

## Analysis of preferences for treatment modalities in outpatients with nocturia with special reference to complementary and alternative medicine

Yukihiro Udo<sup>1)</sup>, Kokoro Hino<sup>2)</sup>, Kosuke Yamamoto<sup>1)</sup>, Eiji Sumiya<sup>2)</sup>,  
Hiroshi Kitakoji<sup>3)</sup>, Masahiro Nakao<sup>\*1)</sup>

<sup>1)</sup> Department of Urology, Meiji University of Integrative Medicine

<sup>2)</sup> Department of Basic Acupuncture and Moxibustion, Meiji University of Integrative Medicine

<sup>3)</sup> Department of Clinical Acupuncture and Moxibustion, Meiji University of Integrative Medicine

### ABSTRACT

**Aim:** Patients with lower urinary tract symptoms (LUTS) tend to seek various treatment modalities. The aim of this study is to examine preferences for treatment modalities and their relationships with the number of nocturia episode and quality of life (QOL) due to nocturia in outpatients with nocturia using a questionnaire with special reference to complementary and alternative medicine (CAM).

**Subjects and methods:** Eighty outpatients who visited our clinic were requested to complete a 3-day bladder diary to confirm that they had nocturia. Those who had one or more nocturnal voidings were also interviewed using an original questionnaire regarding their QOL due to nocturia, which had been modified from a validated Japanese version of the International Prostate Symptom Score (IPSS) QOL index, and their desire to undergo five treatment modalities; i.e., CAM, prescription medication, water and salt intake reduction, taking exercise, and sleep improvement. The patients were asked to rate preferences for each modality using three discrete scales; i.e., "wish to undergo", "undecided (may undergo treatment if strongly recommended)", and "do not wish to undergo". Then, the participants were divided into three groups based on the number of nocturia episodes and their QOL score, which were then compared with each other with regard to their desire to undergo the five treatment modalities.

**Results:** Twenty-seven patients were excluded from the analysis because of incorrect bladder diary recording, and 53 patients were analyzed in this study. There was a significant correlation between the number of nocturia episodes and QOL due to nocturia. Twenty six percent of the patients wanted CAM, 81% desired prescription medication, 38% chose water and salt intake reduction, 62% chose exercise, and 40% opted for sleep improvement. There were significant relationships between number of nocturia episodes and the desire for CAM and medication. There was also a significant relationship between the QOL score and the desire for CAM.

**Conclusion:** Patients with nocturia seek various kinds of treatment, and their choice depends on personal preference, number of nocturia episodes and impaired QOL due to nocturia. Considerable number of patients seek CAM. It is clinically important for physicians to ask nocturics about their treatment preference when deciding on a suitable treatment strategy including CAM.

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**Key words** nocturia, outpatient, treatment modality, complementary and alternative medicine, preference

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\* Correspondence author: Department of Urology,  
Meiji University of Integrative Medicine, Hiyoshi-cho,  
Nantan, 629-0392, Japan  
Tel: +81-771-72-1221, Fax: +81-771-72-0234  
E-mail: m\_nakao@meiji-u.ac.jp

## I. Introduction

Nocturia is defined as the complaint to wake one or more times to void while sleeping by the International Continence Society (ICS)<sup>1)</sup>. It is well known that nocturia is a common disorder affecting the elderly, and there is no difference in its prevalence between men and women<sup>2,3)</sup>. Nocturia leads to many disorders such as sleep deprivation and diurnal fatigue, decreased quality of life (QOL), increased risk of fall at night, and an increased mortality rate, and is perceived to be an important health problem in elderly people<sup>4-8)</sup>.

The causes of nocturia are mainly classified into increasing urine production, decreased bladder capacity and deterioration of sleep, and are associated with various factors such as urological diseases including benign prostate hyperplasia (BPH) and overactive bladder (OAB); systemic diseases including hypertension, diabetes mellitus, heart failure, renal failure, peripheral edema, nephrotic syndrome, hypoproteinemia, liver diseases, and obstructive sleep apnea; poor dietary habits such as excessive intake of water, salt, alcohol, and caffeine; and many factors resulting in sleep disturbance and leading to nocturia such as various kinds of pain and pruritus, pulmonary diseases following cough, heartburn, and mental problems including depression and higher susceptibility to light and noise<sup>1-4)</sup>. Therefore, nocturia has recently been recognized not only as a symptom of lower urinary tract disorders but also as a bothersome clinical entity to which special attention should be paid. Various modalities such as medication, behavioral training, and food and fluid manipulation are used to treat it<sup>9-12)</sup>.

