นิพนธ์ต้นฉบับ

ภาวะปัสสาวะบ่อยในเวลากลางคืนและผลของการใช้ยาเดสโมเพรสซินในการรักษาภาวะปัสสาวะบ่อยจากการสร้างน้ำปัสสาวะพิดปกติ

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บทคัดย่อ

วัตถุประสงค์:ศึกษาอุบัติการณ์ของภาวะปัสสาวะบ่อยในเวลากลางคืนที่มีสาเหตุจากการสร้างน้ำปัสสาวะมากผิดปกติ และผลของยาเดสโมเพรสซินในการรักษาภาวะการสร้างน้ำปัสสาวะผิดปกติในเวลากลางคืน ผลของยาต่อคุณภาพชีวิต และผลความปลอดภัยในการใช้ยา

วัสดุและวิธีการ: ผู้ป่วย 34 ราย ที่ได้รับการวินิจฉัยว่ามีภาวะปัสสาวะบ่อยเวลากลางคืนพบว่า 15 ราย อายุเฉลี่ย 67.87 ปี (ระหว่าง 60-80 ปี) มีสาเหตุจากภาวะสร้างน้ำปัสสาวะมากผิดปกติ ผู้ป่วยจะได้รับการรักษาด้วยเดสโมเพรสซิน ขนาด 0.1 มิลลิกรัมเป็นเวลา 4 สัปดาห์ ผู้ป่วยทุกรายถูกเก็บข้อมูล โดยตอบแบบบันทึก frequency volume chart แบบสอบถาม KHQ และสุขภาพทั่วไป และตรวจเลือดหาระดับโซเดียมในเลือดก่อนเริ่มการรักษาและหลังการรักษา 2 และ 4 สัปดาห์

ผลการศึกษา: ความชุกของผู้ป่วยที่มีภาวะสร้างน้ำปัสสาวะผิดปกติ คิดเป็นร้อยละ 44 ในภาวะปัสสาวะบ่อยเวลากลางคืน ค่าเฉลี่ยความถี่ของการปัสสาวะหลังการรักษาด้วยเดสโมเพรสซินที่ 2 สัปดาห์ ลดลงจาก 2.73±0.34 ครั้ง เป็น 1.6±0.64 ครั้ง ที่ 4 สัปดาห์ เป็น 1.68±0.43 ครั้ง (p=0.002) ปริมาณน้ำปัสสาวะในเวลากลางคืนลดลงจาก 437.39±157.14 ซี.ซี. เป็น 255.74±136.18 ซี.ซี. ที่ 2 สัปดาห์ และ 251.87±127.97 ซี.ซี. ที่ 4 สัปดาห์ (p=0.001) พบว่าหลังรักษาคะแนนคุณภาพชีวิตดีขึ้นทั้ง KHQ และแบบทดสอบสุขภาพทั่วไป ผลข้างเคียงของยามีเพียงเล็กน้อยและไม่พบผู้ป่วยที่มีอาการโซเดียมในเลือดต่ำ

สรุป: ภาวะสร้างน้ำปัสสาวะมากผิดปกติเป็นสาเหตุสำคัญในภาวะปัสสาวะบ่อยในเวลากลางคืน ยาเดสโมเพรสซินมีความปลอดภัยและมีประสิทธิผลดีในการรักษาผู้ป่วยที่มีภาวะสร้างน้ำปัสสาวะมากผิดปกติ

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Nocturia and Efficacy of Desmopressin for Treatment of Polyuric Nocturia

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Abstract

Objective: To investigate incidence of polyuric nocturia in nocturia patient and efiicacy, the effect on quality of life, safety of Desmopressin in treatment of polyuric nocturia.

Patients and Methods: Total 34 patients who were verified nocturia which 15 patients were diagnosed polyuric nocturia were recruited .Average age was 67.87 year (range 60-80 years) Desmopressin (0.1 mg) was given to the patients who was diagnosed polyuric nocturia for 4 weeks. After 2, 4 weeks these people were collected symptom by frequency/volume chart and quality of life by King's Health Questionnaire, General Health questionnaire and blood for electrolyte.

