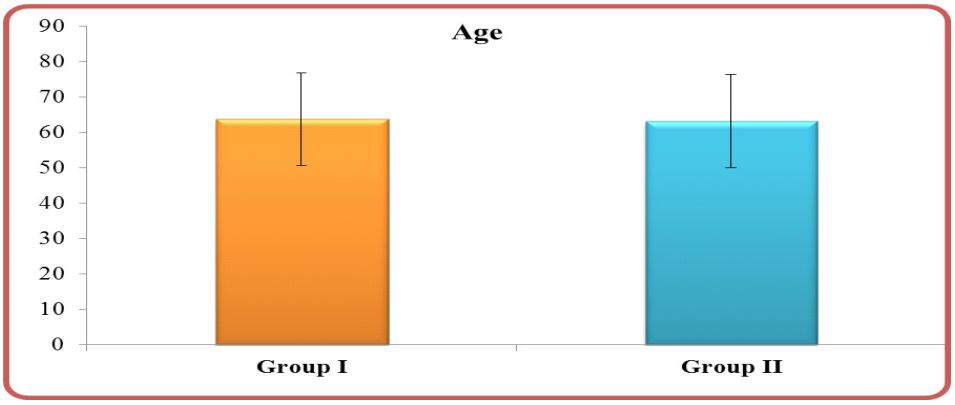


Figure: Age in group I vs. group II.

Sex: Predominant female sex was cleared **(Table 2)**. The percent of sex in group I for female vs. male was 55.8% vs.44.2% (No. 364 vs. 288) and in group II was 52.4% vs.47.26% (No. 205 vs. 186) **(Figure 2)** but with insignificant P-value (0.286) **(Table 2)**.

SEX		Groups					
		Group I		Group II		Total	
		N	%	N	%	N	%
Female		364	55.8%	205	52.4%	569	54.6%
Male		288	44.2%	186	47.6%	474	45.4%
Total		652	100.0%	391	100.0%	1043	100.0%
Chi-square	X^2	1.138					
	P-value	0.286					

Table 2: Sex in group I vs. group II.

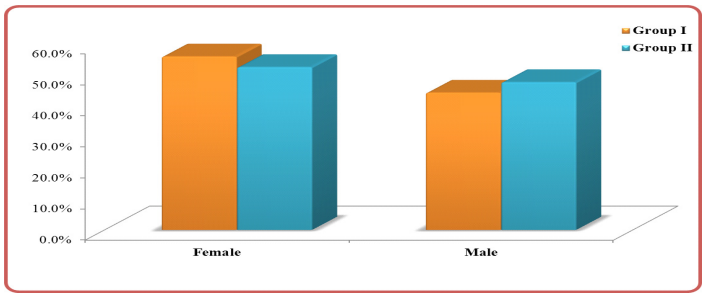


Figure 2: Sex in group I vs. group II.

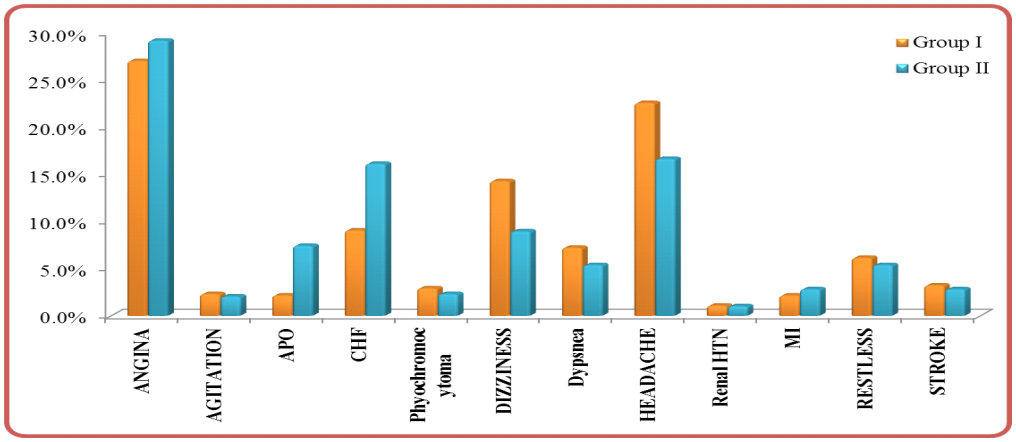
Hypertension-associated conditions: P-value (<0.001) was significant in comparing group I and group II **(Table 3)**. With predominant hypertension-associated conditions in group II vs. group I **(Table 3)** and **(Figure 3)**.

