The Pattern of Management of Nocturnal Enuresis in a Tertiary Hospital in Sudan

Karimeldin M A Salih, MHPE,ESME,MD*,**,*** Mohammed Abbas, MHPE,MD **** Muddathir H Hamad, MD***** Hiba K M Ali, MBBS****** Sarar Mohamed, MD,FRCPCH*******,********,*********

ABSTRACT

Introduction: Childhood enuresis is a stressful condition for both family members and patients. Different strategies can be offered to manage this condition with variable success rates. Data on the treatment of enuresis are scarce in Sudan. We compared the efficacy of treatment with albendazole, desmopressin, and a combination of these two medications.

Methodology: This is a prospective randomized hospital-based study conducted at Khartoum Children Hospital, Sudan. Children aged 5-15 years who presented with enuresis were recruited. Subjects were randomly assigned to one of 3 treatment groups (albendazole, desmopressin, or combination therapy) using a computer-generated table. The participants and clinician were aware of the treatment received by each individual.

Results: A total of 71 children were enrolled; 34 (47.9%) were males and 37 (52.1%) were females. All participants were offered counseling, motivation, and toilet training. Albendazole was administered to 17 patients, desmopressin to 17 patients, and combination therapy was offered to 20 patients. Five patients initially responded to counseling, motivation, and toilet training. Nine of 17 (52.9%) patients responded well to albendazole, 8/17 (47.1%) responded to desmopressin, and finally, 15/20 (75%) responded to combined therapy. Twelve patients declined to continue during non-pharmacological treatment.

Conclusion: Combined albendazole and desmopressin therapy seem to offer a better response in the treatment of children with enuresis.

Keywords: Albendazole, Counseling, Desmopressin, Enuresis, Enterobius vermicularis

---

* Departments of Pediatrics and Medical Education
University of Bisha, College of Medicine
Saudi Arabia.
E-mail: karimeldin641@gmail.com; karimeldin_salih@hotmail.com

** Medical Education Department
College of Medicine
University of Bisha

*** Department of Pediatrics
Faculty of Medicine
University of Bahri, Sudan

**** Department of Paediatrics
College of Medicine
Arabian Gulf University, Bahrain

***** Division of Neurology
Department of Pediatrics
King Khalid University Hospital
King Saud University Medical City
Saudi Arabia

****** College of Medicine
University of Medical Sciences and Technology

******* Department of Pediatrics
Prince Sultan Military Medical City
Saudi Arabia

******** Department of Pediatrics
College of Medicine
Alfaisal University
Saudi Arabia

********* Prince Abdullah bin Khaled Coeliac Disease Research Chair
College of Medicine, King Saud University
Saudi Arabia.

INTRODUCTION

Nocturnal enuresis is characterized by involuntary voiding of urine during sleep in children more than five years of age, with a frequency of two times per week over a period of more than three months[1-6]. The affected child may be symptomatic from the start (primary enuresis) or may have a second period of dryness (secondary enuresis)[7,8]. Nocturnal enuresis may or may not be associated with daytime symptoms[7,8]. The prevalence of enuresis is not accurately known in most parts of the world; may reach up to18.9%[9]. While other studies using different definitions for enuresis, documented a prevalence ranging from 5% up to 33.5%[3,4,10,11]. The pathophysiology of enuresis is attributed to the incoordination between arousal from sleep and the fullness of the urinary bladder beyond its ability during sleep[2], however many factors were incriminated, such as genetic, psychological as well as other organic conditions[12,13].

Different treatment strategies have been postulated with different responses. Some of these interventions were simple, feasible, and acceptable and allow families to adhere to them. Modalities of therapy include counseling, advice on toilet training, motivation, behavioral therapy, and medications[14]. As the current data do not clearly show which pharmacological treatment option is superior, we opted to conduct this study to compare the treatment response to albendazole and desmopressin alone or in combination.

PATIENTS AND METHODS

This prospective, randomized, hospital-based study was conducted at Khartoum Children Hospital, a leading referral pediatric hospital in Sudan over a period of two years. The participants were children aged 5-15 years diagnosed with nocturnal enuresis (night bedwetting) according to standard diagnostic criteria (1-6). All patients who presented with nocturnal enuresis in the emergency room, outpatient clinic, and hospital wards were assessed for inclusion in the study. Children who presented with involuntary voiding of urine during sleep at a frequency of two times per week for more than three months were included. Children were excluded from the study if they had a known cause of enuresis, such as diabetes mellitus, diabetes insipidus, acute kidney injury, chronic kidney disease, or diuretic use. Consent was obtained from the parents or guardians. The first and the second authors assessed the participants. A detailed medical history and clinical examination were performed. Information gathered included the age of onset, duration, and frequency of enuresis and medical history including history of perianal irritation. Clinical examination included growth assessment, abdominal examination, and inspection of the genitalia. A case report form was used to collect the data. All patients received non-pharmacological therapy, including counseling, advice on toilet training, motivation, and behavioral therapy, for 3 months. Patients who continued to have nocturnal enuresis two or more times a week were considered non-responsive to non-pharmacological treatment and were therefore included in this clinical trial. Alarm therapy was not used because it was not available at our hospital. Participants who satisfied the inclusion criteria and failed to respond to non-pharmacological therapy were randomly assigned to receive either albendazole, (group 1), desmopressin (group 2), or a combination of the two medications. A computer-generated table was used for randomization. The patient and treating clinician were all aware of the treatment assigned to each participant. Albendazole was administered at a single dose of 400 mg according to the World Health Organization (WHO) recommendations[15]. Desmopressin was used at a dose of 0.2 mg titrated to a maximum dose of 0.6 mg to achieve the desired effect[14]. The duration of pharmacological treatment was 6 months for each participant. At the end of the 6 months, the participant was labeled by the authors as responsive to the intervention if no nocturnal enuresis was reported in the last three months. The participant was labelled as non-responsive to therapy if nocturnal voiding was reported once or more per week in the last three months of treatment. This study was approved by the ethics committee at Khartoum children's hospital.

