

Language disorders as comorbidity in enuretic children: Prevalence and impact on treatment

Pietro Ferrara^{1,2}, Rosanna Masticci³, Ignazio Cammisa², Chiara Matarrelli², Antonio Gatto³, Gallo Giorgia², Sacco Roberto⁴, Verrotti Alberto⁵

¹Department of Medicine and Surgery, Università Campus Bio-Medico Roma, Italy; ²Operative Research Unit of Pediatrics, Fondazione Policlinico Universitario Campus Bio-Medico, Roma, Italy; ³Department of Pediatrics, Fondazione Policlinico Universitario IRCCS A. Gemelli, Roma, Italy; ⁴Neurodevelopmental Disorders, Campus Bio-Medico University, Rome, Italy; ⁵Department of Pediatrics, Università di Perugia, Perugia, Italy

Abstract. *Background:* Several studies have recorded an association between nocturnal enuresis (NE) and developmental delays. Language disorders are one of the main comorbidities in enuretic children, affecting therapy outcomes and prognosis. *Methods:* The study was conducted within our pediatric outpatient clinic in Campus Bio-Medico University Hospital Foundation of Rome, enrolling 223 enuretic children, of which 20 had language disorders. Data concerning NE were collected through questionnaires, interviews with parents, and bladder diaries. The language disorders were secondarily investigated. The chi-squared test was used to assess the correlation between therapy outcomes and language disorders in enuretic children. *Results:* Our sample consists of 223 enuretic children, with a mean age of 7 years. 211 children were subjected to pharmacological treatments, while 12 children, with mild clinical symptoms, did not take any drugs. It was observed that 48,5% of enuretic children did not respond to therapy or relapsed, while 43% responded in the first cycle. 20/223 (9%) of enuretic children had a language disorder, of which 17 were subjected to pharmacological therapy: 13/17 (76,5%) did not respond to therapies and 4/17 (23,5%) responded ($p = 0.038$). *Conclusion:* Language disorders could impact NE therapy response, underlying the influence of comorbidities and the importance of a global assessment in enuretic children. (www.actabiomedica.it)

Key words: nocturnal enuresis, language disorders, therapy response, children

Introduction

Nocturnal enuresis (NE) is the most common functional disorder in children. It consists of the involuntary loss of urine during sleep which occurs more than twice a week for at least 3 consecutive months in children over the age of 5 (1). According to the International Children's Continence Society (ICCS), NE is defined as monosymptomatic (MNE) if occurs without any other lower urinary tract symptoms and a history of bladder dysfunction, and non-monosymptomatic (NMNE) if it is characterized by a concomitant daytime incontinence (2,3).

NE is a multifactorial disorder: genetic, environmental, and psychological components are the main predisposing factors (4). Nocturnal bladder control is considered a key developmental milestone: NE could be explained by an immaturity of the central nervous system as supported by the finding that premature and low-birth-weight children have a higher risk of NE than normal-birth-weight ones (5,6). It has been observed that there could be a link between NE and developmental delays in areas such as motricity, language, physical growth, and skeletal maturation. This suggests that NE might indicate a possible delay in some spheres of child development. A randomized

controlled trial, known as Quebec Longitudinal Study of Child Development and conducted by Touchette et al., documented that NE influence the developmental milestones in early childhood: motor skills, such as having already sat up without support for 10 minutes at the age of 5 months, and language skills, such as being able to speak 2 words, were reached later by enuretic children (5). Jarvelin et al. showed that enuretic children had greater fine and gross motor clumsiness and perceptual dysfunction, while Birenbaum et al. documented that they had a higher rate of oral language disorders, particularly phonological disorders, and difficulty with speech (7-10). Epidemiological studies showed that enuretic children tend to have more oral language disorders than the non-enuretic ones. According to the research conducted by Boyle and colleagues (12), it was found that a considerable number of children, approximately 5% to 8%, might be struggling with speech or language disorders. Language disorders can be classified as primary when the cause is unknown and secondary when caused by another condition such as hearing impairment, behavioral or emotional difficulties, autism, neurological impairment, or genetic conditions. According to Bishop (13), the term "language disorder" in the DSM-5 (2013) (14) covers a wide range of areas such as phonology, vocabulary, grammar, morphology, narrative skills, and pragmatic language (15). Interventions for children with primary speech and/or language disorders include a range of practices such as methods, approaches, and programs. These interventions aim to facilitate language development or remove barriers that hinder a child's participation in society. Eligibility for intervention is determined based on a combination of standardized assessment (where available), observations of linguistic and communicative performance, and professional judgment. Our observational study aimed to evaluate the prevalence and the impact of language disorders in a sample of enuretic children, aged between 5 and 14 years, focusing on therapy outcome and relapse.