Hypertension-associated conditions		Groups					
		Group I		Group II		Total	
		N	%	N	%	N	%
Angina		176	27.00%	114	29.20%	290	27.80%
Agitation		15	2.30%	8	2.00%	23	2.20%
APO		14	2.10%	29	7.40%	43	4.10%
CHF		59	9.00%	63	16.10%	122	11.70%
Phyochromocytoma		19	2.90%	9	2.30%	28	2.70%
Dizziness		93	14.30%	35	9.00%	128	12.30%
Dypsnea		47	7.20%	21	5.40%	68	6.50%
Headeache		147	22.50%	65	16.60%	212	20.30%
Renal HTN		7	1.10%	4	1.00%	11	1.10%
MI		14	2.10%	11	2.80%	25	2.40%
Restlessness		40	6.10%	21	5.40%	61	5.80%
Stroke		21	3.20%	11	2.80%	32	3.10%
Total		652	100.00%	391	100.00%	1043	100.00%
Chi-square	X^2	39.045					

	P-value	<0.001*					

Note: APO: Acute pulmonary edema, **CHF:** Congestive heart failure, **HTN:** Hypertension, **MI:** Myocardial infarction

Table 3: Hypertension-associated conditions in group I vs. group II.



APO: Acute pulmonary edema, **CHF:** Congestive heart failure, **HTN:** Hypertension, **MI:** Myocardial infarction

Figure 3: Hypertension-associated conditions in group I vs. group II.

Side effects: P-value (<0.001) was significant in comparing group I and group II **(Table 4)**. With predominant side effects in group II vs. group I **(Table 4** and **Figure 4)**. This is indicating that the increase in nitroglycerine i.v. infusion dose is directly related to increasing to the side effects.

Side Effects	Groups		Total			
	Group I	Group II				
	N	%	N	%	N	%
No	597	91.6%	181	46.3%	778	74.6%
Headache	22	3.4%	43	11.0%	65	6.2%
Dizziness	11	1.7%	46	11.8%	57	5.5%
Flushing	1	.2%	5	1.3%	6	.6%
Hypotension	14	2.1%	43	11.0%	57	5.5%
Mixed side effect	0	0.0%	38	9.7%	38	3.6%
Muscle twitches	3	0.5%	11	2.8%	14	1.3%
Reflex tachycardia	4	0.6%	17	4.3%	21	2.0%
Vomiting	0	0.0%	7	1.8%	7	0.7%
Total	652	100.0%	391	100.0%	1043	100.0%
Chi-square	X2	292.755				
	P-value	<0.001*				

Table 4: Side effects in group I vs. group II.