STATISTICAL ANALYSIS

Data were analyzed using the Statistical Package for Social Sciences (SPSS, Version 17). Qualitative data were expressed as numbers and percentages. A p-value of less than 0.05 was used to determine the level of significance, and Student's t-test was used for analyses.

RESULTS

In this study, 71 children with nocturnal enuresis were enrolled: 34 (47.9%) were boys and 37 (52.1%) were girls (table 1). Five patients responded initially to counseling, motivation, and toilet training, and 12 declined to continue non-pharmacological treatment. A total of 54 patients satisfied the diagnostic criteria for nocturnal enuresis and failed to respond to non-pharmacological treatment for 3 months. The 54 participants were randomized to receive albendazole (n = 17), desmopressin (n = 17), or a combination of albendazole and desmopressin (n = 20). Nine of the 17 (52.9%) patients responded well to albendazole, 8/17 (47.1%) responded to desmopressin, and 15/20 (75%) responded to combined therapy (p <0.003) (Table 2).

Table 1: Gender distribution, N=54 children with nocturnal enuresis

Treatment modalities	Participants distribution according to the Sex		
	Male	Female	Total
Albendazole	9	8	17
Desmopressin	6	11	17
Combined therapy	9	11	20
Total	24	30	54

Table 2: Treatment modalities for 54 children with nocturnal enuresis

Treatment modalities	Responded	Not responded	Total	P value
Albendazole	9(52.9%)	8	17	<0.05
Desmopressin	8(47.1%)	9	17	
Combined therapy	15(75%)	5	20	
Total	32(59.3)	22	54	

The p-value for treatment response < 0.05

DISCUSSION

Currently, there is no consensus regarding the management of nocturnal enuresis. Most authorities consider behavioral therapy, such as counseling and family training, as the first option for the management of children with enuresis[16]. Others recommend a combination of alarm therapy and toilet training rather than using each alone[17]. Most pediatricians prescribe desmopressin to children with enuresis when non-pharmacological interventions fail. However, others preferred to start children with enuresis on antidepressants. Recently, albendazole has emerged as an alternative treatment for nocturnal enuresis[18]. In this study, we conducted a randomized, open-label clinical trial to compare monotherapy using albendazole or desmopressin with the combination of these two medications. We found that combination therapy with albendazole and desmopressin for nocturnal enuresis showed a better response than monotherapy, as 75% of the patients who received combination therapy achieved a good response. Interestingly, only 52.9% of the participants who received albendazole had a good response.

To the best of our knowledge, this is the first study in Sudan to discuss the pattern of treatment for enuresis; however, previous studies in Sudan

by Rahim et al (1986)., Karimeldin et al(2013)., and Fatahelrahman et al(2016). explored the epidemiology of nocturnal enuresis in the country[3,4,11].

Aquod et al. conducted a study on Nigerian children with nocturnal enuresis and showed that more than 40% of children with enuresis responded well to albendazole[19]. This is in agreement with our study, which showed a 52.9% response to albendazole monotherapy. Furthermore, 75% of the patients who received a combination of albendazole and desmopressin showed a good response. Albendazole is commonly used to treat E. vermicularis. This infection is prevalent among Sudanese children, with 7.4% being infected in one study[20]. We did not perform stool analysis in our cohort to determine whether the participants were infected with this parasite. The mechanism of action of albendazole in the treatment of nocturnal enuresis is unclear. Itching associated with Enterobius vermicularis infection may predispose patients to enuresis.

The combined therapy of enuresis and albendazole has proven successful in the management of enuresis[21]. A study conducted by Otu-Bassey et al 2011 among a large number of Nigerian children showed a dramatic response in children with enuresis after administration of 400 mg of albendazole given as a single dose[22]. Many theories support a strong association between enterobius, premium itching, and enuresis[22-24]. Therefore, it is not surprising to obtain a good response for enuresis when albendazole is added to the monotherapy, which is supported by other studies[23].

LIMITATIONS

The sample size seems to be small for a common disorder. We were unable to examine the stool of the participant for enterobius which could have identified subjects with infections that predispose to enuresis. Therefore, our results should be interpreted in the context of these limitations. Further studies in different locations may give a better insight into the pharmacological therapy of enuresis.

