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Imidafenacin mediates nocturnal antidiuresis through concentration of urine osmolality

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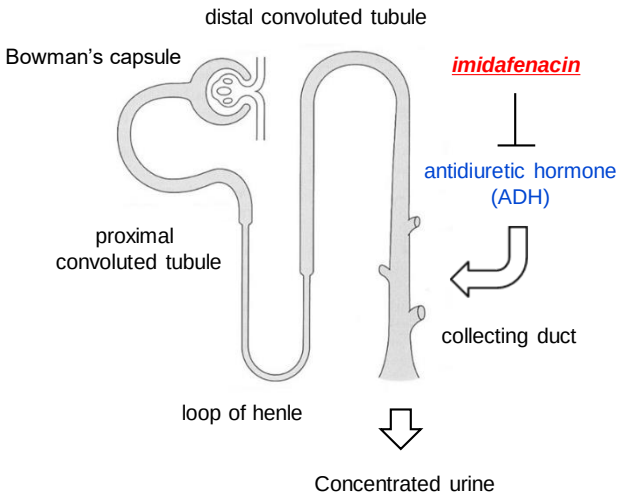
Summary/Conclusion

- This is the first study to evaluate the effectiveness of imidafenacin on concentration of Urine Osmolality (Uosm) in clinical practice.
- We found that the beneficial effects of nocturnal antidiuresis of imidafenacin depend on patient's low baseline levels of Uosm.

Introduction

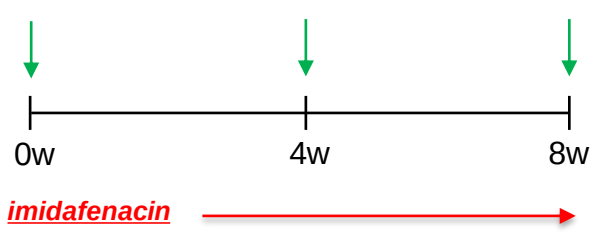
- Imidafenacin with high affinity to muscarinic type 3 receptor is prescribed for alleviating OAB symptoms. Several urologists reported that imidafenacin was effective for decreasing nocturnal urine volume [1,2]. However, However, it remains to be elucidated the mechanism.
- Recently, one basic research suggested that imidafenacin would have facilitative effects on antidiuretic hormone (ADH) related pathway [3]. Figure modified from [4] indicates possible mechanism of imidafenacin mediating that pathway.
- We hypothesized that imidafenacin-induced decrease of urine volume at night might be derived from concentration of urine osmolality (Uosm) based on the report. The objectives are to clarify the mechanism of its antidiuresis and patient's characteristics which respond to its antidiuretic effectiveness in clinical practice.



Methods

- The patients who complained the symptom of nocturia and had not been administered anticholinergic agent entered our study.
- We evaluated the study variables described below every four weeks until the eight weeks visit after administration of imidafenacin.

IPSS (International prostate symptom score)
OABSS (Overactive bladder symptom score)
Uosm at first void in the morning
Estimated 24HUNa (24-hour urinary Na excretion) [5]
Frequency volume charts (FVC)
Npi (Nocturnal polyuria index)



Results

- A total of 56 patients entered our study (Male 36, Female20).
- In all patients, Npi decreased significantly, however Uosm did not change.
- Furthermore, no significant change of 24-hour urine volume and 24HUNa have been observed.

Table1

All patients (n=56) M:36, F:20	baseline	4 week	8 week
24-hour urine volume (ml)	1672±750	1764±819	1567±611
Npi	0.43±0.12	**0.37±0.14†**	**0.39±0.14†**
Uosm (mOsm/l)	496±172	515±185	531±173
24HUNa (mEq)	173±45	175±43	171±44
incidence of nocturia	3.5±1.4	3.2±1.4	3.2±1.5 †
incidence of daytime urination	6.6±2.4	6.1±2.1 †	5.9±2.4 †
IPSS	13.7±6.7	12.4±6.7 †	12.1±6.8 †
OABSS	6.8±3.3	5.4±2.9 †	4.7±2.8 †

Paired t-test was conducted to compare each variable with baseline.
† P＜0.05 was considered as statistically significant.

- We classified the patients into two groups according to baseline Uosm: under and over **500mOsm/l** (Groups A and Groups B, respectively).
- Npi decreased and Uosm increased significantly only in GroupA with low baseline Uosm.

Table2

GroupA (n=29) Baseline Uosm<500	baseline	4 week	8 week
24-hour urine volume (ml)	1796±925	1950±1063	1689±770
Npi	0.43±0.13	0.37±0.12†	**0.35±0.12†**
Uosm (mOsm/l)	360±79	414±147	**461±153 †**
24HUNa (mEq)	172±50	173±40	170±48
incidence of nocturia	3.6±1.5	3.3±1.6	3.0±1.7 †
incidence of daytime urination	7.0±2.7	6.4±2.4	6.8±2.8
IPSS	14.7±7.3	12.5±7.2 †	13.3±7.8 †
OABSS	7.1±3.5	5.0±3.3 †	4.8±3.1 †

GroupB (n=24) Baseline Uosm>500	baseline	4 week	8 week
24-hour urine volume (ml)	1536±419	1542±400	1381±439
Npi	0.41±0.11	0.35±0.13†	0.40±0.13
Uosm (mOsm/l)	660±96.9	646±143.0	595±163.5
24HUNa (mEq)	175.1±42.4	176.2±47.3	171.5±44.0
incidence of nocturia	3.48±1.24	3.41±1.27	3.39±1.30
incidence of daytime urination	6.17±2.18	6.09±1.83	5.49±2.11†
IPSS	12.7±6.25	12.0±6.30	11.4±5.58
OABSS	6.21±3.29	5.60±2.52†	4.86±2.72†

Paired t-test was conducted to compare each variable with baseline.
† P＜0.05 was considered as statistically significant.

Discussions

- Imidafenacin has been reported to have antidiuretic effect by enhancing vasopressin-related responses, [3] thus, we hypothesized that concentration of Uosm could be one of the mechanisms of reducing Npi after imidafenacin treatment based on the previous basic research.
- In all the patients, Npi decreased with no significant change of Uosm.
  The patients with low baseline Uosm (GroupA) significantly decreased their Npi and increased Uosm.
  However, the patients with high baseline Uosm (GroupB) have not achieved sustained decrease of Npi and increase of Uosm.

→ Imidafenacin's antidiuretic effect through vasopressin-related responses is considered to depend on patient's low baseline Uosm.

- Our results have shown that Npi has decreased significantly in all patients after administration of imidafenacin with no significant change of 24-hour urine volume.

→ It was possible that nocturnal urine volume was shifted to daytime as previously reported [1].

- No significant change of 24HUNa was observed.

→ The amount of urinary Na excretion was reported to affect night time urine volume [6].
So this kind of effectiveness on nocturnal urine volume could be excluded.

References

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