Materials and Methods

Children with NE, aged between 5 and 14 years, who were referred to the Pediatric Outpatient Clinic

of Campus Bio-Medico University Hospital Foundation of Rome between September 2020 and March 2022 were eligible for inclusion in the study. NE diagnosis, according to the ICCS definition, is based on anamnestic and clinical evaluation. Data concerning NE were collected through questionnaires and interviews with parents, to which a bladder diary was proposed to record main features (frequency of wetting, urinary volume, daytime incontinence, urgency). During the first examination, we verified the presence of language disorders, previously diagnosed by a specialized center. According to the ICCS recommendations, we provided some advice to parents: dietary recommendations, fluid restriction in the evening, regular bladder emptying before going to sleep, and physical exercises to improve pelvic floor strength. In addition, drug therapy was prescribed: desmopressin if children showed only nocturnal symptoms, oxybutynin if showed diurnal symptoms, and desmopressin in association with oxybutynin if children suffered from both. Each patient was treated and monitored for 3 months. A second examination was conducted to record therapy response and the presence of relapse, defined as more than 1 episode of bed wetting per week. A statistical analysis was conducted using IBM SPSS Statistics 25.0 software (IBM Corporation, Armonk, NY, USA). Statistical analysis data were expressed as mean \pm standard deviation or as frequency and percentage. The chi-squared test " χ^2 " (p -value = 0.05) was used to evaluate the correlation between therapy outcome and language disorders. This study was conducted according to the regulatory standards of Good Clinical Practice and the Declaration of Helsinki and was approved by the Pediatric Unit of Campus Bio-Medico University Hospital Foundation of Rome. Children and their families were asked to participate in the study and signed written informed consent.

Results

Our sample was composed of 223 enuretic children, 157/223 males (70,4%) and 66/223 (28,9%) females. The mean age was 7 years, 99/223 (44,0%) children with monosymptomatic enuresis, of which 65 males (65,7%) and 34 females (34,3%), while

124/223 (55,6%) children have non-monosymptomatic enuresis, of which 92 males (74%) and 32 females (26%). Familiarity was found in 138/223 (61,8%) patients. In the study group 97/223 (43,5%) children were treated with desmopressin, 28/223 (12,6%) with oxybutynin, and 86/223 (38,6%) with both drugs, while 12/223 (5,4%) did not take any therapy. It was observed that 106/223 (47,5%) children did not respond to therapy or relapsed, while 89/223 (39,9%) children responded at the first cycle of treatment. The patients followed also non-pharmacological recommendations: 201/216 (93,1%) filled out a night voiding diary, 106/216 (49,3%) filled out a day voiding diary, 191/216 (88,4%) followed dietary advice and only 34/223 (15,2%) performed breathing exercises (Table 1). Analyzing the clinical characteristics of our patients: 28/223 (13%) had constipation and only 5/28 successfully treated the problem during our clinical follow-up, 9/223 (4,0%) were obese, 10/223 (4,5%) reported allergic history, 3/223 (1,9%) underwent corrective surgery for cryptorchidism. Only 13/223 (5,8%) patients were referred to recurrent urinary tract infections, and 28/223 (12,6%) were referred to encopresis. A total of 21/223 (9,4%) were left-handedness, 16/223 (7,2%) had polythelia, 9/223 (4,0%) had a heart murmur,

Table 1. Study population, pharmacological or not therapies.