Several treatment-seeking surveys of patients with lower urinary tract symptoms (LUTS) have been performed, however, only two studies focused on nocturia<sup>13-15)</sup>. These two studies, which revealed that nocturia only has a minor impact on daily living and that few individuals seek medical care despite its high prevalence, examined only treatment seeking behavior of community-dwelling people, and clinically useful information obtained through them was very sparse<sup>14,15)</sup>. No study has examined seeking treatment for nocturia so far in outpatients. Recently, it is proposed that multicomponent

intervention including pharmacotherapy and lifestyle modification is useful to treat nocturia, because of its multifactorial nature<sup>16)</sup>. Furthermore, patients with LUTS tend to seek various treatment modalities such as prescription medication, physical therapy, self-treatment, coping strategies, and surgery<sup>13)</sup>. Actually, we often experience that many outpatients with LUTS seek less invasive treatments such as over-the-counter drugs and plant extracts belonging to complementary and alternative medicine (CAM) as self-treatment. Therefore, it is thought to be of clinical importance to clarify the preferred treatment remedies of outpatients with nocturia including CAM. The aim of this study is to examine preferences for various treatment modalities with special reference to CAM and their relationships with the number of nocturia episodes and QOL due to nocturia in outpatients using a questionnaire.

## II. Subjects and methods

### Subjects

This study was performed under the approval of the Ethical Committee of Meiji University of Integrative Medicine (Approval no. 17-53). Written informed consent to analyze and publish their bladder diary and questionnaire data was obtained from all subjects.

Between December 2005 and November 2006, 80 outpatients who visited the Department of Urology, Meiji University of Integrative Medicine with various complaints were clarified to have one or more voiding episodes during sleeping using the International Prostate Symptom Score (IPSS).

The patients were requested to complete a 3-day bladder diary to confirm that they had nocturia. The patients underwent a medical interview, urinalysis, routine blood test and prostate specific antigen (PSA), uroflowmetry, and residual urine measurement to make a definite diagnosis. All patients were the Japanese living in rural areas in Kyoto Prefecture, Japan, and interviewed and examined using the Japanese language by one urologist (M.N.). Those who were suspected to suffer from definite pathological disorders such as urolithiasis, bladder cancer, bacterial cystitis, prostate cancer, prostatitis, etc., were excluded from the analysis.

## Questionnaires

Those who had one or more nocturnal voiding episodes were also interviewed by the same urologist (M.N.) using an original questionnaire. The interview was performed before explaining detailed causes of and treatment modalities for nocturia. The questionnaire consisted of two parts. The first part was concerned with QOL due to nocturia and was modified from the validated Japanese version of IPSS QOL index; i.e., “If you were to spend the rest of your life with your nighttime voiding condition just the way it is now, how would you feel about it?” There were seven answer scales; i.e., 0: delighted, 1: pleased, 2: mostly satisfied, 3: mixed (about equally satisfied and dissatisfied), 4: mostly dissatisfied, 5: unhappy, and 6: terrible<sup>17,18</sup>. The second part was related to the desire for each treatment modality. The actual question was “Do you want to undergo the following treatment modalities: complementary and alternative medicine (CAM) including Chinese herbal medicine, acupuncture, and moxibustion; prescription medication; water and salt intake reduction; taking exercise like walking or jogging in the evening; improving sleep conditions by shortening the time spent in bed and making the bedroom dark and calm.” The patients were asked to give their views regarding each modality using three discrete scales; i.e., “wish to undergo”, “undecided (may undergo treatment if strongly recommended)” and “do not wish to undergo”.

## Statistical analysis

The participants were divided into three groups based on the number of nocturia episodes and QOL index due to nocturia, which were compared with each other with regard to their desire to undergo the five treatment modalities. Spearman’s correlation coefficient ( $r_s$ ) and the chi-square test were used for statistical analysis. For all analyses, a P value of less than 0.05 was considered to be statistically significant.

