Abstract

Nocturia is defined as the number of times urine is passed during main sleep. Prevalence of nocturia is around 70% and 11-44% for age group 70-80 and 20-40 years respectively. Although, it is clearly prevalent, nocturia is just seen as a small part of lower urinary tract symptoms (LUTS). The objective of the study was to review nocturia in terms of diagnostic and management strategies among Indonesian urologists. This was a descriptive cross-sectional study. A self-constructed questionnaire was distributed to Indonesian urologists from August 2017 until August 2018 using consecutive sampling method. 124 urologists out of 400 urologists participated. In this study most of the urologists had to face 1-5 cases nocturia per month. Age of patients were mostly 50-65 years old and affecting more men than women (66.9% vs 16.9% respectively). Only 45% of urologists utilized bladder diary regularly to assess nocturia. Nearly 90% urologist opted for lifestyle intervention to manage nocturia. Desmopressin was used by only 20.2% urologists to treat nocturia. Anti-muscarinic and beta-3 agonist were used more often than desmopressin to treat nocturia. To conclude, diagnostic strategies for nocturia are mostly in line with available guidelines except for bladder diary which was only used routinely by 45% of urologists. As for treatment, desmopressin was still prescribed less frequently than OAB drugs for nocturia.

Keywords: nocturia, urology, LUTS, desmopressin, functional.
Introduction
Nocturia is defined as the number of times urine is passed during the period of main sleep. Having woken to urinate for the first, each urination must be followed by sleep or the intention to sleep.¹ It is prevalent across age groups and genders with similar prevalence between men and women of around 70% and 11-44% for age group 70-80 and 20-40 years respectively.² ³ Nocturia is the main cause of sleep disturbance compared to other causes namely anxiety, worries and other causes hence, it is associated with mood disturbance, cognitive and memory impairment, reduced performance at work, increased morbidity and mortality, risk of falling, diabetes, cardiovascular disease and depression.⁴ Although it is clearly prevalent, nocturia has not been the prime research interest as it is just seen as a small part of lower urinary tract symptoms (LUTS) which is usually suggested to be caused by either benign prostatic obstruction (BPO) or overactive bladder (OAB). In reality, the most common cause of nocturia is nocturnal polyuria⁵ which comprises 76-88% of the cases.⁶ Nocturnal polyuria is demonstrated when nocturnal urine output exceeds 20% of 24 hour urine output in the young or more than 33% in the elderly.⁷

Different pathophysiology underlying nocturia such as cardiovascular disease, oedema of the lower limb, sleep apnea, nephrological cause and pharmacotherapy have been identified.⁸ However, this symptom is unfortunately still underdiagnosed and undertreated. In Indonesia the situation is similar where nocturia is often being treated as BPO in men and OAB in most women. Currently there is no national guideline or consensus specific for nocturia. Its management algorithm is usually included in other guidelines such as BPO and OAB. The objective of the study was to review nocturia in terms of diagnostic and management strategies among Indonesian urologists.

Methods
A self-constructed questionnaire was distributed to Indonesian urologists from August 2017 until August 2018 during various urology scientific meeting using a consecutive sampling method. It consisted of nine questions covering characteristics of the urologists, nocturia patients’ characteristics, diagnostic tools and management strategies for treating nocturia. According to Ethics Committee Faculty of Medicine Universitas Indonesia-Cipto Mangunkusumo National Hospital, ethical approval was not required for this study.

Results
One hundred and twenty-four Indonesian urologists out of 400 urologists participated and returned the questionnaire. Most urologists worked in government teaching hospital (41.9%), followed by non-government non-teaching hospital (31.5%) and were mostly in 30-39 age group with two years of work experience. The characteristics of respondents are shown in Table 1.

