Correlations of Thirst With Ejection Fraction and Plasma Sodium Level in Elderly with Chronic Heart Failure

Hubungan Derajat Rasa Haus dengan Fraksi Ejeksi dan Kadar Natrium Plasma pada Gagal Jantung Kronis Usia Lanjut

Sri Lestari, I Dewa Putu Pramantara, Hasanah Mumpuni

ABSTRAK

Latar Belakang: Haus merupakan simptom yang umum dan mengganggu bagi pasien gagal jantung. Banyak pasien gagal jantung usia lanjut mengeluh rasa haus berlebihan. Perjalanan alamiah gagal jantung, terapi farmakologi dan non farmakologi dapat meningkatkan rasa haus. Cardiac output yang rendah dan peningkatan aktivasi sistem neurohormonal seperti sistem renin-angiotensin aldosteron akan merangsang pusat haus di hipotalamus. Hubungan antara rasa haus dengan fraksi ejeksi dan kadar natrium plasma pada pasien gagal jantung kronis usia lanjut belum diketahui.
Tujuan: Tujuan dari penelitian ini adalah untuk mengetahui hubungan antara derajat rasa haus dengan fraksi ejeksi dan kadar natrium plasma pada gagal jantung kronis usia lanjut.
Metode: Penelitian menggunakan metode potong lintang, dilakukan di Bagian Penyakit Dalam dan Bagian Kardiologi RSUP Dr. Sardjito Yogyakarta. Subyek penelitian adalah pasien usia lanjut penderita gagal jantung kelas fungsional III-IV sesuai dengan kriteria NYHA, usia ≥60 tahun. Pengukuran rasa haus dilakukan dengan menggunakan skor VAS. Pemeriksaan fraksi ejeksi dilakukan dengan ekokardiografi. Karakteristik subyek penelitian disajikan dalam bentuk rerata dan simpangan baku. Hubungan antara derajat rasa haus dengan fraksi ejeksi dan kadar natrim plasma dianalisis dengan menggunakan uji korelasi Pearson. Nilai p <0.05 dianggap signifikan.
Hasil: Didapatkan 30 subyek sebanyak 63.3% laki-laki dengan median usia 69.5 tahun. Diperoleh rerata rasa haus 63.67±17.5 mm dan rerata fraksi ejeksi sebesar 41.93±15.5%. Rerata hasil pemeriksaan kadar natrium adalah 139.7±4.1 mmol/l sedangkan rerata osmolalitas plasma 296.4±10.1 mOsm/kg.
Kesimpulan: Pada uji korelasi Pearson didapatkan korelasi antara rasa haus dengan fraksi ejeksi adalah korelasi negatif lemah namun tidak signifikan secara statistic (r=-0.314, p=0.091). Tidak didapatkan korelasi antara rasa haus dengan kadar natrium plasma (r=-0.04 p=0.833).

Kata kunci**:** *usia lanjut, rasa haus, gagal jantung kronis, fraksi ejeksi, natrium plasma*

ABSTRACT

Background: Thirst is a common symptom that disturbs patient with heart failure. Many elderly patients with heart failure get severe thirst. Natural history of heart failure, pharmacological and non-pharmacological therapies could increase the thirst level. Low cardiac output and activation of neuro-hormonal system e.g. renin angiotensin-aldosterone system, would stimulate the thirst center in hypothalamus. Correlations of thirst with ejection fraction and plasma sodium level in elderly with chronic heart failure have not been known yet.
Aims: The aims of this study are to investigate the correlations of thirst with ejection fraction and plasma sodium level in elderly with chronic heart failure. Cross sectional design has been conducted on elderly patients (age of ≥60 years) with heart failure of functional class of III-IV (based on NYHA criteria) in Department of Internal Medicine and Department of Cardiology, Dr. Sardjito General Hospital, Yogyakarta.

Method: Measurement of thirst was done using VAS score, while the investigation of ejection fraction was performed using echocardiography. Characteristics of subjects were presented in the average and standard deviation values. Correlations between thirst with ejection fraction and plasma sodium level were analyzed by using Pearson correlation test with $p < 0.05$ considered to be significant.
Result: There were 30 subjects, 63.3% male, median of age of 69.5 years. The average of thirst value was 63.67} 17.5 mm and the ejection fraction was 41.93} 15.5%. The averages of plasma sodium level and plasma osmolality were respectively 139.7} 4.1 mmole/l and 296.4} 10.1 mOsm/kg.
Conclusion: Pearson correlation test has revealed a weak negative correlation of thirst and ejection fraction ($r= -0.314$, $p=0.091$). On the other hand, there was no correlation between thirst and plasma sodium level ($r=-0.04$ $p=0.833$).