## III. Results

### Patient characteristics

Twenty-seven patients were excluded from the study, because they did not record their bladder

**Table 1** Patient characteristics

No. patients (male/female)	53	(38/15)
Age, mean (SD)	74.9	(6.0)
Chief complaint	n	%
LUTS	47	89.0%
Dull pain in the lower abdomen	1	1.9%
Discomfortness in the lower abdomen	1	1.9%
Microhematuria	1	1.9%
Elevated PSA	1	1.9%
Insomnia	1	1.9%
Lumbago	1	1.9%
Clinical diagnosis	n	%
BPH	25	47.0%
OAB	20	38.0%
Nocturia	3	5.7%
Prostatodynia	3	5.7%
Underactive bladder	2	3.8%
IPSS	mean	SD
Incomplete emptying	1.4	1.5
Frequency	2.7	1.6
Intermittency	1.4	1.7
Urgency	1.7	1.8
Weak stream	2.2	2.0
Straining	1.4	1.7
Nocturia	3.2	1.1
Total	14	7.1

diary correctly or had definite pathological disorders. Therefore, a total of 53 patients (38 males and 15 females; mean age 74.9 plus minus 6.0) were analyzed in this study. As for their chief complaint or their main reason for visiting the clinic, 47 patients (89%) complained of LUTS, and the other patients complained of various symptoms or signs (**Table 1**). Twenty-five patients (47%) were diagnosed with BPH, 20 patients (38%) with OAB, 3 patients (5.7%) with nocturia, 3 patients (5.7%) with prostatodynia, and 2 patients (3.8%) with underactive bladder. The mean IPSS score was 14 plus minus 7.1 (**Table 1**).

### Relationship between the number of nocturia episode and QOL due to nocturia

The association between the number of nocturia episodes and QOL due to nocturia was shown in **Table 2**. A significant correlation was found between them ( $r_s=0.2791$ ,  $p=0.0430$ ).

### Treatment preferences for nocturia

The patients’ treatment preferences were summarized in **Table 3**. Twenty six percent of the

**Table 2** Relationship between the number of nocturia episodes and QOL due to nocturia

No. of nocturia episode	n (%)	QOL due to nocturia							mean (SD)
		0	1	2	3	4	5	6	
1	11 (21.0%)	0	1	2	3	2	2	1	3.5 (1.5)
2	14 (26.0%)	0	1	0	3	5	5	0	3.9 (1.1)
3	18 (34.0%)	0	1	0	6	1	9	1	4.1 (1.3)
4	7 (13.0%)	0	0	1	1	2	3	0	4.0 (1.2)
5 or more	3 (5.7%)	0	0	0	0	0	1	2	5.7 (0.6)
Total	53 (100%)	0	3	3	13	10	20	4	4.0 (1.3)

**Table 3** Treatment preference of the patients (n=53)

Treatment modality	Desired, n (%*)	Undecided, n (%*)	Did not desire, n (%*)
CAM	14 (26.0%)	21 (40.0%)	18 (34.0%)
Medication	43 (81.0%)	5 (9.4%)	5 (9.4%)
Water and salt intake reduction	20 (38.0%)	16 (30.0%)	17 (32.0%)
Exercise	33 (62.0%)	12 (23.0%)	8 (15.0%)
Sleep improvement	21 (40.0%)	16 (30.0%)	16 (30.0%)

\*: percentage of the patients/total patients in each row

patients wanted to undergo CAM, 81% wanted prescription medication, 38% opted for water and salt intake reduction, 62% chose exercise and 40% hoped for sleep improvement.

The relationships between the number of nocturia episodes and QOL score due to nocturia and the desire for each treatment modality were summarized in **Table 4**. There were statistically significant relationships between the number of nocturia episodes and the desire for CAM and medication. There was also a significant relationship between the QOL score and the desire for CAM. Statistically significant result was not obtained through the analyses of the other three modalities; i.e., water and salt intake reduction, exercise, and sleep improvement (**Table 4**).

#### IV. Discussion

Prior studies on seeking treatment for nocturia examined community-dwelling people<sup>14,15</sup>. To the best of our knowledge, this is the first study to investigate the favored treatment modalities for nocturia including CAM in outpatients visiting a medical institution. All subjects were interviewed and examined by one urologist (M.N.) using an original questionnaire, bladder diaries and the necessary work-up.