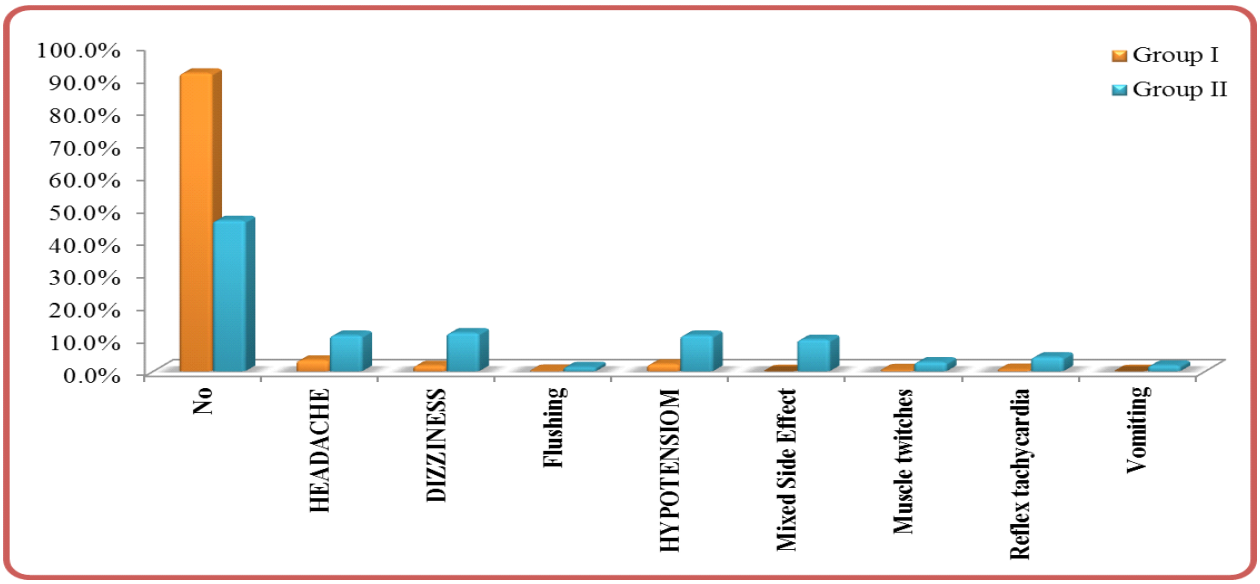
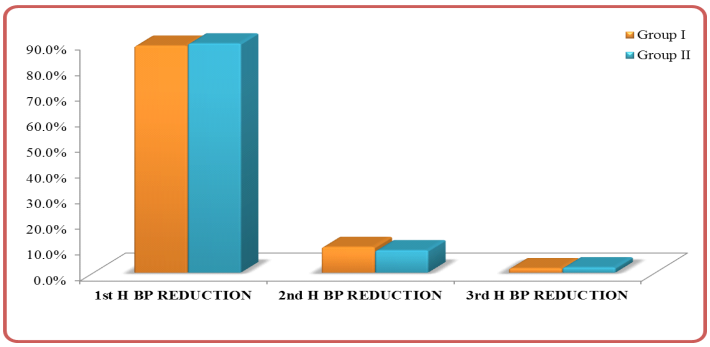


Figure 4: Side effects in group I vs. group II.

Response (Efficacy): P-value (0.735) was insignificant in comparing group I and group II **(Table 5)** in the first three hours' post-nitroglycerine i.v. infusion **(Table 5)** and **(Figure 5)**. This is indicating that there is no significant difference in response for both group after nitroglycerine i.v. infusion.

Response		Groups					
		Group I		Group II		Total	
		N	%	N	%	N	%
1st H BP REDUCTION		576	88.30%	349	89.30%	925	88.70%
2nd H BP REDUCTION		65	10.00%	34	8.70%	99	9.50%
3rd H BP REDUCTION		11	1.70%	8	2.00%	19	1.80%
Total		652	100.00%	391	100.00%	1043	100.00%
Chi-square	X^2	0.616					
	P-value	0.735					
Note: BP: Blood pressure							

Table 5: Side effects in group I vs. group II.



BP: Blood pressure

Figure 5: Response in group I vs. group II.

Conclusion

The author concluded that nitroglycerine is effective and safe in the treatment of hypertensive emergencies with the lowest vs. the remaining other nitroglycerin infusion doses. Regards the drug efficacy, no significant difference between the lowest and remaining other nitroglycerin infusion doses in treating hypertensive crises. Using the lowest nitroglycerin infusion dose in treating hypertensive crises safer, economically saver, and less anxious regards the serious adverse effects. Propylene glycol may be the suggested inducing agent for the side effects and its severity with increasing nitroglycerin infusion doses.