Results: Fifteen patients of 34 patients were diagnosed polyuric nocturia (44%). On the average, frequency of nocturnal void decreased from 2.73±0.34 to 1.6±0.64 at 2 wks and 1.68±0.43 at 4 wks (p=0.002) and nocturnal void volume decreased from 437.39±157. 14 ml to 255.74±136. 18 ml at 2 wks and 251.87±127. 97 ml at 4 wks (p=0.001). The scores of KHQ questionnaire and General Health questionnaire were improved after 4 weeks of Desmopressin. Most adverse events were mild. Serum sodium were >130 mmol/l in 14 patients but one <130 mmol/L at 2 wk follow up. No significant symptom of hyponatremia was shown.

Conclusion: Polyuric nocturia is major cause of nocturia. Oral Desmopressin is effective and well tolerated in treatment of polyuric nocturia patients.

Keywords: Nocturia, Desmopressin, Polyuric Nocturia

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Introduction

Nocturia was defined as waking at night to pass urine more than 1 time per night[1]. Nocturia is a common complaint of urologic patients but under-diagnosis of this disease is demonstrated. Nocturia can cause by overactive bladder, polyuria or both. In fact, patients should receive the correct diagnosis for improvement of sleep disturbance, well being and quality of life. In the past; nocturia is a major problem of men and a common prevalence in advance age[2]. But it would neglect because many other problems seem more necessary than nocturia. Today, nocturia is not a little problem because many elderly people disturbed from this problem more over and over[2,3]. Physicians did not solve this problem and were not concerned about this common symptom. In elderly people, circadian pattern of urine flow is paralled by rhythms of renal plasma flow and glomerular filtrate rate until around age of 60. Greater proportion of urine at night time become evident [2,4,5]. Several studies, elderly people produce urine greater than 33% of all urine volume per day because they decrease antidiuretic hormone (ADH) or vasopressin that can cause polyuric nocturia.

To this point, we think nocturia will improve if we can reduce urine at night time. Desmopressin hormone (Synthetic analogue of vasopressin) should improve the nocturia symptom that cause by polyuria.

Patients and Methods

Thirty four from 58 patients [male 20 patients, female 14 patients; age 60-80 years] with lower urinary tract symptom were diagnosed nocturia and 15 patients [male 9 patients, female 6 patients] were diagnosed polyuric nocturia, this group of patients were collected to take Desmopressin. Between October 2006-February 2007, polyuric patients who had been treated with Desmopressin were included. Patients age >18 yrs were eligible for study if they had nocturia (>1 time void per night) unrelated to diabetes insipid us or excessive/ abnormal fluid intake. Exclusion criteria included DM, CHF with sign of volume overload, previous diagnosis of abnormal ADH, take diuretics at bed time, sleep apnea syndrome and patient in nephrosis status.

All polyuric patients took 0.1 mg of Desmopressin at bedtime. During the study; From 1 hour before bedtime to 8 hours after taking medication, patients were advised to drink only if thirsty and avoid tea, coffee, Cola, alcohol and other liquids with a diuretic effect at night. Patients kept a diary with frequency volume chart to record bedtime and time of rising, time of nocturnal voids, nocturnal urine volume, daily fluid intake and frequency of nocturia. After 2 weeks and 4 weeks of treatment, patients came back to return frequency/volume chart. Patients also answered the questionnaire [KHQ and General Health] that we gave to them before treatment and 4 weeks after received Desmopressin. At the Last week, they were asked for his/her general health symptom and symptoms after taking Desmopressin.

Safety assessment at 2 weeks and 4 weeks, serum sodium levels, vital signs were monitered through-out the study and adverse effect were recorded at OPD Uroclinic.

Study end points

The primary efficacy end point was frequency of nocturnal void and mean of nocturnal void volume per day after treatment compared with baseline before treatment. Secondary endpoint was also assessed effect on quality of life. Safety was evaluated from laboratory data with emphasis on serum sodium and reported adverse events. At last, we can assess the proportion of patients who improve from the treatment.

The primary object were tested using Wilcoxon

rank some test, Results were presented using P values. Questionnaire analysis was based on frequency counts of individual questions. Serum sodium was also calculated with Wilcoxon rank some test. The incidence of polyuric nocturia and nocturia was proportion of population in this study.

Results

In population of the studied, we could demonstrate the proportion of polyuric nocturia and nocturia. The number is 15 out of 34 patients (44%). Average age was 67.87 year (60-80 years). Then we gave polyuric nocturia patients with Desmopressin to measure outcome.

