Commentary

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Low Dose Oxybutynin: A therapeutic Option for Treating Nocturnal Enuresis

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Nocturnal enuresis (NE) affects 15-20% of 5-year-old children, 5% of 10-year-old children, and 1-2% of people aged 15 years and over. Various factors contribute to the development of nocturnal enuresis, most notably genetic factors and stressful early life events. Physiologic disturbances such as nocturnal polyuria, small functional bladder capacity, and decreased arousal response to the full bladder have also been identified [1,2]. NE is classified as monosymptomatic or polysymptomatic. Most children (80% to 85%) with NE only have night wetting and are classified as monosymptomatic. Children with polysymptomatic NE also have daytime bladder symptoms such as urgency, frequency, or other signs of bladder instability [3,4]. Numerous medical regimens have been proposed for PME including behavioral and motivational therapy, alarm aid, and pharmacotherapy which mainly consists of either desmopressin or antimuscarinic agents like propiverine or oxybutynin [5,6]. One treatment regimen for PME, which has been used for many years, is anticholinergic drugs, especially oxybutynin and tolterodine. Oxybutynin is an anticholinergic and antispasmodic agent that decreases uninhibited bladder contractions. It competitively antagonizes the M1, M2, and M3 subtypes of the muscarinic acetylcholine receptor. It also has direct spasmolytic effects on the smooth muscle of the bladder as a calcium antagonist drug [7,8]. Because detrusor hyperactivity plays a part in NE pathogenesis, oxybutynin is suggested to be effective when treating NE. Several studies have been performed in different countries regarding the efficacy of oxybutynin for the treatment of nocturnal enuresis in children. In a study by Friedman et al., oxybutynin proved to be effective in the treatment of polysymptomatic NE, most probably through reduction of bladder instability. It could also be used as an adjunct treatment with desmopressin or imipramine in pediatric patients [9]. Maitham et al reported that the treatment of nocturnal enuresis in children with imipramine was significantly faster and more cost-effective than oxybutynin or non-drug treatment [10]. A double-blind RCT by Montaldo et al showed that anticholinergic agents may play an important role in a subset of children with enuresis who have a restricted bladder capacity and thickened bladder wall [11]. Lovering et al found no evidence that oxybutynin was effective in treating primary enuresis [12]. An observational study by Lee et al revealed that combination therapy with desmopressin plus oxybutynin was significantly faster and more cost-effective than single drug therapy using either desmopressin or imipramine

[13]. In a systematic review, Evans showed that oxybutynin alone had no significant benefit and reported minor side effects in 17% of the subjects with inadequate statistical data [14]. Sajjad et al. also stated that combination therapy appeared safe in treating nocturnal enuresis in older children who had no success with other treatment modalities [15]. In this issue of the *Journal of Pediatric Nephrology,* Naseri et al reported the results of their study on the treatment effects of low dose oxybutynin in childhood nocturnal enuresis [16]. According to their study, low dose oxybutynin alone may have a role in treating nocturnal enuresis, especially in patients with NMNE. However, there are some conflicts about the results of this study. The key question is the criteria for low dose oxybutynin administration or discontinuation of drug, and some issues on the details of the patients are not clear, as well. Meanwhile, climatic conditions alone cannot justify the idea of the researcher in prescribing low-dose oxybutynin and stronger evidence is required. The position of urodynamic studies, VCUG, and radionuclide scan findings, especially in children with NMNE, is not clear. Again, statistical details are sparse, making it impossible to confirm or reject the authors' conclusion that low dose oxybutynin may be superior to the standard dose**.** According to recent studies, evidence supporting the administration of oxybutynin alone for the treatment of nocturnal enuresis is limited and in the review literature, most studies suggest that anticholinergic agents may play an important role in a subset of children with enuresis who have a restricted bladder capacity and thickened bladder wall. It was better if the researchers focused on these issues. In conclusion, according to the findings of this study, it seems that the validity of response to treatment with low dose oxybutynin in children with nocturnal enuresis should be substantiated in future studies with more patients and more defined selection criteria with regards to the limitations. Given the heterogeneous nature of the disease, it is conceivable that a subset of patients with NE may benefit from anticholinergic medications. Finally, it is worth noting that despite its limitations, there are still challenges regarding the treatment of nocturnal enuresis. Ongoing and future researches will better define how and when it should be used in this population of pediatric patients for whom very few treatment options currently exist.

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