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EFFECTIVENESS OF AN ANTI-INFLAMMATORY DRUG, LOXOPROFEN, IN PATIENTS WITH NOCTURIA

Hypothesis / aims of study

Nocturia is a major health problem for benign prostatic hyperplasia (BPH) and/or over active bladder (OAB) patients.[1] Nocturia is a syndrome involving the interruption of sleep by the urge to void. Nocturia impairs quality of life, and is one of the main problems for BPH/OAB patients, along with urinary incontinence and difficulty in urination.[1] Recently, there have been some reports indicating that nonsteroidal anti-inflammatory drugs (NSAIDs) are effective in patients with nocturia. [2,3] But the mechanisms of this preventive effect are not fully understood. Prostaglandins (PGs) have various effects on the kidney, bladder, urethra and sympathetic and parasympathetic nervous systems. PGs inhibit Na^+ tubular reabsorption and ADH, decrease aldosterone secretion and cause glomerular vasodilatation, natriuresis and diuresis. PGs are reported to increase the detrusor tone, relax the urethra and reduce intraurethral pressure. In particular, PGE and PGF increase the tone of the detrusor smooth muscle and enhance micturition. PGs increase acetylcholine from nerves and activate capsaicin-sensitive afferents in the urinary bladder. Loxoprofen sodium (loxoprofen) is one of the most common NSAIDs in Japan, and a potent PG-synthesis inhibitor. Loxoprofen is a non-selective cyclooxygenase (COX) inhibitor, and has fewer side effects in the stomach than other NSAIDs. Loxoprofen's active metabolite inhibits PGE2 production in leukocytes three times stronger than indomethacin. Furthermore, loxoprofen is also reported to have a relatively short half time among NSAIDs. In this study, we attempted to investigate the preventive effect of loxoprofen and its possible mechanism in BPH/OAB patients with nocturia.

Study design, materials and methods

This study was administrated to BPH and/or OAB patients who had presented with nocturia. 15 BPH and/or OAB patients (13 males and 2 females) aged 62-76 (71.1± 1.5) with three or more voids per night were involved in this study. These patients were carefully provided information about the risk and possible side effects of NSAIDs before starting this study. These patients had received standard drug therapy, but still complained of nocturia more than two times per night. Before this treatment, 13 patients were treated with oral alpha-blocker medication (tamsulosin HCl in 8 patients, naftopidil in 4 patients and urapidil in 1 patient), 2 patients with anticholinergic medication (propiverine HCl), and 2 patients with antidepressants (ethyl loflazepate) because of BPH and/or OAB. All patients had undergone general urological studies as well as urodynamic studies in order to establish the proper diagnosis. The patients took a single 60 mg tablet of loxoprofen prior to sleeping at night. Before and one week after the initiation of this therapy, the effects of this treatment were assessed as excellent, improved, unchanged or worsened using a questionnaire and a frequency volume chart before and after the treatment. We also carefully observed the side effects in these patients before and after the treatment. Statistical analyses among the groups were performed using analysis of variance and the multiple comparison Fisher's tests. $P < 0.05$ was regarded as the level of significance.

Results

The patients' background data and the questionnaire data are shown in Table 1. In the questionnaire, 7 patients answered "excellent," 6 patients "improved," 2 patients "unchanged" and no patients answered "worsened". Gastric discomfort and general fatigue were both observed in one patient. The data of the frequency volume chart are shown in Table 2. Our data indicated that the total voids per night and total urine volume per night were significantly reduced after the treatment, and that total voids per day, total urine volume per day and single-voided volume at night were not significantly changed after the treatment.

Interpretation of results

Some reports have indicated that NSAIDs are effective for patients with nocturia. Le Fanu reported that aspirin is effective for symptoms of nocturnal polyuria.[2] Al-Waili reported that indomethacin markedly reduced bed-wetting episodes and decreased the frequency of voiding in enuretics with small or normal functional bladder capacity.[3] Al-Waili suggests that the mechanisms of this effect include decreasing the urine volume, the clearance of free water and urinary electrolytes and possible effects on bladder and urethral contraction, all by means of inhibiting NO and PG synthesis.[3] It is important to investigate the mechanisms of this preventive effect. PGs have various effects on many systems in vivo, including renal and urinary tract system. NSAIDs are reported to reduce GFR and urine volume, to decrease detrusor muscle tone and to increase urethra tone. Thus, the possible mechanisms of this effect are to reduce urine production during sleeping, to reduce detrusor smooth muscle tone and increase urethral tone, or to block the afferent nerve from the bladder. In this study, we demonstrated that loxoprofen significantly reduces nocturia and urine volume during sleeping. Furthermore, there is no significant difference in single-voided volume at night before and after loxoprofen medication. Our data indicated that this effect is caused by a decrease in urine volume at night. As the single-voided volume at night is similar before and after this treatment, loxoprofen appears not to directly affect the lower urinary tract smooth muscle or afferent nerve system.

Concluding message

loxoprofen improves nocturia, and the main mechanism of this effect is by decreasing urine production during sleeping. As NSAIDs have serious side effects in many systems, careful observation is required.

References

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TABLE 1. BACK GROUND OF PARTICIPATED PATIENTS IN THIS STUDY

PATIENT NUMBER		MEDICATION		EVALUATION OF THE TREATMENT	
Male	13	tamsulosin	8	excellent	7
Female	2	naftopidil	4	improved	6
		urapidil	1	unchanged	2
Total	15	propiverine	2	worsened	0
Age	71.1± 1.5	ethyl loflazepate	2	total	15

TABLE 2. ANALYSIS OF FEQENCY VOLUME CHART BEFORE AND AFTER LOXOPROFEN TREATMENT

	Voided /day	voided /night	urine volume (ml) /day	urine volume (ml) /night	single voided volume (ml) /night
Before	9.97 ± 0.81	3.82 ± 0.25	1349 ± 81	567 ± 46	143 ± 13
After	8.99 ± 0.74	1.82 ± 0.27*	1258 ± 91	325 ± 51*	149 ± 10

Data are mean ± S.E.M. of 15 patients in each group. *) Significantly different from Before treatment. $P < 0.05$ is level of significance.

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