	Study population (N=223)
Male, n (%)	157 (70,4)
Age (Y), median (IQR)	7,0 (6,0-9,0)
Therapy, n (%)	12 (5,4)
None	97 (43,5)
Desmopressin	28 (12,6)
Oxybutynin	86 (38,6)
Both	
Therapeutic response at first cycle, n (%)	106 (47,5) **
Absent or relapse response	89 (39,9) **
Complete response	
Night voiding diary, n (%)	201 (93,1)
Day voiding diary, n (%)	106 (49,3) *
Dietary advice, n (%)	191 (88,4) *
Breathing exercises, n (%)	34 (15,2)
Familiarity, n (%)	138 (61,8)

*Evaluated in N=216; **evaluated in N=195.

and 8/223 (3,6%) had hypertension (Table 2). We also analyzed the sleeping characteristics with the following results: restless sleep for 74/223 (33,2%), deep sleep for 26/223 (11,7%), and somniloquy for 21/223 (9,4%). Considering the neuropsychiatric characteristics (Table 3): 23/223 (10,3%) presented hyperactivity, 86/223 (38,6%) had good academic performance and 46/223 (20,6%) presented good social interactions at home or in school. A language disorder was found in 20/223 (9%) of enuretic children, respectively 17 males (70%) and 6 females (30%), of which 17 subjected to pharmacological therapy: 13/17 (76,5%) did not

Table 2. Clinical characteristics of the study population.

	Study population (N=223)
Constipation, n (%)	28 (13,0)
History of allergies, n (%)	10 (4,5)
Headache, n (%)	6 (2,7)
Cryptorchidism, n (%)	3 (1,9)
Encopresis, n (%)	28 (12,6)
Recurrent urinary tract infections, n (%)	13 (5,8)
Left-handedness, n (%)	21 (9,4)
Obesity, n (%)	9 (4,0)
Polythelia, n (%)	16 (7,2)
Hypertension, n (%)	8 (3,6)

Table 3. Neuropsychiatric characteristics.

	Study population (N=223)
Sleep apnea, n (%)	68 (30,5)
Hyperactivity, n (%)	23 (10,3)
Good academic performances, n (%)	86 (38,6)
Delayed language development, n (%)	20 (9,0) *
Good social interactions, n (%)	46 (20,6)
Snoring, n (%)	3 (1,3)
Restless sleep, n (%)	74 (33,2)
Deep sleep, n (%)	26 (11,7)
Sleepwalking, n (%)	1 (0,4)
Somniloquy, n (%)	21 (9,4)

*Evaluated in N=220.

respond to therapy and 4/17 (23,5%) responded, highlighting a lower response to treatment in this category of patients [χ^2 4,286; p-value 0,038, Cramer's V 0,14].

Discussion

NE is a common complaint in children worldwide, often underestimated by parents, with a main impact on a child's development (11-16). NE is defined as the biological expression of neurophysiological immaturity, supported by the greater number of neuropsychiatric and neurodevelopment problems observed (17). Barbour et al. supported a "developmental" concept of NE, based on the disappearance of symptoms dependent more upon age than therapeutic intervention (18). In this way, NE could be due to structural or functional immaturity of nervous pathways, such as developmental delays in language and writing. A pilot study conducted by Kilic et al. compared the neuropsychological development between children with enuresis and healthy children, applying the Wechsler Intelligence Scale for Children-Revised and the Bender Gestalt Visual Motor Detection test. They found that children with NE had lower performance in terms of abstract thinking, correct expression of thought, cause-result relation, short-term memory, and problem-solving ability (17). A study by Esposito et al. showed a higher risk of developing learning disabilities and mild reading difficulties in children with NE, while Lunsing et al. documented that children with NE had more language comprehension and arithmetic problems (19,20). Our study, according to the literature, showed a correlation between NE and development delays, specifically concerning the language sphere. In our study, 9% of the total sample had a language disorder and we documented a statistically higher risk of relapse ($p = 0.024$) in this category of enuretic children. 12/15 (80%) children with enuresis and language disorder did not respond to therapy while 3/15 (20%) responded. Several studies have already shown that a wide range of comorbidities, including oral language disorders, influence the prognosis and the response to the therapy in enuretic children (21-28). Language disorders and NE could be both the expression of a developmental delay, influencing each other. Specifically, the comorbidity of language disorders could be

a risk factor for the persistence of NE and treatment resistance. Our study has some limitations, which can be solved in future studies on this topic. The sample of children with language disorders was small, thus a larger cohort is needed to confirm the correlation between language disorders and relapses in enuretic children. A strict follow-up should be done to evaluate the treatment effects in a larger period.