CONCLUSION

In conclusion, we have shown in this study that combined therapy with albendazole and desmopressin is better than monotherapy.

Authorship Contribution: All authors share equal effort contribution towards (1) substantial contributions to conception and design, acquisition, analysis and interpretation of data; (2) drafting the article and revising it critically for important intellectual content; and (3) final approval of the manuscript version to be published. Yes.

Potential Conflict of Interest: None

Competing Interest: None

Acceptance Date: 11 February 2022

REFERENCES

1. Association AP. Diagnostic and statistical manual of mental disorders: DSM-IV-TR. Washington, DC: American Psychiatric Association; 2000.
2. Arda E, Cakiroglu B, Thomas DT. Primary Nocturnal Enuresis: A Review. Nephrourol Mon. 2016;8(4):e35809.
3. Ahmed FE, Salim EE, Salih KEM. Nocturnal enuresis among Sudanese children with sickle cell disease. Current Pediatric Research. 2016.
4. Salih K, Ahmed FE, Salih A, et al. Characteristics and aetiological factors of nocturnal enuresis in Sudanese children. Health Educ 2013;1(2):40-5.
5. Proserpio P, Terzaghi M, Manni R, Nobili L. Drugs Used in Parasomnia. Sleep Med Clin. 2018 Jun;13(2):191-202.
6. Thurber S. Childhood Enuresis: Current Diagnostic Formulations, Salient Findings, and Effective Treatment Modalities. Arch Psychiatr Nurs 2017;31(3):319-23.
7. Neveus T, Eggert P, Evans J, et al. Evaluation of and treatment for monosymptomatic enuresis: a standardization document from the International Children's Continence Society. J Urol 2010;183(2):441-7.
8. Fritz G, Rockney R, Bernet W, et al. Practice parameter for the assessment and treatment of children and adolescents with enuresis. J Am Acad Child Adolesc Psychiatry 2004;43(12):1540-50.
9. B Lu J, Shi P, An Y. Advances in Treatment of Nocturnal Enuresis in Children. InLower Urinary Tract Dysfunction-From Evidence to Clinical Practice 2019 Oct 15. IntechOpen.
10. Mahgoub MA. Nocturnal enuresis in Sudan. Australasian Med J 2010;3(6):362.
11. Rahim S, Cederblad M. Epidemiology of Nocturnal Enuresis in a Part of Khartoum, Sudan: I. The Extensive Study. Acta Paediatrica 1986;75(6):1017-20.
12. Fagundes SN, Lebl AS, Azevedo Soster L, et al. Monosymptomatic nocturnal enuresis in pediatric patients: multidisciplinary assessment and effects of therapeutic intervention. Pediatr Nephrol 2017;32(5):843-51.
13. Van Herzeele C, De Bruyne P, De Bruyne E, et al. Challenging factors for enuresis treatment: Psychological problems and non-adherence. J Pediatr Urol 2015;11(6):308-13.
14. Vande Walle J, Rittig S, Bauer S, et al. Practical consensus guidelines for the management of enuresis. Eur J Pediatr 2012;171(6):971-83.
15. Barkley S, Boisson S, Moja L, et al. Preventive chemotherapy to control soil-transmitted helminth infections in at-risk population groups: guideline. 2017.
16. Robson WLM. Current management of nocturnal enuresis. Current opinion in urology. 2008;18(4):425-30.
17. Glazener CM, Evans JH, Peto RE. Complex behavioural and educational interventions for nocturnal enuresis in children. Cochrane Database Syst Rev 2004(1):CD004668.
18. Zaffanello M, Giacomello L, Brugnara M, et al. Therapeutic options in childhood nocturnal enuresis. Minerva Urol Nefrol 2007;59(2):199-205.
19. DiBianco JM, Morley C, Al-Omar O. Nocturnal enuresis: A topic review and institution experience. Avicenna J Med 2014;4(4):77-86.
20. Karrar Z, Rahim F. Prevalence and risk factors of parasitic infections among under-five Sudanese children: a community-based study. East Afr Med J 1995;72(2):103-9.
21. Costache C, Jalali-Zadeh B. Enterobius vermicularis (Pinworms) infection and enuresis (bedwetting) case report. Revista Scientia Parasitologica 2009;10(1):79-81.
22. Otu-Bassey IB, Useh MF, Alaribe AA. The post—treatment effects of enterobiasis on the occurrence of enuresis among children in Calabar, Nigeria. Asian Pac J Trop Med 2011;4(4):315-9.
23. Otu-Bassey IB, Ejezie GC, Epoke J, et al. Enterobiasis and its relationship with anal itching and enuresis among school-age children in Calabar, Nigeria. Ann Trop Med Parasitol 2005;99(6):611-16.
24. Konanahalli P, Menon P, Walsh MY, et al. Enterobious vermicularis (pinworm) infestation of the vulva: report of 2 cases of a pseudoneoplastic lesion mimicking squamous carcinoma. Int J Gynecol Pathol 2010; 29(5): 490-3.