

POPULARIZING SUMMARY

Nocturia, arising during sleep because of the need to pass urine, is a most bothersome symptom which degrades sleep quality, leading to daytime fatigue while impacting general health and quality of life in both patients and bedmates. In more severe cases, life expectancy may be significantly shortened by the condition.

Nocturia stems from a vast set of causes, touching a diverse population. Prior studies indicated that nocturia is both common and bothersome in men and women; responsiveness to treatment tends to vary with its many causes. We felt that research on cause and corresponding treatments would illuminate how the condition presents across varying populations of men and women of differing age categories, while estimating the prevalence of the condition. Only then could we successfully discover and optimize diagnostic tools, management plans, and therapeutic strategies and make progress towards our goal – to create evidence-based individualized treatment plans for our patients.

Our research revealed that there is a significant association between age and cause of nocturia. As individuals age, nocturia shifts from predominantly issues with bladder storage capacity in younger patients (<50 years) towards overproduction of urine at night in older patients (>70 years). This motivated us to more keenly customize our diagnostic tools and adjust our clinical approach to meet each patient's individualized needs.

To do so, we focused first on patients presenting with nocturia due to small bladders, a subset of patients who were less frequently studied and for whom existing management methods had failed to provide clinically significant relief. Our analysis suggested that, for those with small bladders, behavioral modifications (drinking according to thirst rather than a pre-supposed goal) may be more effective than intervention with certain widely used bladder and/or prostate medications. This highlighted a gap in our therapeutic toolbox – that no medication had a clinically significant effect on bladder capacity, day or night.

But what about those conditions for which drug therapy does exist? We investigated whether a novel formulation of desmopressin, a drug which causes the kidneys to temporarily hold back from excreting water, had a clinically significant impact in the treatment of patients with nocturia. Our trial uncovered an innovative, clinically effective, and safe treatment for patients with nocturia – the desmopressin orally disintegrating tablet. Outcomes correlated with dosing, with a greater reduction in nocturnal voids and nocturnal urine volume associated with larger doses of desmopressin administered.

While the aforementioned finding helped pave the way forward for targeted drug design and therapy optimization, it was meaningful only insofar as the population which stood to benefit was known. It was in an effort to define this population that we conducted a review of >10 years of outpatient records: data which was leveraged to publish the first prevalence estimate of the Nocturnal Polyuria Syndrome (NPS). NPS is thought to cause excessive urine production at night in patients who are otherwise completely healthy. Data demonstrated that NPS represented a significant proportion of those presenting with nocturia, between 17-41%, illuminating a population of patients for whom desmopressin may reasonably be considered as “replacement therapy” for inadequate nocturnal production of the body's own hormone designed to spare water from unnecessary expulsion by the kidneys with resultant nocturia.

The body of work described herein represents more than two decades of research which shaped the diagnosis and classification of nocturia, informed its treatment, and motivated improvement in patient-centered outcomes. Notwithstanding our contributions to the field, many questions remain unanswered. It behooves us, therefore – myself, my broader research team, fellow physician-scientists, and successors – to continue our investigation into and advancement of the field.