Review article

Challenging factors for enuresis treatment: Psychological problems and non-adherence

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Summary

The evidence for organic pathogenetic factors in enuresis and the discovery of effective therapies targeting the bladder and/or nocturnal diuresis have overwhelmed every potential role of psychological factors in pathogenesis and treatment. However, psychopathology is still important in enuresis because according to the document of the International Children’s Continence Society (ICCS) 20–30% of the children with enuresis have at least one psychological/psychiatric disorder at rates two times higher than non-wetting children. The most common comorbid disorder with enuresis is attention deficit hyperactivity disorder. The aim of this review is to translate the existing evidence on the importance of a psychological screening into daily clinical practice of the medical practitioner. The use of the minimal psychological screening tool should be considered mandatory in each primary setting. If psychological problems are indicated, referral of the patient to a multidisciplinary setting should be considered, not only to allow psychological assessment to screen for a possible psychopathology, but also since therapy resistance might be expected. This review concentrates on two items from psychopathology/psychotherapy that might predict insufficient treatment response: the psychological comorbidities as described according to the DSM-5 criteria and the underestimated importance of therapy adherence. Adherence is a cornerstone of effective therapy in enuresis. It is a problem involving the doctor, the patient, and the parents. Increasing adherence takes effort and is time-consuming. But it is worthwhile knowing that several studies have demonstrated that high adherence is associated with high therapy success of enuresis. Eventually, this is the ultimate goal of treatment.
Introduction

Psychological factors have been widely accepted as playing a major role in the pathogenesis of nocturnal enuresis. Research has clearly demonstrated that a major role should be given to a discrepancy between nocturnal diuresis volume and functional bladder volume overnight in combination with deficient arousal and/or sleeping disorders [1]. This evidence for organic pathogenetic factors and the discovery of effective therapies targeting the bladder and/or nocturnal diuresis have overwhelmed every potential role of psychological factors in pathogenesis as for psychotherapy in treatment in medical literature. Patients are now seen by clinicians rather than psychologists, but medical doctors are often not armed to identify psychopathology in a consultation of 10–20 min, neither do they have the time nor the specific techniques to motivate parents and children to adhere to the therapy.

Psychopathology is an important co-existing factor in enuresis. In the general population, 10–15% of the children have a comorbid clinical behavioral disorder. In children with enuresis, the rate is doubled according to the document of the International Children’s Continence Society (ICCS) [2]. More specific, 20–30% of children with nocturnal enuresis fulfill the criteria of at least one disorder in the International Classification of Diseases-10 (ICD-10) or Diagnostic and Statistical Manual of Mental Disorders IV-TR (DSM-IV-TR). Moreover, regardless of the type of monotherapy, the success rates are disappointing (23–60%) [2–6] with a rather high relapse rate. Although a bias in patient selection cannot be neglected, this study aims to elaborate on psychological comorbidity as a possible explanatory factor for the insufficient response rate. Not only psychological/psychiatric disorders but also subclinical symptoms (sadness, feeling upset, burden, etc.) as well as difficulties in therapy adherence are discussed in this paper.

Especially in primary care, these psychological factors are often far beyond the primary interest of the clinician. Moreover, convincing studies of these comorbidities are based on an extensive psychological assessment [2,7], making this not realistic and accessible for clinicians in primary and secondary care. The aim of this review is to translate the existing evidence on the importance of psychological screening into daily clinical practice of the medical practitioner. Therefore, this review concentrates on two items from psychopathology/psychotherapy that might predict insufficient treatment response: the psychological comorbidities as described according to the DSM-5 criteria and the underestimated importance of therapy adherence.

Insufficient treatment response as a consequence of psychological problems

Psychological symptoms

Subclinical symptoms

Subclinical behavioral signs and symptoms, such as sadness, moodiness, feeling upset, embarrassment, humiliation, and guilt, are common and understandable reactions towards the wetting problem and are not disorders per se [2]. Children with enuresis experience a high level of stress, causing those symptoms. Moreover, they have a lower quality of life [8]. In a large population-based study, 36.7% of the children consider enuresis highly endorsed as a difficulty, ranking eighth behind other stressful life events [9].

