TREATMENT OF ENURESIS NOCTURNAE IN CHILDREN WITH CEREBRAL PALSY

Miodrag Stosljevic and Milosav Adamovic

Faculty of Special Education and Rehabilitation,
University of Belgrade, Serbia

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SUMMARY

This paper theoretically elaborates on enuresis nocturnae treatment in children with cerebral palsy. We have described definitions and types of enuresis in the introduction, and then we have presented enuresis prevalence in common population and CP children to argue that CP children have much higher prevalence of enuresis in comparison to ordinary children. Following to this, we have shown ethyopatogenesis of enuresis with special attention to the development of this condition in children. The last chapter deals with the treatment itself based on medical therapy, and a selected medicine desmopressin. Conclusion suggests that in our opinion the most efficient treatment in children with CP is precisely medical, unlike integral treatment of this condition in ordinary children.

KEY WORDS: enuresis nocturnae, cerebral palsy, desmopressin

INTRODUCTION

Bedwetting presented a condition in which a child, older than four, cannot control started urinating process during the sleep, although the organs in question have no apparent problems functioning whatsoever (Stošljević, 2005). Many authors have dealt with defining this problem of bedwetting in their literature. Here are some of the definitions quoted according to chronological order of their occurrence: Somatic and psycho-functional urinating disorder with non-organic impairment (Tramer, 1949), involuntary urination in children older than
four (Weber, 1967.), night wetting does not need surgical intervention (99%) unlike incontinence (1%) where this intervention is necessary (Maizels, 1999)

Actually the last quoted definition of enuresis presents the basic distinction between enuresis and incontinence, a pathological state of being incapable of retaining the urine consciously and voluntarily with obvious organic ethyopatognesis. Therefore, enuresis triggers a question of consciousness and other psychological functions, while incontinence happens in preserved consciousness, and in most cases it is possible to precisely determine the causes and mechanisms of the development of this disorder.

The definition of bedwetting raises a question whether enuresis is a symptom or a disease, or something else? We share an opinion that enuresis is not a symptom, and especially not a disease, but a transitory condition of parasomnia in developmental age. Accordingly, enuresis falls into a sort of sleep disorders because parasomnia is a condition when a person behaves during the night in a way acceptable for a state of being awake, but not while asleep as well. Besides enuresis, there are other parasomnias like somnabulism (moonwalking), pavor nocturnum (night fear), incubus (nightmare) etc.

According to the moment in which the act of urinating occurs, there are following types of wetting: bedwetting (enuresis nocturna), day wetting (enuresis diurna) and urination while laughing, also called “giggle wetting”.

With regard to the moment of occurrence and its duration there are two kinds of bedwetting: primary; if a child hasn’t stopped urinating since it was born and secondary; if a child has had „a dry period“ of at least six months. Primary enuresis (synonyms: persistent, inborn) is mostly hereditary. Most children with bedwetting (85%) have this type of enuresis. It is very important for doctors to know that primary enuresis is more difficult to treat than secondary. Secondary (synonyms: acquired, relapse) enuresis appears in 15% children with bedwetting, and more frequently with children who have established the control of urination later than usual. It is most frequent in children aged between five and eight. In most cases, its development is psychogenic and some psychoanalytic authors suggest that it is a regressive phenomenon on neurological basis in direct relation with low level of frustration tolerance. This fact is essential for developing the least frustrating way of treatment of secondary enuresis in children.

Day wetting is important to parents only if it is associated with night wetting or if it is a consequence of some other disease. There is not much information about Enuresis diurnain literature probably because of the fact that it is more easily treatable than bedwetting and because
of the fact that in most cases it is of organic origin as well. There are some interesting statements by authors who argue that bedwetting and day wetting are “like sisters” and are not supposed to be separated clinically on everyday basis. Weinberg (1973.) published an interesting research that revealed diurna is more common in children with depression, which poses a question of enuresis diurna actually being a monosymptomatic depression. It is of high importance for doctors to know that diurna is not wetting during an afternoon nap, but only wetting in alert and preserved consciousness.