| Characteristics of Respondents | Frequency (%) |
|-------------------------------|--------------|
| Age (years)                   |              |
| 25-29                         | 27 (22%)     |
| 30-39                         | 51 (41%)     |
| 40-49                         | 31 (25%)     |
| 50-60                         | 14 (11%)     |
| > 60                          | 2 (1%)       |
| Work experience (years)       |              |
| <1                            | 6 (4.8%)     |
| 1                             | 14 (11.3%)   |
| 2                             | 30 (24.19%)  |
| 3-5                           | 29 (23.4%)   |
| 5-10                          | 22 (17.7%)   |
| 11-20                         | 22 (17.7%)   |
| >20                           | 1 (0.08%)    |
| Types of hospital/clinic      |              |
| Government teaching hospital  | 52 (41.9%)   |
| Government non-teaching hospital | 39 (31.5%) |
| Private non-teaching hospital | 24 (19.4%)   |
| Teaching private hospital     | 4 (3.2%)     |
| Private clinic                | 5 (4%)       |
| Location of practice          |              |
| Jabodetabek                   | 32 (25.8%)   |
| Java non Jabodetabek          | 64 (51.6%)   |
| Outside Java                  | 28 (22.6%)   |

Most of the urologists had to face up to 1-5 cases nocturia per month which means 12 – 60 cases per year. Age of patients were mostly 50-65 years old and affecting more men than women (66.9% vs 16.9% respectively). Nocturia was more commonly seen together with other storage symptoms (43.4%) and rarely seen as an only symptom (9.7%). Most patients had experienced the symptoms between 1-3 months before they sought help. The characteristics of nocturia patients are described in Table 2.
Table 2. Nocturia Cases Managed by Urologists

| Nocturia Cases Managed by Urologists | Total |
|-------------------------------------|-------|
| Mean Number of Cases (per month)    |       |
| 1-5 cases                           | 61 (49.2%) |
| 6-10 cases                          | 24 (19.4%) |
| 11-20 cases                         | 15 (12.1%) |
| >20 cases                           | 24 (19.4%) |
| Age Group (years)                   |       |
| <18                                 | 18 (14.5%) |
| 18-30                               | 4 (3.3%) |
| 30-49                               | 5 (4%) |
| 50-65                               | 62 (50%) |
| >65                                 | 35 (28.2%) |
| Gender                              |       |
| Men                                 | 83 (66.9%) |
| Women                               | 21 (16.9%) |
| Equal number of patient gender      | 20 (16.1%) |
| Period of Chief Complaint           |       |
| <2 weeks                            | 5 (4.1%) |
| 2-4 weeks                           | 20 (16.1%) |
| 1-3 months                          | 40 (32.3%) |
| >3 months                           | 34 (27.4%) |
| >6 months                           | 25 (20.2%) |
| Nocturia Symptoms                   |       |
| Only nocturia symptoms              | 11 (9.7%) |
| Accompanied by storage symptoms     | 58 (43.4%) |
| Accompanied by voiding symptoms     | 34 (28.3%) |
| Equal number of storage and voiding | 21 (18.6%) |

Table 3. Diagnostic Tools Used for Nocturia

| Diagnostic Tools for Nocturia (n=124) | Total |
|---------------------------------------|-------|
| Anamnesis                             | 122 (98.4%) |
| Physical examination                  | 107 (92.7%) |
| Bladder diary                         | 77 (65.6%) |
| Urinalysis                            | 94 (79.8%) |
| Blood Glucose level                   | 54 (45.2%) |
| Renal function test                   | 32 (53.4%) |
| Uroflowmetry                          | 19 (36.3%) |
| PVR                                   | 18 (33.9%) |
| Diabetes insipidus examination        | 20 (16.1%) |
| Abnormal cardiac function test        | 16 (12.9%) |
| Sleep disturbance examination         | 4 (3.2%) |
| Urodynamics                           | 13 (13.7%) |
| Urinary tract ultrasound              | 84 (67.7%) |
| Cystoscopy                            | 1 (0.8%) |

For diagnostic purposes, most Indonesian urologists used history (98.4%), physical examination (92.7%), urine analysis (79.8%) and urinary tract ultrasound (67.7%). Bladder diary was utilized by 55.6% of urologists to diagnose nocturia and only 45.2% of them regularly asked nocturia patients to fill out bladder diary. Diagnostic tool(s) chosen for nocturia are depicted in Table 3.

Regarding nocturia treatment education and lifestyle intervention were the most prescribed followed by oral pharmacotherapy namely anti muscarinic (65.3%), beta-3 agonist (28.2) and desmopressin (20.2%) as seen in Table 4.