The preferences for five treatment modalities in nocturics were examined in this study (**Table 3, 4**). In particular, 26% of the outpatients wished to undergo treatment involving CAM. CAM is considered to be a treatment that complements and/or substitutes for conventional medicine and includes various modalities such as plant extracts, dietary supplements, acupuncture, moxibustion, yoga, and aromatherapy<sup>19,20</sup>. Plant extracts such as saw palmetto extracts, rye pollen extract, eviprost, Chinese herbal medicines, etc., are also useful to treat LUTS due to BPH and OAB and are used in Japan and many Western countries<sup>19-28</sup>. Among Chinese herbal medicines, pilot studies have reported that Gosha-jinki-gan and Saireito improved nocturia in patients with BPH and OAB<sup>25-28</sup>. Acupuncture is also a useful modality for treating OAB<sup>29,30</sup> and seems to be useful to treat nocturics with decreased bladder capacity. Tomita et al performed a randomized controlled trial and revealed that moxibustion is efficient at reducing frequent urination during sleeping<sup>31</sup>. Several treatment modalities belonging to CAM have been found to be useful for treating nocturia. Recently, many people have made use of various kinds of CAM to maintain good health in Japan<sup>32,33</sup>. Therefore, physicians should be aware that a considerable number of outpatients with nocturia

**Table 4** Relationships between treatment preference and the number of nocturia episodes and QOL due to nocturia

No. of nocturia episodes	n	CAM			P
		Desired, n (%*)	Undecided, n (%*)	Did not desire, n (%*)	
1	11	0 (0.0%)	7 (64.0%)	4 (36.0%)	0.0185
2	14	8 (57.0%)	3 (21.0%)	3 (21.0%)	
3 or more	28	6 (21.0%)	11 (39.0%)	11 (39.0%)	
QOL score					
0 or 1	3	0 (0.0%)	0 (0.0%)	3 (100.0%)	0.0286
2 to4	26	4 (15.0%)	12 (46.0%)	10 (38.0%)	
5 or 6	24	10 (42.0%)	9 (38.0%)	5 (21.0%)	
No. of nocturia episodes	n	Medication			P
		Desired, n (%*)	Undecided, n (%*)	Did not desire, n (%*)	
1	11	9 (82.0%)	2 (18.0%)	0 (0.0%)	0.0380
2	14	11 (79.0%)	3 (21.0%)	0 (0.0%)	
3 or more	28	23 (82.0%)	0 (0.0%)	5 (18.0%)	
QOL score					
0 or 1	3	1 (33.0%)	1 (33.0%)	1 (33.0%)	NS
2 to4	26	24 (92.0%)	1 (3.8%)	1 (3.8%)	
5 or 6	24	18 (75.0%)	3 (13.0%)	3 (13.0%)	
No. of nocturia episodes	n	Water and salt intake reduction			P
		Desired, n (%*)	Undecided, n (%*)	Did not desire, n (%*)	
1	11	2 (18.0%)	4 (36.0%)	5 (45.0%)	NS
2	14	7 (50.0%)	4 (29.0%)	3 (21.0%)	
3 or more	28	11 (39.0%)	8 (29.0%)	9 (32.0%)	
QOL score					
0 or 1	3	1 (33.0%)	0 (0.0%)	2 (67.0%)	NS
2 to4	26	6 (23.0%)	9 (35.0%)	11 (42.0%)	
5 or 6	24	13 (54.0%)	7 (29.0%)	4 (17.0%)	
No. of nocturia episodes	n	Exercise			P
		Desired, n (%*)	Undecided, n (%*)	Did not desire, n (%*)	
1	11	7 (64.0%)	4 (36.0%)	0 (0.0%)	NS
2	14	7 (50.0%)	3 (21.0%)	4 (29.0%)	
3 or more	28	19 (68.0%)	5 (18.0%)	4 (14.0%)	
QOL score					
0 or 1	3	1 (33.0%)	1 (33.0%)	1 (33.0%)	NS
2 to4	26	15 (58.0%)	7 (27.0%)	4 (15.0%)	
5 or 6	24	17 (71.0%)	4 (17.0%)	3 (13.0%)	
No. of nocturia episodes	n	Sleep improvement			P
		Desired, n (%*)	Undecided, n (%*)	Did not desire, n (%*)	
1	11	4 (36.0%)	3 (27.0%)	4 (36.0%)	NS
2	14	7 (50.0%)	4 (29.0%)	3 (21.0%)	
3 or more	28	10 (36.0%)	9 (32.0%)	9 (32.0%)	
QOL score					
0 or 1	3	1 (33.0%)	0 (0.0%)	2 (67.0%)	NS
2 to4	26	8 (31.0%)	8 (31.0%)	10 (38.0%)	
5 or 6	24	12 (50.0%)	8 (33.0%)	4 (17.0%)	

\*: percentage of the patients/total patients in each row

wish to undergo less invasive treatment modalities such as CAM.