“Giggle wetting” occurs in children while laughing. It is more common in hypotonic children, but in CP children as well, but unless it is associated with two previously mentioned kinds of wetting it is not a warning sign for starting a treatment (Stošljević, 2005).

Prevalence

Bedwetting is present in 15% of five-year-old children, in about 10% of seven-year-old children and in about 2% of fifteen-year-olds. This data suggest that the number of children with bedwetting decreases with age which is in relation to central nervous system maturation. Therefore, it is impossible to determine the prevalence of enuresis because „a certain number of parents don’t think it is of great importance and don’t consider it to be a disease, while others hide it like a big family secret“. (Perez, according to Popov, 1976). Gumus et al (1999) proved in their research the prevalence of 10.6% in girls and 16.9% in boys, which is 13.7% on average. They collected the data on sample of 2000 children between ages seven and eleven. Dahm et al. (1997) acknowledged the prevalence of 13.4% in seven-year-old girls and of 22.2% in boys of the same age, with 50% of children displaying secondary enuresis. The same authors revealed that 5.4% of girls and 8.2% of boys have had wetting problems at least once a week. From the aforementioned, it is obvious that bedwetting is more frequent in boys than in girls. Another research (Zarovski et al., 2008) suggests that 24.6% of children with CP have enuresis nocturnae which is much higher prevalence than in ordinary children with monosymptomatic enuresis.

Ethiopathogenesis

Bedwetting causes could be: hereditary, organic, functional and psychogenic, but enuresis can be of unknown origin as well.

The hereditary background of bedwetting has been proved. In terms of statistics, there is a 40% chance of night wetting if one of the parents had the same experience, and 70% chance if both parents had it. From our standpoint, what one inherits directly is not night urination but only some of its predispositions (e.g. inherited deep sleep disorder) (Stošljević, 2005).
From medical point of view, organic causes of bedwetting may ensue due to urogenital tract impairment, Spinabifideoccultae, or some other organic disorder like CP. Most common changes in urogenital tract likely (but not certain) to cause enuresis are fibrositasvesicaeurinariae, reflux vesicoureteralis, spasms in urethral opening, diverticulosis vesicaeurinariae, underdeveloped trabecular system, stricturauretrae, calculosisvesicaeurinariae, phimosis, tumors etc. It is still not clear how CP affects bedwetting, but the majority of children have a disturbed hormonal system in which vasopressin plays an important role regulating the urinary function. Disturbed vasopressin release affects the development of enuresis no matter what.

The most important functional causes of nocturnal enuresis are deep sleep, low bladder capacity, ostipation, hypersensitivity to some kinds of food and drinks and higher urine production. Each of these can trigger enuresis development in children with CP, but special attention must be given to ostipation, since intestinal peristalsis is common with these children. Psychological causes of nocturnal enuresis development are in close relation to enuretic child’s character, habits and family psychodynamics, but immediate surroundings can trigger nocturnal enuresis as well. These causes are multiplied in children with the fact of having CP in the first place. The most common psychological causes of enuresis development include hyperactivity (ADHD syndrome), stress, habitual polydipsia (drinking habit) and stimulation of negative behaviour. Enuresis in CP children can also be caused by compulsive water drinking.

**Diagnostics**

Children always feel a certain amount of fear when they go to a doctor. If that fear is stronger than usual, while examining an enuretic child, a doctor might get a distorted picture of its psychological status. In order to avoid this situation, and make a child feel more comfortable at the doctor’s, parents are supposed to prepare a child for this upcoming experience. A successful preparation should include the following steps:

- Explain the reasons of the examination to a child
- Inform him on the exact time of the examination
- Make sure that the child recognises the doctor as someone who will help him solve the night wetting problem
- Explain that the examination is not painful like for example taking a blood sample or getting an injection
- Tell your child that the doctor will ask him questions about his bladder and bowels emptying, and that he shouldn’t be ashamed because this is going to help him be cured
Since doctor does not know the terms used inside the family to designate emptying habit, a child must be familiar with words like “stool” and “urination”. If a child refuses going to a doctor parents can make a trial visit in order to get to know the doctor and the space where the child will be examined the next time.

