CORRELATION OF OVERACTIVE BLADDER (OAB) PATIENT'S URINE NERVE GROWTH FACTOR LEVEL (NGF) WITH THE DEGREE OF OVERACTIVE BLADDER'S SYMPTOM

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Abstract: Overactive bladder (OAB) are conditions of urinary urgency with or without incontinence symptomps, and are usually followed with frequency and nocturia. OAB's primary mechanism is inflammation in the bladder, with proof of nerve damage from inflammation in the bladder, enhancing secretion of Nerve Growth Factor (NGF). NGF is involved as chemical mediator from pathologic changes induced by stimuli to Afferent Nerve C and reflex from the bladder. New researchs are focused to find tools that are more effective and simple to detect OAB and assessing the degree of severity as sson as possible, one of the being the NGF levels in urine.
Objective: To assess the correlation between OAB patient's urine NGF with the severity degree of OAB Symptoms
Method: This is a correlation analytic study with crossectional design, assessing OAB patient's urine NGF level with severity degree of OAB symptoms using Spearman test with confidence interval of 95%.
Results: This study shows that OAB patients have urine NGF level with mean 295,65 ± 69,898 pg/ml with NGF level increase along with the severity of symptoms. Median of 273.50 pg/mL with lowest 221 pd/mL and highest 525 pg/mL. According to correlation test, shows that there is significant positive strong correlation between Urine NGF with degree of symptom, assessed using OABSS with R = 0.796 and p = 0.001.
Conclusion: There is significant positive strong correlation between Urine NGF with degree of symptom severity in OAB patients.

Keywords: NGF, overactive bladder.

Preliminary

The picture of overactive bladder (OAB) has changed dramatically in the last 20 years. A quarter of a century ago this complex phenomenon did not even exist. Only in the early 2000 did the concept of this syndrome emerge which was made from four closely related symptoms that we now call OAB. [1] Overactive bladder (OAB) is a condition of urinary urgency with or without incontinence, and is usually accompanied by frequency and nocturia. Urgency is a core symptom of the presence of OAB. [2,3,4] Frequency of urgency symptoms can be caused by psychological factors, increased urine production, a great desire to urinate due to central nervous system (CNS) lesions, and excessive detrusor activity (DO). [2]

The prevalence of OAB varies among populations, because the number of women who seek help and report symptoms depends on the social acceptance of incontinence. As a result of ignorance, shame and sometimes believing that incontinence is somewhat 'normal' due to birth and aging, many women suffer for years not yet seeking medical care. Overall, the prevalence rate of OAB in large population-based studies ranges from 7–27% in men and 9–43% in women. The overall prevalence in women over 40 years is 16.6% in Europe. In addition, the prevalence tends to increase with age. A study in the United States found that the incidence of OAB was 48.3% in women and 60.5% in men. Studies in Asia also cite a similar prevalence of OAB, even though only one in five patients usually seek treatment for the reasons mentioned earlier. [4]

There are scores for validated OAB symptoms developed for clinical use and research purposes. OAB symptom score (OABSS) is a tool designed recently to evaluate patients with OAB symptoms and is popular in the Asia-Pacific region. [4] OABSS is used to define and classify mild, moderate or severe degrees of OAB

The main mechanism of OAB is caused by the inflammatory process that occurs in the bladder, where there is evidence that nerve damage due to inflammation in the bladder can increase neutropics such as Nerve Growth Factor (NGF) . Nerve Growth Factor (NGF) is one of the neurotropic factors needed for the maintenance of sensory neurons. It is known that too much NGF expression can cause bladder hyperactivity.

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Nerve Growth Factor / *Nerve Growth Factor* (NGF) is a neurotrophic factor that induces the growth, differentiation, and survival of neurons specific targets. NGF is released by smooth muscle and urothelium as chemical mediators in the bladder. [2] NGF has been involved as a chemical mediator of pathological changes induced in afferent C nerve stimulation and bladder reflex activity.