Conclusion

NE is a multifactorial condition, influenced by a lot of comorbidities and factors.²⁵⁻²⁹ Pediatricians should have a global approach to children, paying more attention and identifying the comorbidities to suggest a complete and multidisciplinary treatment. NE and language disorders, whether associated or not, often represent a source of discomfort for the child, who may feel inferior or penalized compared to their peers. For this reason, all the professional figures who interact with children play a fundamental role, from school educators to pediatricians, to improve quality of life and prevent psychological consequences.

Abbreviations: NE= Nocturnal enuresis; ICCS= International Children's Continence Society; MNE= Monosymptomatic nocturnal enuresis; NMNE= non-monosymptomatic nocturnal enuresis.

Authors Contribution: Conceptualization, P.F.; validation, A.G.; data curation, R.M. and E.C.; methodology, R.M.; writing, C.M. and G.G.; resources, S.R. and V.A. All authors have read and agreed to the published version of the manuscript.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

References

1. Nevés T. Pathogenesis of enuresis: Towards a new understanding. *Int J Urol.* 2017 Mar;24(3):174-182. doi: 10.1111/iju.13310.
2. Ferrara P, Del Volgo V, Romano V, Scarpelli V, De Gara L, Miggiano GAD. Combined dietary recommendations, desmopressin, and behavioral interventions may be effective

