

Isosorbide Dinitrate in Treatment of Episodic Resistance and Urgency Hypertension

Hassan Khuder Rajab

Department of Pharmacology, College of Medicine, Tikrit University, Iraq

Corresponding Author: Hassan Khuder Rajab

Background: Hypertension is a major health problem throughout the world for its high prevalence and its association with increased risk of cardiovascular disease. Isosorbide dinitrate is used in such cases of hypertension as rapid acting vasodilator with a duration of action of ≥ 1 hour as a result of its enhancement effect on cGMP. However, the total sublingual dose should be adjusted to avoid excessive effects. This study was designed to determine its efficacy in episodic resistance & urgency hypertension.

Patients and methods: Sixty five outpatients were included in this study, they were divided into two groups, 1st group, consisted of 42 outpatients newly diagnose hypertensive, 2nd group consisted of 23 old hypertensive patients with episodic attack of hypertension that resist drugs. Patients were treated with isosorbide dinitrate tablets 5 mg sublingually, blood pressure was measured after 3, 7, 10, 60 and 120 minutes. Blood samples were collected from all patients to investigate lipid profile and a questionnaire was prepared to record the characteristics of patients.

Results: -61.9% and 52.2% of the patients in the first and second group respectively complained hyperlipidemia. The blood pressure reduced in all patient toward normal level, time need to reduce blood pressure start at 3 minutes up to 15 minute and only 2 patients in second group need up to 20 minutes to the onset of blood pressure reduction. The recorded side effects included mild headache in 16(38%) and 13 (56.5%), and postural hypotension in 5(11.9%) and 2 (8.7%) in the first and second groups, respectively.

Conclusion: Isosorbide dinitrate may safely used to treat urgency and resistance case of hypertension, it was able to reduce blood pressure within minutes.

Keywords: isosorbide dinitrate, emergency hypertension, episodic hypertension

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I. INTRODUCTION

Hypertension is a major health problem throughout the world for its high prevalence and its association with increased risk of cardiovascular disease⁽¹⁾. It was very prevalent and was estimated to affect more than 25% of people. In united state at age over 65 years old, more than 60% are hypertensive⁽¹⁻³⁾. Advance in the diagnosis and treatment of hypertension have play a major role in recent dramatic declines in coronary heart disease and stroke mortality. For individuals aged 40-70 years each increment of 20 mmHg in systolic blood pressure or 10 mmHg in diastolic pressure double the risk of cardiovascular diseases. Change of lifestyle and close follow-up should be implement in the treatment of hypertension, while drug therapy need if there was an evidence of target organ damage or high cardiovascular risk profile⁽⁴⁾. Refractory hypertension may result of genuinely resistance hypertension characterize by persistence elevation of blood pressure in absence of target organ damage. Episodic hypertension in which episodic symptoms accompanied transient elevation of blood pressure. Emergency hypertension referred to more sever hypertension states and defined as an acute ,life threatening states due to sudden rise in blood pressure resulting in complaints and damage to the structure of some organs, when systolic/diastolic pressure reach 220 mmHg/120 mmHg^(5,6). This study was designed to determine its efficacy in episodic resistance & urgency hypertension.

II. PATIENTS & METHODS

This study was carry-out in Kirkuk city (Feb. 2018 till Oct. 2018). Sixty five patients were included in this study, they were divided into two groups, The first group consisted of 42 newly diagnose hypertensive outpatients (19 male and 23 female), their mean systolic- diastolic blood pressure was 187 mmHg -113 mmHg .The second group consisted of 23 old hypertensive patients (15 female and 8 male), their mean systolic-diastolic pressure was 194 mmHg -127 mmHg, they were on hypotensive treatment, but presented as episode of elevated blood pressure resist reduction in spite of continuation of daily treatment. All patients were treated with isosorbide dinitrate tablets of 5 mg sublingually, blood pressure was determined after each 3, 7, 10, 60 and 120 minutes of the treatment. A questionnaire was prepared to investigate the characteristics of patients

(age, sex, familial history of hypertension, previous drug history, medical history, previous attack of episode hypertension, type of drug used to control blood pressure, smoking, alcohol drinking, job, socioeconomic state and anxious state). Blood samples were taken to estimate lipid profile. Chi square test was used to determine the significance between the groups.

III. RESULTS

The average of patients age in the first and second groups was 45.44 and 56.2 years old respectively, and male percent in the first and second groups was 45.3% and 54.7% and female was 34.7 and 65.3 respectively. Smokers percent was 58% and 56.5%, alcohol drinkers percent was 4.7% and 4.4%, the percent of patients with positive family history of hypertension was 66.6% and 78.2%, the percent of patients with good socioeconomic state was 42.8% and 34.8% of, the percent of patients with positive history of previous attack of episodic hypertension was 7.14% and 17.4%, 57.2% and 47.8% were anxious and 61.9% and 52.2% of the patients with hyperlipidemia in the first and second groups respectively (table 1).