Research Method

This study is a correlative analytic study with a *cross - sectional* approach that assesses the correlation between urine NGF levels in patients with OAB and their severity. Previous researchers will look for women with a diagnosis of OAB and then assess the levels of urine NGF and its severity using OABSS.

The place of this research was conducted at the Department of Obstetrics and Gynecology, Faculty of Medicine, University of North Sumatra - RSUP. H. Adam Malik Medan and USU Hospital. This research was conducted from April 2019 until the number of samples were met and after obtaining ethical clearance from the Research Ethics Commission of the Faculty of Medicine, University of North Sumatra. The research sample was paramedics who experienced symptoms of OAB in H. Adam Malik General Hospital and USU Hospital that met the inclusion and exclusion criteria taken with *consecutive sampling techniques* until the minimum sample size was met.

Researchers conducted a study of female paramedias who experienced OAB. Then anamnesis (age, parity and history of illness), physical examination, antopometric records, such as height and weight. Then the research subjects were asked to fill in the OABSS questionnaire and then the OABSS score was calculated to assess the severity of the OAB. To rule out the presence of other diseases, a KGD examination is done while using a stick to rule out any DM disease and a urinalysis check is done to rule out a urinary tract infection. Then urine was taken to assess urine NGF levels and OABSS scores.

Samples were processed using a *sandwich kit* with Enzyme linked immunosorbent assay (ELISA) analysis in accordance with manufacturer's instructions used to quantitatively detect urine NGF levels. The results of this study are presented in the frequency distribution table. To assess the frequency distribution of the characteristics of the study sample based on operational definitions and NGF levels based on the severity of the OAB, a Univariate statistical analysis was performed. To assess the relationship of the severity of OAB with the characteristics of patients with OAB, *Fisher's Exact Test was used* . To assess the correlation between urine NGF levels and the severity of OAB based on OABSS scores, a normality test is first performed, then a Bivariate analysis is performed using the *Correlation-Regression test (Spearman Test* if the data is not normally distributed or *Pearson Test* if the data is normally distributed) using the level 95% confidence.

Research Results

The study is using a group of paramedics women who suffer from OAB as the subject of research which numbered 40 people. Researchers searched for samples using *overactive bladder symptom scores* (OABSS). Characteristics of research subjects can be seen from the following table

Table 1 Characteristics of Research Subjects

Characteristics	People with OAB	
	N	%
Parity		
Primipara	0	(0 %)
Sekundipara	15	(37.5%)
Multi-Parallel	25	(62.5%)
BMI		
Normoweight	9	(22 , 5%)
Overweight	31	(77 , 5%)
Age		
4 5 - 50 years	7	(17 , 5%)
5 1 - 55 years old	33	(82 , 5%)
OAB degree		
Mild	20	50%
Moderate	13	32.5%
Severe	7	17.5%
Total	40	(100%)

Table 2. Relationship of OAB Severity based on OABSS and Characteristics of OAB Sufferers

Characteristics	Research subject			Total		Value of p
	OAB degrees are based on OABSS			n	%	
Parity	**Light**	**Is**	**Weight**			
Sekundipara	13 (32.5%)	1 (2.5%)	1 (2.5%)	15	(37.5%)	.001
Multi-Parallel	7 (17.5%)	12 (30%)	6 (15%)	25	(62.5%)	
BMI						

Normoweight	5 (12.5 %)	2 (5%)	2 (5%)	9	(22.5%)	.321
Overweight	15 (37.5%)	11 (27.5 %)	5 (12.5%)	31	(77.5%)	
Age						
4 5 - 50 years	5 (12.5%)	2 (5%)	0 (0%)	7	(17.5%)	
5 1 - 55 years old	15 (37.5%)	11 (27.5%)	7 (17.5%)	33	(82.5%)	0.316

*** Fisher's Correlation Test**

In the OAB group with a moderate degree, the majority were multipara parity of 12 people (30%) and in the sekundipara parity group, there was only 1 person (2.5%). Based on statistical tests with the *Fisher Exact* test obtained p value <0.05 (p = 0.001) which indicates a significant relationship between parity and degree of OAB. In the moderate-level OAB group, 11 people (27.5%) overweight and others with 2 people (5%) normoweight. In the moderate-level OAB group also generally with age 51-55 years as many as 33 people (82.5%) and others with age 45-50 years as many as 2 people (5%). Based on statistical tests with the Fisher exact test obtained p value> 0.05 in both of them which showed no significant relationship between BMI and age with OAB degrees.