Reference

1. Varon J and Marik PE (2003) Clinical review: The management of hypertensive crises 7: 374-384. Crit Care 7 374-84.
2. Kaplan NM (2005) Kaplan's Hypertensive Crises, Kaplan's Clinical Hypertension, 9th ed (2005). Can J Cardiol 23: 605.
3. Hebert CJ and Vidt DG (2008) Hypertensive crises. Prim Care 35: 475-487.
4. McRae RP Jr and Liebson PR (1986) Hypertensive crisis. Med Clin North Am 70: 749-767.
5. Rodriguez MA, Kumar SK, De Caro M (2010) Hypertensive crisis. Cardiol Rev 18: 102-107.
6. Gifford RW Jr (1991) Management of hypertensive crises. JAMA 14: 829-835.
7. Hopkins C and Brenner BE (2018) Hypertensive Emergencies.
8. Burris JF (1985) Hypertensive emergencies. Am Fam Physician 32: 97-109.
9. Varon J and Marik PE (2000) The diagnosis and management of hypertensive crises. Chest 118: 214-27.
10. Haas AR and Marik PE (2006) critical care issues for the nephrologist: Current Diagnosis and Management of Hypertensive Emergency. Semin Dial 19: 502-512.
11. Phan DG, Dreyfuss-Tubiana C, Blacher J (2015) Hypertensive Emergencies and urgencies, Presse Med 44: 737-744.
12. Phillips RA, Greenblatt J, Krakoff LR (2002) Hypertensive emergencies: diagnosis and management. Prog Cardiovasc Dis. 45: 33-48.
13. Milan A, Puglisi E, Ferrari G, Fabbri A, Rabbia F et al. (2010) Hypertensive emergency and urgency: clinical update. [Article in Italian] G Ital Cardiol (Rome) 11: 835-848.
14. Varon J (2018) Treatment of acute severe hypertension: current and newer agents. Drugs 68: 283-297.
15. Slama M and Modeliar SS (2006) Hypertension in the intensive care unit. Curr Opin Cardiol 21: 279-287.
16. Ahmed N, Wahlgren N, Brainin M, Castillo J, et al. (2009) Relationship of blood pressure, antihypertensive therapy, and outcome in ischemic stroke treated with intravenous thrombolysis: retrospective analysis from Safe Implementation of Thrombolysis in Stroke-International Stroke Thrombolysis Register (SITS-ISTR). Stroke 40: 2442-2449.
17. James PA, Oparil S, Carter BL, Cushman W C etal. (2014) Evidence-Based Guideline for the Management of High Blood Pressure in Adults,Report Fromthe PanelMembers Appointed to the Eighth Joint National Committee (JNC 8), American Medical Association JAMA 1-14 .
18. Prisant LM, Carr AA, Hawkins DW (1993) Treating hypertensive emergencies. Controlled reduction of blood pressure and protection of target organs. Postgrad Med Feb 93: 92-110.
19. Koziolek MJ and Lüders S (2015) Blood pressure treatment in the acute stage of stroke. Dtsch Med Wochenschr 140: 1587-1592.
20. Rhoney D and Peacock WF (2009) Intravenous Therapy for Hypertensive Emergencies, Part 1. Am J Health Syst Pharm 66: 1343-1352.
21. Estafanous FG (1989) Hypertension in the surgical patient: management of blood pressure and anesthesia. Cleve Clin J Med 56: 385-393.
22. Bussmann WD, Kenedi P, von Mengden HJ, Nast HP et al. (1992) Comparison of nitroglycerin with nifedipine in patients with hypertensive crisis or severe hypertension. Clin Investig 70: 1085-1088.
23. Garcia JY and Jr. Vidt DG (1987) Current management of hypertensive emergencies. Drugs 34: 263-278.
24. Hollander JE (2018) Cocaine intoxication and hypertension. Ann Emerg Med 51: S18-S20.
25. Barton JR (2008) Hypertension in pregnancy. Ann Emerg Med 51: S16-S17.
26. Diercks DB and Ohman EM (2008) Hypertension with acute coronary syndrome and heart failure. Ann Emerg Med 51: S34-S36.
27. Salgado DR, Silva E, Vincent JL (2013) Control of hypertension in the critically ill: a pathophysiological approach. Ann Intensive Care 3: 17.
28. Ghiadoni L, Ghiadoni L, Huang Y, Magagna A, Buralli S, et al. (2001) effect of acute blood pressure reduction on endothelial function in the brachial artery of patients with essential hypertension J Hypertens 19: 547-551.