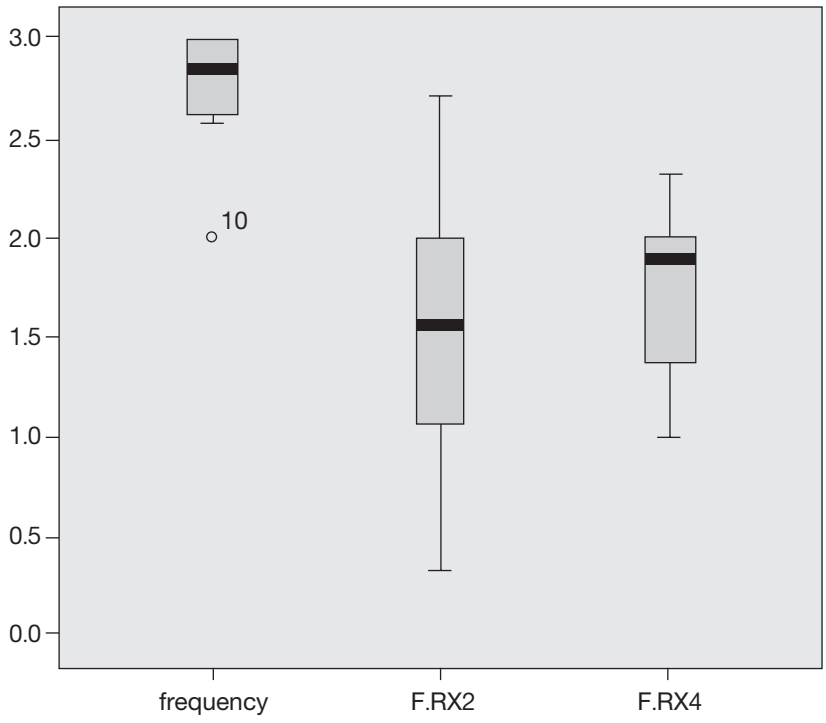
From statistical analysis of frequency/volume chart, the mean frequency of nocturnal void, volume of nocturnal void were decreased as shown in Table 1 and graph 1, 2

Both frequency and nocturnal void volume were significantly improved.

Table 1 *Result of Desmopressin Treatment.*

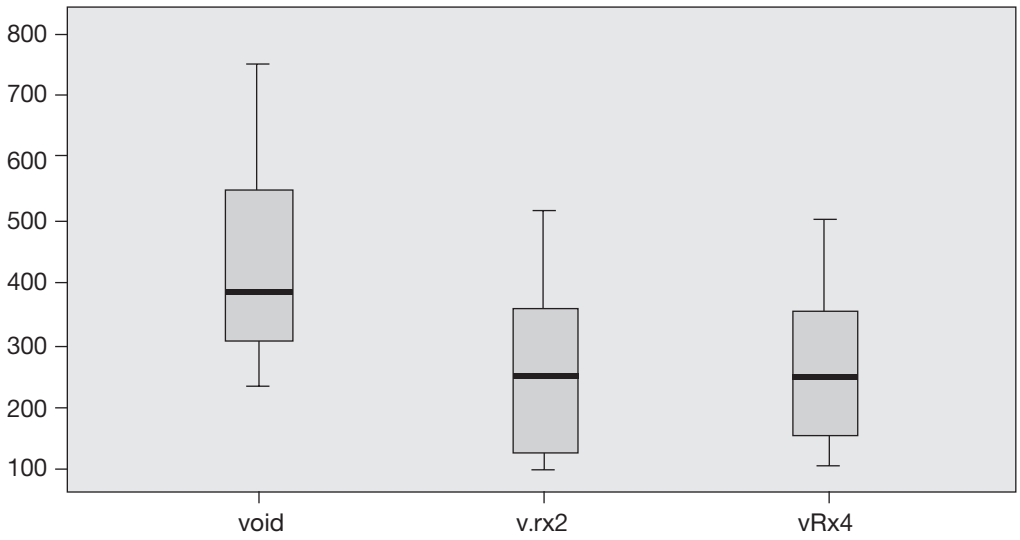
Parameter	Baseline	2 wks after Rx	4 wks after Rx	P value	proportion	% improved
frequency	2.72 ± 0.34	1.60 ± 0.64	1.68 ± 0.43	p=0.002	13/15	87
Nocturnal void volume	437.39 ± 157.14	255.74 ± 136.18	251.87 ± 127.97	p=0.001	14/15	93