Blood pressure was significantly reduced toward normal level in all patients in both groups but at different period of time, time need to reduce blood pressure start at 3 minutes up to 15 minute and only 2 patients in second group need up to 20 minutes to reduce their blood pressure. However, blood pressure was reduced to normal in the majority (61.9%) of the patients of the first group after 7 minutes, while it reduced to normal limit in the majority of the patients in the second (56.5%) group after 10 minutes (table 2). The characteristics of the 2 patients who need more time to reduce their blood pressure were (their age 61 y, heavy smokers, anxious and under stress with recurrent attack of episode of hypertension, not take their medication regularly and with hyperlipidemia).

Blood pressure measurements after 1 and 2 hours were still within or near normal level, (systolic 14.6±3 and diastolic 87.1±2). So patients need to intake their prescribed medications after lowering the episode attack of hypertension.

The most recorded side effects was mild headache within 3 minute of using isosorbide dinitrate in 16(38%) and 13(56.5%), postural hypotension within 5 minute after starting therapy was 5(11.9%) and 2(8.7%) in the first and second groups respectively, no other side effects were recorded (table 3).

Table 1: patients characteristics.

Characteristics	First group		Second Group		Chi square	
Sex	Male	19	45.3%	8	34.7%	
	Female	23	54.7%	15	65.3%	
Smoking	Smokers	25	59.5%	13	56.5%	P=0.8143 ^{NS}
	Non smokers	17	40.5%	10	43.5%	
Alcohol	Drinker	2	4.7%	1	4.4%	P=0.9393 ^{NS}
	Non drinker	40	95.3%	22	95.6%	
Family history of hypertension	Positive	28	66.6%	18	78.2%	P=0.3257 ^S
	Negative	14	33.4%	5	21.8%	
Socioeconomic state	Good	18	42.8%	8	34.8%	P=0.5251 ^{NS}
	Poor	24	57.2%	15	65.2%	
episode of hypertension*	Positive	3	7.14%	4	17.4%	P=0.2024 ^S
	Negative	39	92.86%	19	82.6%	
Anxious state	Anxious	24	57.2%	11	47.8%	P=0.4712 ^S
	Quiet	18	42.8%	12	52.2%	
Hyperlipidemia**	Positive	26	61.9%	14	60.8%	P=0.9346 ^{NS}
	Negative	16	38.1%	9	39.2%	

*: History of previous attack of episode of hypertension or resistance hypertension, **: positive hyperlipidemia (elevation of total cholesterol and triglyceride). NS: non significant and S: significant.

Table 2: time of onset of blood pressure reduction in both groups.

Group	3 minutes	7 minutes	10 minutes	20 minutes
First	2	26 (61.9%)	14 (33.3%)	Nil
Second	Nil	8 (34.7%)	13 (56.5%)	2

Table 3: side effects occurred in both groups

		1 st group	2 nd group	Chi square
Headache	Positive	16 (38%)	13 (56.5%)	P=0.1539 ^S
	Negative	26 (62%)	10 (43.5%)	
Postural hypotension	Positive	5 (11.9%)	2 (8.7%)	0.6898 ^{NS}
	Negative	37 (88,1%)	21 (91.3%)	

NS: non significant and S: significant .

IV. DISCUSSION

Our results showed that many factors were participated as risk factors in hypertension. A significant difference was recorded in the incidence of hypertension and episode of attack of hypertension among smoker, alcoholic and patients with hyperlipidemia, since these factors were considered as risk factors in hypertension. Furthermore, these factor delayed the response to the treatment as decrease the efficacy of hypotensive management^(2-3, 11) as recorded in our study.

Our study showed that the onset of action of sublingual isosorbide dinitrite started within 3 minutes, which was in agreement with that found by Graig and Stitzel⁽⁸⁾ who mentioned that the onset of action of isosorbide dinitrite sublingually occurred within 2-3 minutes, which attributed to high vascularization of the sublingual are which facilitated rapid absorption.

The current study also showed that the duration of action of isosorbide dinitrate extended up to 2 hour to keep blood pressure normal or near normal, this in agreement with Graig *et al.*,⁽⁸⁾ who demonstrate that the duration of action of sublingual isosorbide dinitrite could be extended from 1 up to 8 hours for oral slow release isosorbide dinitrate. On the other hand Brunton and Partker⁽⁹⁾, mentioned that the half life of isosorbide dinitrate reached 45 minutes while its metabolites both isosorbide -2- mononitrite and isosorbide -5- mononitrite extended the duration of action up to 3-6 hours. However, Graig and Stitzel⁽⁸⁾ found that the duration of action of sublingual isosorbide dinitrate was 1-2 hours.

A significant differences were obtained in the occurrence of postural hypotension between the first and second groups, which could be attributed to previous usage of different in the second group rather than the first group. While no significance in the occurrence of headache between both group (38%) and (56.5%), these results were in agreement with many other authors⁽¹⁰⁻¹³⁾.

V. CONCLUSION

Isosorbide dinitrate may safely used to treat urgency and resistance case of hypertension, it was able to reduce blood pressure within minutes.

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