Enuresis might also be a risk factor for the psychological well-being of the parents, especially the mothers, and can compromise their responsiveness towards the child. Mothers of children with enuresis report a lower quality of life, in terms of anxiety and depression, more stress and more intensity of pain than mothers of healthy children [10,11]. Moreover, they appear to be less accepting and more punishing than mothers of continent children [12].

If enuresis is left untreated it may lead to impaired quality of life not only in childhood but also in adulthood. Successful treatment leads to an improved quality of life according to the child [13]. Psychological symptoms will resolve by attaining continence, while manifest disorders or clinical symptoms usually do not [2].

Clinical symptoms

Most at risk to have a psychological disorder are older male children with a low socio-economic status who are admitted to a specialized clinic for secondary and/or non-monosymptomatic nocturnal enuresis [2,14,15]. One can differentiate among externalizing, internalizing, or other disorders. Externalizing disorders are behavioral disorders with visible behavioral symptoms, for example conduct disorder and attention deficit hyperactivity disorder (ADHD). Introversive and emotional symptoms, such as anxiety and depression, are internalizing disorders. Finally, some disorders could not fit between the previous two, such as autism spectrum disorder or anorexia.

Research on internalizing problems is rare. Internalizing problems may have a negative effect on self-esteem and vice versa. Several studies have shown that the self-esteem of children with enuresis is decreased [16–19]. In contradiction to our research group, who did not find lower self-esteem in children with enuresis than in healthy controls [20]. The main reason for this is that our study group not only used parent reports but also child reports. The parents reported more internalizing problems, probably because they are more attentive to those problems than parents of controls. Self-esteem can increase after successful treatment of enuresis [19]. There is a need for more formal and systematic evaluations of internalizing problems in children with enuresis.

Although internalizing problems can be present, externalizing disorders predominate [2]. The most specific comorbid disorder with enuresis is ADHD [21]. In an epidemiological study 9.6% of the children with enuresis had ADHD symptoms compared with 3.4% who only had ADHD and not enuresis [22]. Our research group confirmed the increased prevalence rate of ADHD in children with enuresis [7,23]. Children with enuresis from the tertiary care sample have a 3.4 times increased chance of having comorbid ADHD compared with children with enuresis admitted to non-tertiary care, corresponding to a prevalence rate of 28% and 10%, respectively [23]. Overall, 40% of the children with enuresis in our tertiary research group had ADHD. Fifteen percent were diagnosed with the
combined presentation of ADHD and 22.5% met the criteria of the predominantly inattentive presentation of ADHD [24]. Data revealed that a higher age (9–12 years) was associated with a higher prevalence of ADHD. Nocturnal polyuria had a significant higher incidence in the predominantly hyperactive/impulsive presentation of ADHD but there was no significant difference in bladder function between enuretic children with and without a comorbid diagnosis of ADHD [24]. At 2-year follow-up 73% of the baseline ADHD diagnoses could be reconfirmed. At 4-year follow-up a substantial number of children still met the criteria for ADHD (64%), even after becoming dry. The prevalence rate of enuresis decreased much faster than that of ADHD, suggesting the presence of a psychiatric syndrome rather than a coping behavior [7].

How to improve treatment response: psychological screening

Despite the fact that all experts and guidelines agree on the importance of the comorbidity rate of psychological problems in children with enuresis and recommend a psychological assessment, in the medical setting of a 10–15-min consultation, general practitioners and pediatricians are hardly touching the problem. Most of the available psychological screening tools are validated in psychological settings and time-consuming that they cannot be extrapolated into a primary or even a secondary medical consultation. A short psychological screening instrument as a first step in every new patient is mandatory [2]. Our research group has developed a Short Screening Instrument for Psychological Problems in Enuresis (SSIPPE) [25]. The questionnaire can be used for every new patient by the medical doctor. It consists of 13 dichotome items screening three major domains. The first domain is emotional problems such as anxiety and depression. The last two domains screen for ADHD: inattention problems and hyperactivity or impulsivity symptoms. If two or more items are scored positive on a domain, psychological screening by a psychologist is required.