Graph 1 *frequency parameter after Desmopressin treatment*



F.RX2 = frequency of void at 2 weeks, F.RX4 = frequency of void at 4 weeks

Graph 2 *Nocturnal void volume after Desmopressin treatment*



v.rx2 = void volume (ml) at 2 weeks, vRX4 = void volume (ml) at 4 weeks

Quality of life

The two exploratory questions by KHQ questionnaire and General Health questionnaire revealed difference in quality of life score that reached statistical significance. (Table 2 and Graph 3)

Adverse effects

Two patients complained of dizziness and headache after Desmopressin administration. No serious side effects occurred. The mean serum sodium level decreased during treatment [Table 3 and Graph 4]. The decrease level was pronounced after 2 weeks of treatment. One patient had serum sodium below than 130 mmol/L, but he had no symptoms. Although people in this study had lower serum than baseline in the first 2 week statistically (p=0.001) but in 4 weeks, the mean serum sodium was not statistically changed. No symptoms of hyponatremia were revealed. There were mild non-specific symptoms such as headache and dizziness.

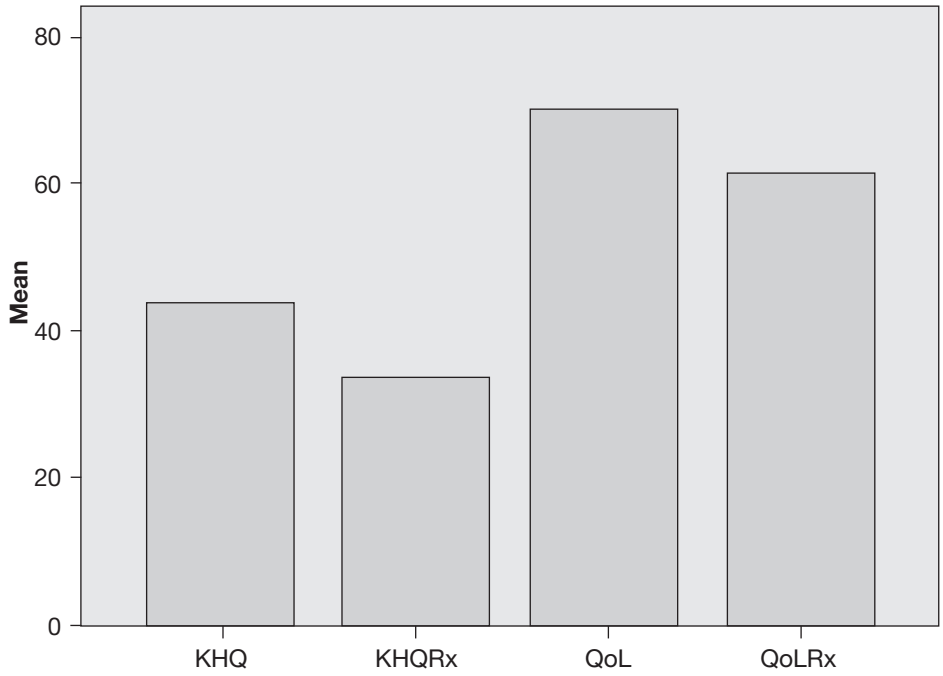
Discussion

Nocturia influences general health and quality of life. One consequence of nocturia is sleep deterioration that increases day time sleepiness, loss of energy[6]. Nocturia people were also prone to different somatic symptoms such as muscle clamps in calves, leg tinglings[7]. It was also found that noc-

Table 2 *Effect of Desmopressin in quality of life*

parameter	pretreatment	postreatment	P value
KHQ score	43.73 ± 4.65	33.87 ± 6.40	p=0.001
General Health score	70.47 ± 4.67	61.47 ± 4.22	p=0.001