Keywords: thirst, elderly, chronic heart failure, ejection fraction, plasma sodium level

INTRODUCTION

Heart failure has been being a heavy burden for people due to high cost of care, lowering the quality of life, and lowering the expectation of life. Heart failure incident amounted to 10 per 1000 of population of age of over 65 years. The age of 80 years has the risk to have heart failure about 20% for both male and female.[1] Heart failure incidents in developing countries increase from 1.5-4% to 6.7-9%,[2] while number of people of more than 60 years old has been predicted globally to be twofold in 2025 and threefold in 2050.[3] In the last several years, several studies have proven that plasma sodium level during admission to the hospital can be independent predictor to the increase of re-hospitalization and mortality for hospitalized patient with heart failure. The decrease of 3mEq/L of plasma sodium level at the time of admission to the hospital has correlation with to relative increase of 20% of re- admission in 90 days after discharged from hospital.[4]

Thirst is one of common symptom that disturbs the patients with heart failure. Pharmacology and non-pharmacology therapies and natural heart failure history can increase thirst. Thirst can be caused by several factors that correlated to the heart failure. Pathophysiology of heart failure with low cardiac output and the increasing neuron-hormonal system activation i.e. renin-angiotensin-aldosterone will stimulate the center of thirst in hypothalamus. Experiences have revealed that numbers of patients with heart failure feel excessively thirsty. This symptom is paradoxical since the thirst sensing ability decreases in elderly.[5] Studies which compared thirst in elderly with and without heart failure has shown that patients with heart failure experienced more significantly intensive thirst than the control group.[6]

Correlations of fluid balance with thirst have been investigated widely for young and healthy people,[7] but have not been conducted for elderly. The aims of this study were to understand the correlation of thirst level with ejection fraction and plasma sodium level in chronic heart failure in elderly.

MATERIAL AND METHODS

Study was proposed by using cross section study design, at Department of Internal Medicine and Department of Cardiology Dr. Sardjito General Hospital, Yogyakarta. Study was conducted on March 2013 until adequate number of samples collected. Subjects of

Study were the elderly patient with heart failure who hospitalized in intensive cardiac care unit (ICCU) or Internal Medicine Ward, Dr. Sardjito, General Hospital. Criteria of inclusion were patients with heart failure: functional classes of III-IV based on NYHA criteria, age ≥ 60 years, agree to be subject of study. Criteria of exclusion were subjects with chronic kidney disease, liver cirrhosis, severe cognitive impairment, diarrhea, vomiting, and fever. Informed consent was applied to give information to patients and/or their family and to request to be subjects of study. Subjects were examined with *Mini Mental State Examination*/MMSE. If subjects were suffering from severe cognitive impairment, they were excluded.

The eligible subjects were interviewed, to have physical examination, and to get blood examination in laboratory. Thirst examination was done by using VAS score method i.e. by marking the 100 mm line which describes the level of thirst of subjects. Score 0 described that subjects were not thirsty, while score 100 meant very thirsty. Examination was carried out in the morning, before patients got diet and medicine. Demographic data, laboratory test result during admission to the hospital, given treatment, and fluid balance were obtained from medical record. Examination of fraction ejection was performed during treatment by cardiologist and echocardiography officer using echocardiography Vivid Pro.[7] Fraction ejection was measured using M-mode method. If there was segmental kinetic disorder, it was measured using Simpson method. Continuous data with normal distribution were presented in average value and standard deviation, while data with non-normal distribution were presented in median, minimum and maximum. Correlation between thirst level with fraction ejection and plasma sodium level was analyzed using Pearson correlation test. The criteria of correlation strength (r) were very weak (r= 0-0.2), weak (r= 0.2-0.4), medium (r= 0.4-0.6), strong (r= 0.6-0.8). Value of $p < 0.05$ was considered significant. Data analysis was performed using computer program.

