The allele frequency of C825T GNB3 gene in hypotension

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Abstract. Hypotension is signed by the systolic blood pressure less than 90 mmHg and the diastolic less than 60 mmHg. The prevalence of orthostatic hypotension is high, about 10-33%. Genetic polymorphism one of factors influenced the prevalence of blood pressure abnormality. GNB3 gene located at chromosome 12p13 influenced blood pressure by their involved in the second messenger during the transduction pathway. The survey conducted to 54 volunteers (29 normotension and 25 hypotension). The peripheral blood was collected from brachial vein. GNB3 gene were analysis by PCR-RLFP. DNA extraction was processing by *GeneJET Genomic DNA Purification Kit*. The genotype frequency of CC: CT:TT was 12%:72%:16% in hypotension, while 21%:52%:17% in normotension. The allele frequency of C:T was 48:52% in hypotension and 46,5:53,5% in normotension. The frequency allele of C and T were difference between hypotension and normotension (p=0.005). Concluded that C825T of GNB3 gene associated with hypotension evidence.

1. Introduction

Hypotension is the condition signed by the systolic blood pressure less than 90 mmHg and the diastolic less than 60 mmHg. Symptoms of hypotension are related to the cerebral hypoperfusion. Insufficient of cerebral oxygenation causing headedness, dizziness, weakness, difficulty to think, headache, syncope, or feeling faint [1].The prevalence of hypotension in old population are high. Previous studies have revealed an increase in the prevalence of orthostatic hypotension with increasing of age. Orthostatic hypotension can be detected in approximately 6% of middle-aged individuals [2]. The prevalence of 65 years old population is 20% and increased until 30% at the age of 75 years. Orthostatic hypotension is often associated with such comorbidities as hypertension or diabetes. Presence of orthostatic hypotension increases mortality and coronary event risk [2][3].

Hypotension was caused by many factors included nutrition, genetic, lifestyle, obesity and other diseases. Intake natrium influenced the blood pressure by their ability to re-tent body fluid and increased blood volume. Orthostatic hypotension was triggered by autonomic disorder with brain, autonomic disorder with spinal cord involvement and autonomic neuropathies, both acute and chronic [4]. Previous study had demonstrated that 30–50% of the individual risk comes from genetic factors [5].

There are many genetic factors influenced the blood pressure [6]. The GNB3 gene encodes the G protein β3 subunit, located on chromosome 12p13. G protein is a family of proteins that are involved in second messengers during signal transduction. The function of GNB3 is to integrate signals between receptors and effectors [7]. The C825T GNB3 polymorphism occurs because thymidine replaces the cytosine found in exon 10 GNB3 [8]. Many studies concluded the association between

C825T GNB3 polymorphism and the prevalence of hypertension [9][10][11]. This study assessed the relationship between the polymorphism of the GNB3 C825T gene and the evidence of hypotension based on the role of this polymorphism on the pathophysiology of blood pressure.

2. Methods

2.1. Participants of study

This study was a survey during 2019. A total fifty-five participants were recruited, they were normotension (29 participant) and hypotension (25 participant). The inclusion criteria were (1) hypotensive people who have blood pressure <100/70 mmHg (2) normotensive people or have normal blood pressure: systolic 110 or 120 mmHg, and diastolic 70 or 80 mmHg. All participant signed the agreement of inform consent.

2.1.1. Gene and allele analysis

The gene detection was conducted at the Laboratory of Molecular Biology, Department of Biology, Universitas Negeri Semarang. Blood sample was collected from brachial vein. DNA extraction was carried out using the GeneJET Genomic DNA Purification Kit. Polymorphism detection was carried out using the PCR-RFLP method.

3. Result and Discussion

3.1. The characteristic of participant

The participants of hypotension patient were older than the normotension. Most of hypotension participants were female. The participants have similar body weight, body height and body mass index. All data were presented in Table 1.

Table 1. The characteristic of participants

No	Variable	Hipotension (n=25)	Normotension (n=29)
1	age (year)	33,84	24,58
2	Body weight (kg)	56,84	57,62
3	Body height (cm)	159,76	162,93
4	BMI	22,18	21,70
5	Sex		
	Female	88%	38%
	Male	12%	62%

3.2. Genotype and allele frequency

Frequency of genotype was analyzed by Fisher's test to know the correlation between genotype and evidence of low blood pressure.

Table 2. Genotype frequency of hypotension dan normotension

Genotype	Hypotension (N=25)	Normotension (N=29)	P *value*
CC	3 (12%)	6 (21%)	0,089
CT	18 (72%)	15 (52%)	
TT	4 (16%)	8 (27%)	

Table 3. Allele frequency of hypotension dan normotension

Alel	Hypotension (n=25)	Normotension (n=29)	*P value*
C	24 (48%)	27 (46,5%)	0,005
T	26 (52%)	31 (53,5%)	

This research aims to determine the genotype of hypotension patients based on the GNB3 gene expression. The second purpose was to analyze the correlation of the C825T polymorphism of the GNB3 gene with the evidence of hypotension. Although many data of the polymorphism of the GNB3 gene has been reported in Asian and European population, but no data had been reported in Indonesian.

We didn't find the correlation between polymorphism of the GNB3 gene and hypotension based on the genotype frequencies between hypotension and normotension groups. However, the allele frequency was a significant difference between hypotension and normotension groups. It suggested the role of allele C and T of GNB3 gene on hypotension. There was only a little data suggested the correlation between polymorphism and hypotension evidence. The variation of association between polymorphism and blood pressure suggested that regulation of blood pressure was complex. Interaction among predisposition factors involved genetic, lifestyle, nutrition and others resulted difference changes. The nervous system has an important contribution to reduce post exercise blood pressure [12]. For the post exercise hypotension patients, the greater effect is accompanied by a reduction of cardiac output due to a smaller increase in heart rate and cardiac sympathovagal balance [13]

The age of hypotension participants involved in this study was older than normotension participants. This condition might influence the result based on sample setting. The Finnish study reports a very high prevalence of orthostatic hypotension in elderly people over 75 years, which can be attributed to differences in the study population and methodology [14]. Orthostatic hypotension in the elderly is associated with decreased baroreceptor sensitivity and decreased elasticity and strength of limb muscles [15]. Pathological changes that occur in old age lead to failure or decrease in autonomic reflex function which results in orthostatic hypotension and slow reaction time [16]. The association between orthostatic hypotension and the G protein subunit (GNAS1) T131C and G protein b subunit (GNB3) C825T polymorphism was suggested in previous study. G protein subunit (GNAS1) T131C encode sympathetic nerve components that might be involved in predisposing to orthostatic hypotension. The continuous increase of the activation of protein G will reduce the capacity of further activation of the sympathetic nervous system under stimulated conditions, such as standing. The interaction between the T825 allele and the age factor of the baroreceptor reflex system can increase the prevalence of orthostatic hypotension [17]

The genetic predisposition of orthostatic hypotension has not been explored comprehensively. The small population-based studies indicate that gene polymorphisms related to protein G, GNAS1 and GNB3 which affected on cardiovascular tone and reactivity [17], Insulin Promoter Factor 1 (PDX1) at chromosome 13 which involved in beta cell function can be associated with postural changes in systolic blood pressure [18].

4. Conclusion

Genetic is one of many factors influenced blood pressure. The study understanding role of genetic factor on hypotension provide the genetic-based therapy in future. This study appeared that C825T of GNB3 gene associated with the hypotension evidence. Small participants in this study was the limitation beside the difference age of participants. Future research was needed to explore the involved of C825T of GNB3 gene in the blood pressure.

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