Doctors should know that examination of enuretic child is specific because of the possible psychogenic ethyopathogenesis. Owing to this, we always advise doctors not to wear white coats that can frighten children but to make enuretic clinic look quite plain, i.e. to resemble hospitals as little as possible. In practice, we have seen children reacting to hospital smell, so a separated examination room would be recommendable. This is also significant from the point that many parents want to keep this bedwetting problem a secret, so a separated clinic and waiting hall would be more acceptable. Before the examination itself, a doctor is going to ask a child and parents a few questions about his bladder and bowel emptying habit. These questions examine the urgency and frequency of urination, presence of pain during urination, urinary infections, frequency and the manner of bowel emptying etc.

**Treatment**

Each enuretic child is «sui generis», i.e. a clinical entity on its own, which does not mean there is just one treatment protocol applicable to all children, but it implies that the treatment must be adapted to each child separately. Secondly, the treatment plan is made in several stages according to ethyopathogenetic factors determined in the diagnostic process. Thirdly, an ideal treatment would imply a team of experts in the field, including, for example, a psychologist and a defectologist helping a doctor and parents to administer the treatment properly.

The treatment consists of several parts:

- Adopting a hygiene-diet system of living and obeying the general rules of treatment
- Performing exercises for CNS maturation, relaxation, enhancing attention stability, developing child’s imagination
- Applying medical therapy

This kind of integral treatment applied with enuretic children on everyday basis is unfortunately impossible to apply with CP children because of their condition, so we are forced to use the third kind of treatment, that is, a medical therapy. It is necessary to emphasise that medical therapy presents a supplementary part of the therapy. Therefore, we conclude that medical therapy is not causal therapy as well, which does not imply that successful treatment is possible without medications. On the contrary, medical therapy is mandatory and the only possible type of therapy in CP children.
There is a wide range of medications that are being used in treating enuretic children nowadays. The older generation of doctors applies Imipramine, a medicine that Mac Lean found to be effective in improving the condition of enuretic children by its anti-cholinergic effect in 1960 (Stošljević et al, 2003). However, a range of contemporary studies found that Imipramine has various side effects like sleep disorder, heart toxicity, weight loss, and a temporary hair loss. In any case, Imipramine has a similar effect to oxybutynine, so when there is a need to apply anti-cholinergics we suggest using the other one.

A certain number of doctors still suggest Noxenur (atropine-sulfate) application in enuresis treatment. We must admit having positive experiences in using this medicine, but since it has been outdated, we prefer not to use it in everyday clinical practice. In this case, like previous, Noxenur is supposed to be replaced by oxybutynine, since it is more effective and less harmful alternative.

Hence, there are two contemporary medicines that can help in treating enuretic children. Both medicines lower the intravesicular pressure, but in different ways and through different mechanisms. These two medicines are oxybutynine (Ditropan) and desmopressin (Minirin).

Oxybutynine (Ditropan) is parasympatholytic which reduces the intensity and frequency of vesicular contractions and prolongs bladder emptying. Therefore, this is the suggested medicine when it comes to low bladder capacity or bladder instability. It is never applied separately, but only as supplementary part of the main treatment course. It is available as syrup or as 5mg tablets. The dosage depends on the age. Five to seven year olds take half a tablet at 8a.m., then half a tablet at 4p.m., and half a tablet before they go to sleep. Eight to twelve year olds take half a tablet at 8a.m., then half a tablet at 4p.m., and half a tablet before they go to bed, while children older than twelve take half a tablet at 8a.m., then half a tablet at 4p.m., and 1-2 tablets before they go to sleep. The medicine has significant antimuscarine side effects like dry mouth, constipation, blurred vision, nosebleed. It is not recommended for use in asthmatic children since it can induce an attack. It is rarely applied in our practice and always according to strict indications mentioned above.