Results

Study was carried out during March-June 2013 and involved 30 subjects. The characteristics of subjects are presented in

Table 1. Baseline Characteristics of Study Subjects

Variable	N (%)	Average ± SD	median (minimum-maximum)
Age (years)			69.5(62-88)
Sex			
Male	19(63.3)		
Female	11(36.7)		
Creatinine on admission (mg/dl)		1.5±0.5	
Edema of Leg	6(20)		
Breath frequency (/minute)			22(18-28)
Diuretic Therapy	26(86.7)		
Fluid balance			
Input of fluid (cc)		1281±301.3	
Output of fluid (cc)		2058±567.7	

N: number of subjects, SD: standard deviation; cc: centimeter cubic

Table 2. Thirst, ejection fraction, plasma sodium level and plasma osmolality

Variable	Average ± SD
Thirst/VAS (mm)	63,67±17,5
Ejection fraction (%)	41,93±15,5
Sodium (mmole/l)	139,7±4,1
Blood glucose level (mg/dl)	122,2±40,6
BUN (mg/dl)	28,9±14,9
Plasma Osmolality (mOsmol/kg)	296,4±10,1

SD: standard deviation; VAS: *visual analog score*; BUN: *blood urea nitrogen*

Tabel 3. Results of Pearson correlation test of thirst with several variables

Variables	Pearson correlation coefficient (r)	p
Ejection Fraction	-0.314	0.091
Plasma sodium level	-0.040	0.833
Plasma Osmolality	0.067	0.724
Fluid Input	0.025	0.896

Table 1. Subjects consisted of 63.3% male and median of ages was 69.5 years. Most subjects got diuretic therapy (86.7%). Clinically, 80% of subjects did not experience leg edema, median of breath frequency of 22 (18-22)/ minute. Average fluid input was 1281} 301.3 cc, whereas output of fluid was 2058}567.7 cc. Fluid input consisted of fluid given by oral and parenteral. Applied parenteral fluid was solution of sodium chloride 0.9%, dextrose 5% and Ringer Lactate. Thirst was measured using *Visual Analog Score* (VAS), it was found that average thirst level was 63.67}17.5 mm.

All subjects underwent examination of ejection fraction using echocardiography. It was found that average ejection fraction was 41.93} 15.5%. Average plasma sodium level was 139.7} 4.1 mmole/l, while average osmolality was 296.4} 10.1 mOsm/kg. Examination results are presented in Table 2.

The results of Pearson correlation test have revealed that thirst and ejection fraction have a weak negative-correlation (r= -0.314, p= 0.091), but statistically not significant. Correlation test of thirst and plasma sodium level has shown that there is no correlation (r= -0.04; p= 0.833) Pearson correlation test has revealed that there is no correlation (r= 0.067, p= 0.724) between thirst and plasma osmolality, and there is also no correlation (r= 0.025, p= 0.896) between thirst and fluid input. Complete results are listed in Table 3.

Most subjects in this study got diuretic therapy. Unpaired t-test has been performed to investigate whether diuretic therapy causes thirst due to normal distribution of data. It has been found that there is no difference of thirst between group with and without diuretic therapy (p= 0.094, CI 95% 15.7(-2.9-34.4). The results are listed in Table 4.

Normal interval of plasma sodium level is 135-145 mmole/l 8.9. Based on that interval, plasma sodium levels during measurement of thirst were categorized into three groups: group

Table 4. Difference of thirst with and without diuretic therapy

	n	Average ± SD	Average difference (CI: 95%)	p
Thirst with diuretic therapy	26	65.7±17.2	15,7(-2.9-34.4)	0.094*
Thirst without diuretic therapy	4	50±14.1		

n: number of subjects; SD: standard deviation; CI: confidence interval; * unpaired t-test

Table 5. Differences of thirst based on plasma sodium level and plasma osmolality

	n	Average thirst ± SD	median of thirst (maximum-minimum)	p
Sodium (mmol/l)				0.754*
Sodium <135	4	57.5±18.9	65(30-70)	
Sodium 135-145	23	65.2±17.8	70(30-100)	
Sodium >145	3	60±17.3	50(50-80)	
Plasma Osmolality (mOsmol/kg)				0.444*
Osmolality <285	3	53.3±20.8	60(30-70)	
Osmolality 285-295	8	71.3±21.7	70(40-100)	
Osmolality >295	19	62.1±14.7	60(30-80)	