Prescription medication was found to be the most preferred treatment with 81% of the subjects wishing

to receive medication. At present, desmopressin, diuretics including furosemide, alpha-1 blockers for BPH, and anti-muscarinic agents for OAB are utilized as nocturia pharmacotherapies<sup>9,10,34,35</sup>.

Among these, desmopressin seems to be most useful for reducing frequent nocturnal voidings<sup>2,9)</sup>. Our study revealed that 89% of the subjects visited our clinic with complaints of LUTS and many of them desired to receive medication. It is worth noting that the majority of patients visiting medical institutions with nocturia wish to undergo medical treatment involving drugs.

It is important to reduce the intake of water and salt to improve 24 hour and nocturnal polyuria<sup>12)</sup>. In our previous study, the 24 hour urine volume was an important factor affecting the number of nocturia episodes in the examinees without 24 hour polyuria<sup>36)</sup>. Matthiesen et al reported that salt excretion in urine was significantly higher in nocturics than non-nocturics<sup>37)</sup>. Although the reduction of water and salt intake seems to be useful to treat nocturics, 38% of patients wished to reduce their taking of water and salt, which was smaller than the percentages who wanted to receive medication and exercise in our study. It is worth noting that relatively few patients wanted to change their daily dietary habits to improve their nocturia.

Through exercise like jogging and walking, sleep condition seems to improve, which also leads to an increase in nocturnal bladder capacity<sup>11)</sup>. Sixty-two percents of patients wanted to exercise to treat their nocturia, which was higher than the percentages who opted to undergo CAM, water and salt intake reduction, and sleep improvement. It is speculated that patients who visit hospital to receive treatment for LUTS hope to become healthy through exercise.

Forty percent of the patients preferred sleep improvement, which was almost the same as the percentage who preferred to reduce their water and salt intake. Recently, nocturia has been recognized to be related to sleep conditions<sup>4)</sup>. In particular, length of sleep duration seems to be independently related to nocturia, and sleep reduction seem to be useful for reducing the number of nocturia episodes<sup>38,39)</sup>. Making the bedroom dark and calm also seems to lead to deeper sleep and improve nocturia<sup>4)</sup>. However, elderly people tend to stay in bed for longer than youths<sup>40)</sup>, and it is worth noting that quite number of outpatients did not want to change their sleep habits to treat their nocturia.

Two studies examining community dwelling people revealed that many elderly people think

nocturia is not a serious health problem and a few nocturics seek medical care<sup>14,15)</sup>. Recently, it is proposed that multicomponent therapy including pharmacotherapy and lifestyle modification is effective to treat nocturia<sup>16,36,41)</sup>. Furthermore, treatment modalities desired to undergo by patients with LUTS varied among them<sup>13)</sup>. It was also clarified through our analyses that outpatients with nocturia tend to hope for various treatment modalities based on their preference. Accordingly, personal choice seems to be especially important to decide individual treatment strategy including CAM for nocturia.

In general, number of nocturnal voiding is closely related to treatment strategy of nocturia. Tikkinen et al reported that nocturia with two or more voidings seems to be meaningful and should be interfered clinically<sup>42)</sup>. Our study also revealed that there were significant relationships between number of nocturia episodes and desire for CAM and medication.

Several studies have also clarified that the degree of bother due to nocturia correlates with the frequency of nocturia episodes<sup>42,43)</sup>. There seems to be a considerable degree of relationship between number of nocturia episodes and QOL due to nocturia in our study (**Table 2**). We did not examine degree of bother due to nocturia closely, however, it is presumed that some of the subjects suffered from non-bothersome nocturia in our study<sup>44,45)</sup>. In addition, Endeshaw performed a questionnaire-based survey in community-dwelling older adults and revealed that nocturics who have difficulty going back to sleep are different from those who have no difficulty from a viewpoint of impaired QOL/bother due to nocturia<sup>46)</sup>. In our study, the proportion of patients who hoped for CAM was much higher in those who had decreased QOL due to nocturia than in those who did not. Therefore, asking the patients whether their nocturia is bothersome or not is thought to be clinically important for the evaluation and treatment of nocturics. We used a modified IPSS QOL index to ask nocturia specific QOL question in this study. Although this method is not standard and is too simple for analyzing the bother caused by nocturia<sup>47,48)</sup>, the IPSS QOL index seems to be useful for evaluating nocturics; therefore, in the clinical setting, physicians should ask about impaired QOL/bother due to nocturia using a

simple questionnaire such as the IPSS QOL index.