During a psychological screening the psychologist will gather information by observation of the child and the parents, asking questions about the present and history, and use a standardized broadband questionnaire to further explore possible psychological problem areas. Commonly used is the Child Behavior Checklist (CBCL) [26]. The CBCL measures emotional, social, and behavioral problems in 1.5–18-year-old children. The questionnaire can be filled in by the parents (CBCL), the teacher (Teacher Report Form), and the child (if at least 11 years old; Youth Self Report). If these informants report (sub)clinical scores on psychological problems, a comprehensive psychological assessment should follow [2].

The aim of a full psychological assessment is to investigate if a child has a diagnosis according to the standardized DSM-5 or ICD-10 classification system. Assessment is not standardized, it is individualized to the patient and his/her family and to the concerns of either the medical staff, the patient, and/or the family. It consists of a detailed history, observation and exploration of the child and family functioning, a mental state examination, questionnaires, and intelligence and other formal psychological tests depending on the specific psychological concerns [2]. After completion of the assessment findings should be discussed with the patient and the parents. If necessary, psychological therapy can be advised.

Insufficient treatment response as a consequence of non-adherence

Adherence

An insufficient treatment response is attributable to various factors but little attention has been given to poor attendance and poor compliance/adherence. Both are the most basic necessities for effective treatment [27]. Treatment attendance, as defined by Nock and Ferriter, refers to delivery of the agreed upon treatment participants (e.g., parents, children, etc.) to the treatment setting for scheduled appointments [27]. Compliance has been defined by the World Health Organization as “the extent to which a person’s behavior — taking medication, following a diet, and/or executing lifestyle changes — corresponds with agreed recommendations from a healthcare provider” [28]. The term adherence is preferred because it implies a more active participation in collaboration with the healthcare provider. In contrast, the term compliance has a more passive connotation due to its obedience and acquiescence to the orders of the healthcare provider [27]. Treatment attendance and adherence are considered related but distinct constructs: one can attend but not adhere, but also one can stop attending but continue to adhere [27].

There is an overall non-adherence rate of about 50%; therefore, non-adherence is a general public health problem [29]. In pediatrics, adherence is even more complex, since we are not only dealing with the patient, but also with the parents and other care-givers (school, babysit, grandparents) [27].

Baeyens et al. investigated treatment adherence in enuresis regarding standard urotherapy and medication [30] and found an average adherence rate of 70%. In line with studies of other conditions the highest adherence was reported for medication intake. Adherence with urotherapy was considerably lower. But extrapolating these results into general practice is difficult, since the study was performed in a multidisciplinary setting, in which more time can be given in explaining the therapy and coaching the patients.

The adherence rate using desmopressin was studied in a large international study [31]; 81—91% ingested all medication as instructed during the first 4 weeks of treatment. However, the proportion of fully adherent patients decreased to 77% during the first 3-month treatment period and decreased even further to 71% during the second 3-month treatment period. Moreover, it is well recognized that in clinical trials patient motivation and adherence are stronger than in everyday clinical practice. Furthermore, in clinical trials patients were informed that adherence would be recorded, which may have further encouraged adherence. This suggests that the adherence rate in clinical practice will be even lower. In other studies, the adherence rate with desmopressin ranged from 67% [32] to 94.5% [33], mainly due to different adherence definitions and different sample sizes [31].

A comorbid psychological disorder can negatively affect treatment adherence, resulting in worse success rates [34].

Crimmins et al. [34] investigated in a retrospective study
the influence of ADHD on treatment adherence. Using timed voiding as treatment, 48% of families of children with ADHD reported non-adherence compared with only 14% of the control families. Using the alarm as treatment, non-adherence was also significantly higher in children with ADHD (38%) than children without ADHD (22%) [34]. If psychological treatment is offered, adherence to treatment will ameliorate and therapy outcome will improve [30].

Several other factors predict adherence and might be barriers to treatment: concrete stressors and obstacles (e.g., waiting time) [27,35], doctor–patient relationship [27,29], perceived relevance of the treatment [27,30,31], treatment demands (such as duration, administration frequency, formulation, cost, and adverse effects) [27,36], parental involvement and support [37], and patient-related factors such as age and gender [38,39].