SD: standard deviation; * Kruskal-Wallis test

of plasma osmolality of < 285 mOsm/kg (3 subjects (10%)), group of plasma osmolality of 285-295 mOsm/kg (8 subjects (26.7%)) and group of plasma osmolality of >295 mOsm/kg (19 subjects (63.3%)). Kruskal-Wallis test has been conducted to investigate the differences of thirst for three different groups of plasma osmolality and plasma sodium level. It has been found that the value of p is 0.754 (p= 0.754) for thirst with plasma sodium level and 0.444 (p=0.444) for thirst with plasma osmolality. It means there is no difference of thirst between three different groups. Results are listed in Table 5.

DISCUSSION

Thirst is subjective feeling for patient with heart failure. It can only be measured by asking to the person. Thirst should be considered to be a problem if patients are prevented to respond a thirst signal naturally i.e. drink water, or if thirst does not decrease by drinking the water.[10] Visual Analog Score (VAS) that used in this study has been validated and used to evaluate patients with heart failure.[11] The average value of thirst of subjects was 63.67} 17.5 mm. Waldreus *et. al.* (2011) compared thirst in elderly with acute decompensated heart failure to elderly with other disease as the control group. They found that medians of thirst were 75 mm and 25 mm, respectively. Thirst of elderly with acute decompensated heart failure was threefold of thirst of control group. Holst *et al.* (2008) compared limited fluid input to 1.5 liter/day to free fluid input of 30-35 ml/kg body weight/day on quality of life, physical capacity, thirst and treatment in hospital for patients with stable heart failure

(age of 70}10 years). They found that thirst level was 51 mm for group of limited fluid input and 23 mm for group of free fluid input ($p< 0.001$). The study to investigate effect of sodium input and fluid input of patients with heart failure on quality of life appetite, and thirst had been conducted by using random prospective study. The study compared group of intervention (fluid was limited to 1.5 liter and sodium 5 g/day) to control group (individual diet, information from the nurse to not drink too much and to consume salt carefully) for patients with stable heart failure (age of 74 years). It was found that thirst levels of two groups were 54 and 50 mm shifted to 46 and 48, respectively. After 12 weeks the result was not statistically significant).[12]

In stable heart failure, thirst level is lower compared to acute compensated heart failure; however it is still higher than healthy control group. The fact has shown that thirst increases for heart failure and increases further for acute compensated heart failure.[10] In this study, the average ejection fraction was 41.93} 15.5%. The result of study conducted by Holst *et al* (2008) revealed that ejection fraction was <45%, while Philipson *et al* (2013) found the ejection fraction was 34%. Waldreus *et al.* (2011) obtained average ejection fraction of 32} 12%, from measurement of 13 subjects of total 23 subjects of elderly with heart failure. In this study, thirst with ejection fraction have negative correlate ($r= -0.314$, $p=0.091$), decreasing ejection fraction results in increasing thirst level and conversely, increasing ejection fraction results in decreasing thirst level. Ejection fraction represents cardiac output. The decrease of cardiac output stimulates baroreceptor artery in sinus caroticus and arcus aorta, further will stimulate the thirst center and secretion of vasopressin. Activation of baroreceptor also stimulates secretion of rennin and angiotensin II from kidney that also stimulate thirst center.[13] There is no existing study that correlate thirst and ejection fraction. It was found that average plasma sodium level was 139.7} 4.1 mmole/l. There was no correlation of thirst and plasma sodium level ($r=-0.04$, $p=0.833$) using Pearson correlation test. Average plasma sodium level in this study is similar to that of study conducted by Holst *et al* (2008) for elderly patients with heart failure, about 40} 3 mmole/l. While Waldreus *et al* (2011) reported the value of plasma sodium level of 140.1} 3.7 mmole/l for elderly patients with acute decompensated heart failure. The plasma sodium level is still in normal range and not to be reason of increasing the thirst.[6] The study on adults that experience dehydration due to exercise, thirst has positive correlation with plasma sodium 14.9. Average plasma osmolality during thirst measurement being conducted was 296.4} 10.1 mOsm/kg.