There are some limitations in this study. First, the number of examinees was small. Therefore, expanding the number of subjects seems to be necessary to obtain standard data of Japanese elderly people. Second, our hospital belongs to a university that educates acupuncturists, moxa-cauterizer, and judo healing therapists, and it also contains the Center of Acupuncture Science of Meiji University of Integrative Medicine. Therefore, some of our patients may visit our hospital seeking oriental medicine-based treatment and so our subjects may not be representative of ordinary Japanese patients. Third, we did not ask the subjects whether they had tried self-treatments such as CAM; over-the-counter drugs; and coping strategies such as reducing their water, alcohol, and/or caffeine intake<sup>13)</sup>. Analysis of this information may have affected the results of this study. Furthermore, patients using CAM or other self-treatments do not usually reveal this information, and physicians should ask patients directly about their self-treatments or coping strategies<sup>19,33)</sup>. Further studies examining many patients visiting various kinds of medical institutions are necessary to clarify the preferred treatment modalities of patients with nocturia.

## V. Conclusion

Patients with nocturia seek various kinds of treatment modalities and their treatment choice depends on personal preference, the number of nocturia episodes, and impaired QOL due to nocturia. Considerable number of patients seek CAM. It is clinically important for physicians to ask nocturics about their preferred treatment modality when deciding on a suitable treatment strategy including CAM.

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# 夜間頻尿を有する外来患者における治療法選択に関する検討 —補完代替医療を中心に—

有働 幸紘<sup>1)</sup>, 日野こころ<sup>2)</sup>, 山本 浩介<sup>1)</sup>,  
角谷 英治<sup>2)</sup>, 北小路博司<sup>3)</sup>, 中尾 昌宏<sup>1)</sup>

<sup>1)</sup> 明治国際医療大学泌尿器科学教室

<sup>2)</sup> 明治国際医療大学基礎鍼灸学教室

<sup>3)</sup> 明治国際医療大学臨床鍼灸学教室

**要 旨** 【目的】 下部尿路障害を有する患者は種々の治療法を希望する傾向があるため、夜間頻尿を有する外来患者における各種治療法の選択と夜間排尿回数および夜間頻尿による生活の質（QOL）との関係について、補完代替医療を中心に検討した。

【対象と方法】 2005年12月から2006年11月の間に、明治国際医療大学泌尿器科外来を受診した80名の患者に対して、夜間頻尿の有無を確認するために3日間の排尿日誌の記録を依頼した。1回以上の夜間排尿が確認された者に対して、国際前立腺症状スコア（IPSS）QOL indexを改変した夜間頻尿によるQOLと5種類の治療法すなわち補完代替医療（CAM）、薬物療法、水分塩分の減量、運動、睡眠の改善に対する受療希望に関する質問票を用いた面接調査を行った。各治療法に対して「受けたい」、「わからない（必要なら受ける）」、「受けたくない」の3項目から回答を得た。さらに対象者を夜間の排尿回数と夜間頻尿によるQOLから、それぞれ3つのグループに分類し、各治療法に対する希望について比較検討した。

【結果】 排尿日誌の記録の不備などにより、27名の患者が除外され、最終的に53名が対象となった。夜間の排尿回数と夜間頻尿によるQOLには有意な相関があった。各治療法に対して「受けたい」と回答した患者の割合は、それぞれCAMが27%、薬物療法は81%、水分塩分の減量は38%、運動は62%、睡眠の改善は40%であった。夜間の排尿回数とCAMや薬物療法に対する受療希望との間に有意な相関が示された。また夜間頻尿によるQOLとCAMに対する受療希望の間にも有意な関連が認められた。

【結語】 夜間頻尿患者の求める治療法は様々であり、その選択は個人的な希望や夜間の排尿回数、夜間頻尿によるQOLに基づいていた。また相当数の患者がCAMを希望していた。CAMを含め患者に適した治療法を決定する際は、夜間頻尿患者において種々の治療に対する彼らの希望を尋ねることが臨床上特に重要であると考えられた。

**Key words** 夜間頻尿, 外来患者, 治療方法, 補完代替医療, 選択