- first-line treatment in resolution of enuresis. *Urol J*. 2015; 12: 2228-2232.
3. Haid B, Tekgül S. Primary and secondary enuresis: pathophysiology, diagnosis, and treatment. *Eur Urol Focus*. 2017; 3:198-206. doi: 10.1016/j.euf.2017.08.010.
 4. Ferrara P, Ianniello F, Romani L, Fabrizio GC, Gatto A, Chiaretti A. Five years of experience in nocturnal enuresis and urinary incontinence in children: where we are and where we are going. *Urol Int*. 2014;92(2):223-9. doi: 10.1159/000354388.
 5. Touchette E, Petit D, Paquet J, Tremblay RE, Boivin M, Montplaisir JY. Bed-wetting and its association with developmental milestones in early childhood. *Arch Pediatr Adolesc Med*. 2005; 159:1129-34. doi: 10.1001/archpedi.159.12.1129.
 6. Meadow SR, MacKeith R, Kolvin I. Bladder control and enuresis. London: Heinemann Medical; J.B. Lippincott [for] Spastics International Medical Publications; 1973.
 7. Birenbaum TK, Cunha MC. Oral language disorders and enuresis in children. *Pro Fono*. 2010; 22:459-64. doi: 10.1590/s0104-56872010000400017.
 8. Leković V. Occurrence of tics, enuresis and hyperkinetic behavior in children with language disorders. *Med Pregl*. 1993; 46:53-5.
 9. Järvelin MR. Developmental history and neurological findings in enuretic children. *Dev Med Child Neurol*. 1989; 31:728-36. doi: 10.1111/j.1469-8749.1989.tb04068.x.
 10. Essen J, Peckham C. Nocturnal enuresis in childhood. *Dev Med Child Neurol*. 1976; 18:577-89. doi: 10.1111/j.1469-8749.1976.tb04204.x.
 11. Ferrara P, Autuori R, Dosa F, Di Lucia A, Gatto A, Chiaretti A. Medical comorbidity of nocturnal enuresis in children. *Indian J Nephrol*. 2019; 29:345-352. doi: 10.4103/ijn.IJN_319_18.
 12. Boyle J, Gillham B, Smith N. Screening for early language delay in the 18-36 month age-range: the predictive validity of tests of production and implications for practice. *Child Language Teaching & Therapy* 1996;12(2):113-27.
 13. Bishop DV. Ten questions about terminology for children with unexplained language problems. *Int J Lang Commun Disord*. 2014 Jul-Aug;49(4):381-415. doi: 10.1111/1460-6984.12101.
 14. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th Edition. Washington (DC): American Psychiatric Publishing, 2013.
 15. Adams C, Lockton E, Freed J, et al. The Social Communication Intervention Project: a randomized controlled trial of the effectiveness of speech and language therapy for school-age children who have pragmatic and social communication problems with or without autism spectrum disorder. *Int J Lang Commun Disord*. 2012 May-Jun;47(3):233-44. doi: 10.1111/j.1460-6984.2011.00146.x.
 16. Chan IHY, Wong KKY. Common urological problems in children: primary nocturnal enuresis. *Hong Kong Med J*. 2019; 25:305-11. doi: 10.12809/hkmj197916.
 17. Kılıç A, Övünç Hacıhamdioğlu D, Tural E, Karademir F. Evaluation of neuropsychological development of children diagnosed with primary monosymptomatic nocturnal enuresis: A pilot study. *Turk J Urol*. 2020; 46:320-5. doi: 10.5152/tud.2020.19122.
 18. Barbour RF, Borland EM, Boyd MM, Miller A, Oppe TE. Enuresis as a disorder of development. *Br Med J*. 1963; 2:787-90. doi: 10.1136/bmj.2.5360.787.
 19. Esposito M, Carotenuto M, Roccella M. Primary nocturnal enuresis and learning disability. *Minerva Pediatr*. 2011; 63:99-104.
 20. Lunsing RJ, Hadders-Algra M, Touwen BC, Huisjes HJ. Nocturnal enuresis and minor neurological dysfunction at 12 years: a follow-up study. *Dev Med Child Neurol*. 1991; 33:439-45. doi: 10.1111/j.1469-8749.1991.tb14904.x.
 21. Ferrara P, Corsello G, Sbordone A, Nigri L, Ehrlich J, Pettoello-Mantovani M. Foster care: a fragile reality needing social attention, and economic investments. *J Pediatr*. 2016; 173:270-271.e1. doi: 10.1016/j.jpeds.2016.02.036.
 22. Karakas HB, Mazlumoglu MR, Simsek E. The role of upper airway obstruction and snoring in the etiology of monosymptomatic nocturnal enuresis in children. *Eur Arch Otorhinolaryngol*. 2017 Jul;274(7):2959-2963. doi: 10.1007/s00405-017-4558-z.
 23. Ferrara P, De Angelis MC, Caporale O, et al. Possible impact of comorbid conditions on the persistence of nocturnal enuresis: results of a long-term follow-up study. *Urol J*. 2014 Sep 6;11(4):1777-82.
 24. Yavuz A, Bayar G, Kilinc MF, Sariogullari U. The Relationship Between Nocturnal Enuresis and Spina Bifida Occulta: A Prospective Controlled Trial. *Urology*. 2018 Oct;120: 216-221. doi: 10.1016/j.urology.2018.07.038.
 25. Garcovich S, Gatto A, Ferrara P, Garcovich A. Vulvar pyoderma gangrenosum in a child. *Pediatr Dermatol*. 2009 Sep-Oct;26(5):629-31. doi: 10.1111/j.1525-1470.2009.01005.x.
 26. Ferrara P, Costa S, Rigante D, et al. Intramedullary epidermoid cyst presenting with abnormal urological manifestations. *Spinal Cord*. 2003 Nov;41(11):645-8. doi: 10.1038/sj.sc.3101482.
 27. Ferrara P, Giorgio V, Vitelli O, et al. Polythelia: still a marker of urinary tract anomalies in children? *Scand J Urol Nephrol*. 2009;43(1):47-50. doi: 10.1080/00365590802442086.
 28. Ferrara P, Ianniello F, Cutrona C, et al. A focus on recent cases of suicides among Italian children and adolescents and a review of literature. *Ital J Pediatr*. 2014 Jul 15;40:69. doi: 10.1186/s13052-014-0069-3.

Correspondence:

Received: 5 April 2024

Accepted: 15 October 2024

Rosanna Masticci, MD

Department of Pediatrics, Fondazione Policlinico

Universitario "A. Gemelli" IRCCS

Largo Agostino Gemelli, 8, 00168, Rome, 00168 Italy.

E-mail: rosanna.masticci01@icatt.it

ORCID: 0009-0007-3584-5387