Graph 3



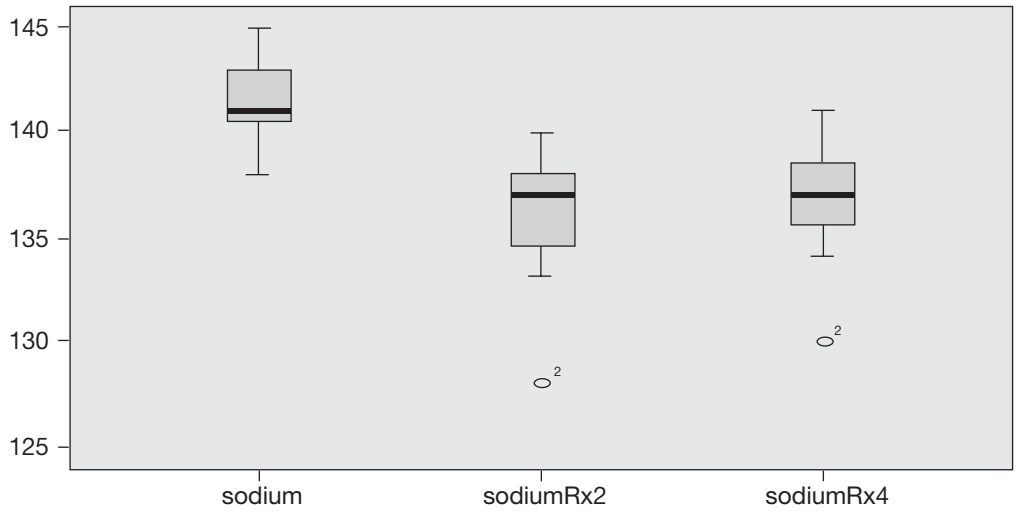
KHQ = KHQscore pretreatment, KHQ Rx = KHQscore posttreatment

QoL = General Health score pretreatment, QoLRx = General Health score post treatment

Table 3 *Serum sodium (mmol/L)*

case	baseline	2 wks after treatment	4 wks after treatment
1	143	140	140
2	139	128	130
3	145	139	141
4	138	133	134
5	141	137	137
6	145	138	138
7	143	135	136
8	145	138	138
9	141	134	135
10	139	134	134
11	141	137	137
12	143	139	140
13	140	137	138
14	141	137	139
15	143	136	136

Graph 4 *Serum sodium parameter after Desmopressin treatment.*



turia was the most common symptom among patients with isolated systolic hypertension[8] and influenced irregular heart beats, DM, stroke. As mentioned earlier,[9-11] nocturia effects on well-being and quality of life were noted. Therfore, we have examined such patients to determine the alternative treatment on nocturia,which is not simply limited to antimuscarinic or anticholinergic drug[12].

There were 3 main pathophysiologic categories for nocturia[13]: nocturnal polyuria (in which a relatively higher proportion of urine is produced and voided during night time compared with day time), low bladder capacity (caused by obstruction, DI or cystitis) and mixed nocturia (combination of nocturnal polyuria and low bladder capacity), however the major of mechanism in nocturia is polyuric nocturia and mixed type.

In this study; we collected data of patients aged 60-80 years. The results of nocturia and polyuric nocturia in population are as same as the previous report[14]. Decreasing polyuria at night time will improve their nocturia and quality of life. A factor resulting in polyuric state is decrease in ADH (Antidiuretic Hormone) or Vasopressin. Taking Desmopressin will improve this symptom. There was a relationship between ADH and elderly: in old age; ADH is decreased and sensitivities of kidney with ADH are decreased that influence in decreasing the concentration of urine[15]. Desmopressin (Minirin) which is a synthetic analogue of vasopressin should improve polyuric noturia people. In Sweden, UK, the Nether-lands,Denmark and USA. Desmopressin has been used in tritration dose for 3 weeks which are different from this study. Results of Oral Desmopressin is an effective and well-tolerated treatment for patients with nocturia[16,17]. The studies confirm the efficacy of antidiuretic effect of Desmopressin that results in higher clinical response, which decrease in the number of nightly voids and decrease in void volume. The results of exploratory questionnaire also indicated an improvement in quality of life.

This study was based on safety consideration. We used low dose of Desmopressin because Thai people were different from foreign people in body weight and BMI. The dose for Thai people should further investigate in the future. Hyponatremia is only serious potential adverse effect associated with the use of Desmopressin in nocturia[18,19]. In this study,

only one patient had serum sodium value <130 mmol/L indicative of clinically relevant hyponatremia (at 2 weeks after treatment). But in 4 weeks, he returned to normal serum sodium and no change in serum sodium was statistically significant. All patients had no symptoms of hyponatremia. They had mild symptoms such as headache and dizziness. We note that treatment of Desmopressin is safe.

The impact of Nocturia on quality of life is being recognized[19]. In this study, The scores from KHQ questionnaire and General Heallth quality of life scores were improved after treatment. These results may prove to determinine the effects on this treatment.

Conclusion

Polyuric nocturia is main cause of Nocturia. Oral Desmopressin is effective and well tolerated treatment for polyuric nocturia.

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