Table 4. Choice of Therapy for Nocturia

| Choice of Therapy for Nocturia (n=124) | Total |
|---------------------------------------|-------|
| Education and lifestyle modification  | 110 (88.7%) |
| Desmopressin                          | 25 (20.2%) |
| Antimuscarinic                        | 81 (65.3%) |
| Beta 3 agonist                        | 35 (28.2%) |
| Imipramine                            | 17 (13.7%) |
| Anti diuretics                        | 4 (3.2%) |
| Sleeping medication                   | 2 (1.6%) |
| Physiotherapy                         | 23 (18.5%) |
| Consultation to specialist/sub-specialist | 18 (14.5%) |
| Alpha Blocker                         | 2 (1.6%) |
| Operation                             | 2 (1.6%) |

Discussions

Nocturia has been reported to be the most common lower urinary tract symptom. An internet cross-sectional study done in United States, United Kingdom and Sweden involving 21,000 participants revealed that nocturia is the most prevalent symptom with rates of 69% and 76% of men and women respectively.\(^9\) This is in contrast with this study where Indonesian urologists are facing more men with nocturia than women. This might be because men rather than women tend to seek treatment from urologists. Nocturia is more prevalent in older age group as has been reported in several studies.\(^2,3\) Another recent retrospective cross-sectional study involving 22,300 individuals reported that 24% had nocturia and the median age for nocturia group was 55.2.\(^10\) This is in agreement with this study, the most common age seen with nocturia was above 50 years old. Around this age metabolic syndrome, comorbidities, prostate enlargement, menopause which could contribute to nocturia may have already occurred.
Nocturia can be one of the symptoms of OAB spectrum alongside of other storage symptoms such as urgency, urinary incontinence and frequency. Most of Indonesian urologists faced nocturia complaint with other storage symptoms followed by combination with voiding symptoms.

Almost all urologists used history and physical examination as diagnostic tools for nocturia. This is in accordance with available guidelines which state that history and physical examination are recommended for diagnosis. Through history taking it is pivotal to get information on LUTS, haematuria, dysuria, cardiac, respiratory, neurological, sleep, gynaecological, psychiatric problem(s), drinking and eating habits and medication affecting diuresis. Physical examination consists of cardiac, respiratory, abdominal, prostate, female pelvic and ankle edema assessment.

The European Association of Urology (EAU) and ICS also recommend urine analysis to rule out infection, haematuria and diabetes. This study shows that urine analysis was used by nearly 80% of urologists. According to ICS consensus it is recommended to diagnose nocturnal polyuria in nocturia patients using a bladder diary before treating them with desmopressin although there was no consensus on how many days the bladder diary should be. Parameters of bladder diary most commonly used for nocturia are maximum voided volume, voiding frequency and ratio of nocturnal compared to the total 24-hour urine production.

This current study describes that only 45% of Indonesian urologists routinely utilized bladder diary to assess nocturia, probably because it is challenging and time consuming for both the patient and the physician. Assistance from a trained nurse, caregiver, and or family might be one of the solution.

Life style intervention such as change of diet, weight loss, physical exercise and modification of fluid intake are considered relevant in nocturia. Most urologists (nearly 90%) opted for lifestyle intervention.

Desmopressin was used by only 20.2% Indonesian urologists to treat nocturia despite the fact that it is the only evidence-based pharmacotherapy for nocturia. Reports from several studies have concluded that the use of desmopressin in clinical setting is still rare due to limited knowledge about the drug, dosage and safety profile especially the risk of hyponatremia specifically in the elderly.

Nocturia patients are usually treated first with OAB/BPO drugs rather than desmopressin as also demonstrated in this study, where anti muscarinic and beta-3 agonist (OAB drugs) was used more often than desmopressin to treat nocturia.

Conclusion
Nocturia is prevalent and remains a challenge for urologists. Diagnostic strategies are mostly in line with available guidelines except for bladder diary which was only used routinely by 45% of the respondents. As for treatment, desmopressin was still prescribed less frequently than OAB drugs for nocturia. It is pivotal to establish our own national guideline for nocturia and to raise awareness on the importance of bladder diary for diagnosis and desmopressin as the first line pharmacotherapy for nocturia.

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