Table 3. NGF levels based on severity of OAB

OAB degree	Urine NGF levels					N	%
	The mean	Elementary school	Median	Min	Max		
Severe	407.86	84.30	412.0	249	525	7	17.5
Moderate	304.77	30.18	302.0	251	373	13	32.5
Mild	250.45	19.04	249.5	221	289	20	50.0
Total OAB	**295.65**	**69.90**	**273.50**	**221**	**525**	**40**	**100**

Table 3 explains that in patients with OAB the mean value of urine NGF is higher at severe degrees of 407.86 ± 84.30, lower at moderate degrees of 304 ± 30.18 and mild degrees of OAB at 250.45 ± 19.04

Table 4 Correlation of OABSS Score with Urine NGF levels in OAB Patients

	The mean	Elementary school	Median	Value of r **	Value of p
OABSS score	5.9	3.51	5,0	0, 796	.001
Urinary NGF levels	295 . 65	69 . 898	273 . 50		

**** Spearman Correlation Test**

Table 4 explains that based on the AOBSS score it had a mean of 5.9 ± 3.51 and a median of 5.0 while the NGF level had an average of 295.65 ± 69,898 and a median of 273.50. Based on the Spearman Correlation statistical test obtained r = 0.59 and p <0.05 (p = 0.001) which indicates a significant positive correlation between strong levels of urine NGF with a score based on OABSS which means that the heavier the severity of the OAB sufferers the higher the NGF levels urine

Discussion

The results of this study indicate that in patients with OAB they have a urine NGF level with an average of 295.65 ± 69.889, pg / ml where the level increases with the degree of severity. The median value obtained was 273.50 pg / mL with a minimum content of 221 pd / mL and a maximum level of 525 pg / mL. Based on the correlation test, there was a significant positive correlation between strong NGF levels and the severity of OAB which was assessed based on OABSS with r = 0.796 and p = 0.001.

This suggests that high urine NGF levels play an important role in mediating the sensation of urgency in OAB. Similar results were explained by Kuo et al in his study which concluded that patients with dry OAB and wet OAB had significantly higher urine NGF levels compared to the control group and patients with increased bladder sensation [1.24]

Research by Basok et al (2015) states that urinary NGF and NGF / Cr levels were significantly highest in wet OAB and second highest in dry OAB compared to controls.

The study by Tzu Liu et al (2008) found significantly greater increases in urine NGF levels in patients with OAB and 47 patients with BOO / DO than in the control group with values of p = 0.002 and p 0.0001, respectively.

Tzu Liu et al (2010) analyzed urine NGF and NGF / Cr levels among controls, dry OAB women and wet OAB based on age (≥ 55 vs <55 years) and BMI (<20, 20-30 and> 30) and get results that show no significant differences between subgroups in the OAB group, except for dry OAB. Digesu et al (2001) investigated a group of 843 women classified with OAB, and 457 (54.2%) were found to have a urodynamically proven DO. Hyman et al (2001) also found a higher incidence of DO associated

with urge incontinence (wet OAB) compared with urgency and frequency symptoms, nocturia, or difficulty urinating (75% vs 36%) with LUTS. Overall, these clinical observations suggest that urine NGF levels are strongly associated with symptoms of urgency, and higher urine NGF levels may have an impact on DO. [6]

Conclusion

Mean and median levels of urine NGF in patients with OAB are higher in severe degrees, lower in moderate degrees and mild OAB degrees. Based on the correlation test shows that there is a significant strong positive correlation between urine NGF levels and degrees of OAB ($r = 0.59$), $p = 0.001$

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