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29. Goodhart DM and Anderson TJ (1998) Role of nitric oxide in coronary arterial vasomotion and the influence of coronary atherosclerosis and its risks. Am J Cardiol 82: 1034-1039.

30. Cotter G, Einat M, Edo Ki, Zwi F, Rami M et al. (1998) Randomized trial of high-dose isosorbide dinitrate plus low-dose furosemide versus high-dose furosemide plus low-dose isosorbide dinitrate in severe pulmonary edema. Lancet 351: 389-393.

31. Sage PR, Lande IS, Stafford I, Catherine L. Bennett, Phillipove G et al. (2000) Nitroglycerin tolerance in human vessels: evidence for impaired nitroglycerin bioconversion. Circulation 102: 2810-2815.

32. Horowitz JD (1992) Role of nitrates in unstable angina pectoris. Am J Cardiol 70: 64B-71B.

33. Mansoor GA and Frishman WH (2002) Comprehensive management of hypertensive emergencies and urgencies. Heart Dis 4: 358-371.

34. Mancia G and Grassi G (2008) Manual of Hypertension of The European Society of Hypertension. Pp: 251.

35. Bussmann WD and Schupp D (1978) Effect of sublingual nitroglycerin in emergency treatment of classic pulmonary edema. Minerva Cardioangiol Sep 26: 623-632.

36. Hocker S, Morales-Vidal S, Schneck MJ (2010) Management of arterial blood pressure in acute ischemic and hemorrhagic stroke. Neurol Clin 28: 863-886.

37. Aronow WS (2017) Management of hypertension in patients undergoing surgery. Ann Transl Med 5: 227.

38. Domenighetti G and Perret C (1982) Variable hemodynamic response to sodium nitroprusside in hypertensive crisis. Intensive Care Med 8: 187-891.

39. Thomas G1, Shishehbor MH, Bravo EL, Nally JV (2012) Renal denervation to treat resistant hypertension: guarded optimism. Cleve Clin J Med 79: 501-510.

40. Opie LH and Gersh BJ (2012) Drugs for the heart, Heart Failur, Nitrate, 8th ed. 6: 187. Elsevier Health Sciences.

41. Kaplan KJ, Taber M, Teagarden JR, Parker,et M, Davison R et al. (1985) Association of methemoglobinemia and intravenous nitroglycerin administration. Am J Cardiol 55: 181-183.

42. Figueras J, Lldon R, Cortadellas J (1991) Rebound myocardial ischaemia following abrupt interruption of intravenous nitroglycerin infusion in patients with unstable angina at rest. Eur Heart J 12: 405-411.

43. Munzel T, Kurz S, Heitzer T, Harrison D (1996) New insights into mechanisms underlying nitrate tolerance. Am.J Cardiol 77: 24-30.

44. Opie LH and Gersh BJ (2012) Drugs for the heart, Which Therapy for Which Condition? Nitrates in AMI, 8th ed, 12: 486.

45. $C_3H_8O_2$.

46. Opie LH and Horowitz JD (2012) Nitrate Preparations: Doses, Preparations, and Duration of Effects 8th ed Drugs for the heart, Nitrates and Newer Antianginals 2: 44.

47. Janusz S (1991) Propylene Glycol.

48. Flanagan RJ, Braithwaite RA, Brown SS, Widdop B, de Wolff FA (1995) The International Programme on Chemical Safety: Basic Analytical Toxicology, WHO.

49. IPCS (2009) Poisons Information Monograph 443. Propylene glycol.

50. Propylene glycol (2010) National Library of Medicine HSDB Database. Hazardous Substances Databank Number: 174.

51. Organization for Economic Cooperation and Development (2001) Screening Information Data Set for 1,2-Dihydroxypropane, CAS No 57: 55-56.

Citation: Elsayed YMH (2019) Nitroglycerin in Suboptimal Versus the Remaining Doses in Hypertensive Crises Regards Propylene Glycol; Efficacy and Safety (Nitroglycerin On Trace Study); Retrospective Observational Study. Ann Med & Surg Case Rep: AMSCR-1000021