Result of Pearson correlation test has shown that there no correlation between thirst and plasma osmolality ($r=0.067$, $p=0.724$). Previous study on healthy elderly (>65 years) that aimed to investigate effect of lack of fluid and hyper-osmolality stimulant on thirst has been performed. It has revealed that elderly have higher initial osmolality, so that they need higher operating osmolality point to trigger thirst sensation.[15] Study on healthy elderly (age of 67-75 years) showed that long-term deficiency of water can increase the plasma osmolality more than 296 mOsm/kg, followed by decreasing of subjective thirst. After they were given water, they consumed less water than young people, and plasma osmolality shifted to lower level (average 290 mOsm/kg) after deficiency of water in the same period.[16] Another study that aimed to investigate correlation of thirst and plasma osmolality was performed on patients with cancer, who

hospitalized. It was obtained 88 subjects (average age of 61} 14 years) with the plasma osmolality of 256–307 mOsm/kg (median 280). There is no significant correlation between thirsts with BUN level, creatinine, plasma sodium and plasma osmolality.[17] For the patients with chronic kidney disease who has been getting haemodialysis regularly, thirst has no correlation with plasma osmolality, however it has correlation with angiostensin II level and plasma rennin activity.[18] Several factors affect uniquely on drinking behavior of humankind, for example dry mouth (xerostomia) factor and food intake factor.[19] According to Holst *et al* (2008), diuretic therapy will lead to xerostomia. In the epidemiology 10 study which was retrospective observational, comparative and multicenter in Reims, France, it was found that 287 (37.3%) of 769 subjects (average age of 84.6} 8.4 years) experienced xerostomia. The increasing age (OR=1.56, 95% CI (1.30-1.88) p<0.0001) and anticholinergic medicine (OR=1.35, 95% CI (1.05- 1.73), p=0.02) caused xerostomia.[20] The incidence of xerostomia was notinvestigated in this study; however there was no subject who got anticholinergic therapy. Factors that influence thirst in heart failure; correlate with treatment (limitation of fluid and diuretic therapy), heart failure condition (NYHA functional class, clinical stability), demography (age) and emotion (anxiety)[10]. In this study, it was found that average fluid input 1281□ } 301.3 cc, and there was no correlation between thirst and fluid (r=0.025, p=0.896).

Fluid input comprised parenteral and oral input. Parenteral fluid was sodiumchloride 0.9%, dextrose 5% and Ringer Lactate. Effects of various fluids on thirst have been investigated by Zerbe and Robertson (1983). They reported that hypertonic sodium chloride and manitol caused the fast increase and parallel of plasma osmolality, and both hypertonic sodium chloride and manitol stimulated thirst.[21] Sodium chloride 0.9% solution and dextrose 5% solution are isotonic fluids that do not disturb osmotic balance between intracellular fluid and extracellular fluid.[22] Ringer lactate solution is isotonic fluid with osmolality of 276 mOsm/kg, potassium and calcium contents which are similar with normal plasma, so that Ringer Lactate does not disturb osmotic balance between intracellular fluid and extracellular fluid.

Holst *et al* (2008) reported that limitation of fluid input until 1.5 liter/day for elderly with stable chronic heart failure significantly influenced thirst (VAS 51 mm) compared to free fluid input (30-35ml/kg body weight/day)(VAS 23mm, p<0.001).[23] Whereas study on elderly with stable heart failure by Philipson *et al* (2013) revealed that limitation of fluid input until 1.5 liter/day and salt consumption of 5 g/day compared to control group resulted in no statistically significant difference of thirst (average initial thirst level 54 and 50 mm shifted to 46 and 48 mm after 12 weeks.[12] There are weaknesses in this study. First, patients or subjects with heart failure, both with low and normal ejection fraction are involved, so that the collected samples are not homogenous. Secondly, factors influencing the thirst that have not been excluded in this study are xerostomia and anxiety.

CONCLUSIONS

There is negative correlation between thirst and ejection fraction for elderly with chronic heart failure, however it is not statistically significant. On the other hand, there is no correlation between thirst and plasma sodium level for elderly with chronic heart failure. It is necessary to conduct similar study with samples of patients of elderly with

chronic heart failure and low ejection fraction, and it is also important to control all factors influencing thirst. There are factors that correlate with thirst for patients of elderly with chronic heart failure. These factors are essential to be studied comprehensively by conducting further study to explore prevalence, degree and source of excessive thirst for patients with heart failure.

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