Some formulations are more predisposed to non-adherence than others. Adherence of the intake of desmopressin tablets without drinking and not allowed to chew on in young children who cannot swallow a tablet is simply not feasible. Therefore the oral lyophilisate formula might resolve this problem in young children.

A low adherence rate negatively influences therapy outcome of enuresis. The study of Baeyens et al. [30] found that, based on both parent and child reports, higher levels of adherence result in greater therapeutic success after 6 months of treatment.

A large international study clearly demonstrated that high treatment adherence was associated with a greater response. Patients who were 100% adherent to desmopressin were 46.6% responders compared with the less than 50% adherent patients who were just 25% responders [31].

**How to improve treatment response: assessment and improvement of adherence**

Non-adherence can be intermittent or continuous, voluntary or involuntary, and may be specific to single or multiple interventions, which makes reliable measurement problematic [40]. The accuracy and reliability of measurements of adherence vary with the method used. Adherence can be measured for example by 24-h recall interview, counting medication/prescriptions, automated devices, and a diary.

Because of the big taboo of enuresis and social desirability, children will not take the drugs or use the alarm when others can observe it (at school, visitors, sleepovers, camps) and they will not communicate their non-adherence to the doctor at the next visit. Active and non-judgmental questioning on the reasons for the difference between dry and wet nights might explain this observation.

Measuring adherence and social desirability can lead to an overestimation of therapy adherence, especially in clinical practice.

Strategies to improve adherence aim to change the perceived barriers to treatment [27]. Strategies can be educational or behavioral, although an approach that combines both is usually most effective [37,40]. Adherence could be increased by education of the patient and parents on the condition and the specific treatment guidelines by brochures, DVDs, mp3 messages, smart phone apps, and interactive webpages [30]. Patients should be well informed about the consequences of non-adherence. During consultation, this requires full information and time to discuss this, in a language appropriate for both the parents and the child. Non-judgmental questioning about regimen behavior and continuous feedback and reinforcement at subsequent visits of the information are advised [29]. The medical staff has to stress the importance of both child and his/her family, and treatment goals should be set in collaboration with the child and his/her family [37]. Moreover, they should have a high index of suspicion for non-adherence when the anticipated clinical response does not occur. If difficult aspects and difficult (social) contexts for adherence can be anticipated, the patient and the parents are more prepared and less willing to decrease their adherence to treatment guidelines or even give up treatment. Supervision and training of the medical staff is required.

Behavioral methods have proven to be quite successful in improving adherence and include many simple techniques the provider can easily introduce into practice, for example the use of (social) rewards to increase motivation [39]. Use creative and original methods that do concern the child. Let patients indicate in a diary whether they were adherent with treatment guidelines. The diary functions as a (self)-controlling mechanism to increase adherence [31].

Cues and reminders may be useful tools to improve adherence and can be provided by phone, email, text messages, and smart phone apps [37]. A note on the bathroom mirror, mobile phone alarm, and linking medication administration times to routine daily events such as bedtime or teeth brushing may also help patients in remembering to take their medication.

**Conclusion**

In the past decades the role of psychological factors in the pathogenesis of nocturnal enuresis has changed from a primary causal factor to a consequence or comorbidity. The evidence for underlying organic factors has led to a more rational therapeutic approach with higher success rates. Moreover, it has also largely diminished the feelings of guilt for the child and the parents. However, the involvement of psychopathology is now underestimated; nevertheless, there is enough evidence that psychological comorbidity coincides with therapy resistance. Therefore, the use of the minimal psychological screening tool should be considered mandatory in each primary setting. If psychological problems are indicated, referral of the patient to a multidisciplinary setting is recommended, since therapy resistance is expected. Moreover, in every refractory patient, a full psychological screening and a high suspicion of non-adherence is required. Adherence is a cornerstone of effective therapy in enuresis. It is a problem involving the doctor, the patient, and the parents. Increasing adherence takes effort and is time-consuming. But it is worthwhile knowing that several studies have demonstrated that high adherence is associated with high therapy success of enuresis. And at the end, this should always be the ultimate goal of treatment.
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