Desmopressin (I-diamino-8-D-arginin-vasopressin; Minirin, DDAVP) is the synthetic analogue of vasopressin, and the fact that this medicine is intensely exploited in our everyday practice obliges us to further elaborate on it in terms of clinical aspects of desmopressin application. Desmopressin reacts on renal V2 receptors as direct agonist regulating the volume and osmolarity of urine. Indications of this medicine application are nocturnal enuresis condition, central diabetes insipidus and the bladder capacity test.
Since 1970, when chemists developed the substance called desmopressin acetate, a great number of researchers have started studying this medicine. Dimson first published in The Lancet magazine of 1977 that desmopressin has positive effects on bedwetting, not only central diabetes insipidus which used to be the main indication for desmopressin application (Stošljević et al., 2003). These findings carried out the revolution in the field of nocturnal enuresis treatment, and therefore we can ascertain that desmopressin has been used for more than a quarter of a century as a selected medicine in enuretic treatment.

However, is desmopressin as ideal as it seems at first sight? Of course not, since this medicine, like all other medicines, have its shortcomings and side effects.

The main disadvantage of desmopressin, which troubles the most practitioners, is a significant recidivism rate (up to 80%) in the process of enuretic children treatment. During our lectures we repeat time and time again that medical therapy, and desmopressin therapy as well, is not causal but supplementary to the main treatment course. So, the great number of relapses happen because most doctors apply desmopressin in isolation, and not as a supplement to the main part of the treatment. We responsibly acknowledge that desmopressin application in correctly carried out main therapy course leads to recovery in 98% of cases.

The second shortcoming of this medication has been observed with a number of children that do not react to medical therapy. Causes vary from some children not absorbing sufficient amount of the medication (if applied via nasal spray), over nasal mucosal inflammation, nasal congestion, to upper respiratory tract infection. Absorption of this medicine taken orally can be significantly reduced if a previous meal consisted of more than 27% of fat of animal origin. A range of scientific papers have shown that a hereditary component is in direct negative correlation with enuretic child’s response to desmopressin. A certain number of children have such low bladder capacity that desmopressin cannot prevent its fast filling. As we stated above, Oxybutyninis recommended in these cases.

Desmopressin's side effects are «in nucleo» its advantages over other medication of the same kind. The most significant side effect of desmopressin therapy is so called „water poisoning“ with consequential hyponatremia. This side effect is experienced only in cases when patients don’t follow doctor’s instructions not to drink any liquid two hours before and eight hours after taking the medicine. Remaining side effects include headache, nausea, stomachache and epistaxis, but rhinitis and mucal congestion as well in case of nasal application of this medicine. 6%-8% patients report these symptoms but they are more
unpleasant than life threatening. In case of experiencing these symptoms, it is necessary to quit therapy.

If you apply desmopressin you need to be familiar with its interactions with other medicines. Tricyclic antidepressants, selective serotonin inhibitors, Karabamazepine and Chlorpromazine can cause additional diuretic effects, while Indomethacin (NSAID) can cause hyponatremia. Loperamid can cause overdose because it triples the concentration of desmopressin in plasma. Although this medicine is metabolised through the liver, interaction with medicines has not been observed.

The dosage of this medicine is very simple. Starting dose is 0.1-0.2 mg, and maximum dose is 0.4 mg. The medicine is taken immediately before going to sleep. It is available as spray, that is applied nasally, and as 0.2 mg tablets. The spray is more efficient in treating enuresis than tablets, but some shortcomings have been observed too, e.g. the basic prerequisite of application possibility is unobstructed upper respiratory tract. This implies that pathological processes in upper respiratory tract disable nasal spray application. A drug-holiday of about 7-15 days is recommended after 90 days of application of this medicine.

After this detailed elaboration there still remains a question of choosing desmopressin for preferred medicine in enuretic treatment in CP children. The answer lies in the following reasons:

The aim of medical therapy is reducing intravesicular pressure, and desmopressin has the most efficient and fastest influence on it, This medicine has the lowest number of contraindications and side effects in comparison to other medicines
Dosage is very simple, so there is not a threat of overdose, In most patients its effects are momentary, i.e. 2-3 after application, so it is considered to be the ideal solution in cases with urgent and short term solutions to enuresis (e.g. school trips, curriculum based field trips etc.),
Desmopressin provides strong support to the main treatment course in terms of motivating the patient, because a dry child experiences a significant boost of motivation to persist in treatment course during the first 15-20 days of treatment. As shown above, consistency and persistence are the main prerequisites for successful treatment.

It is now necessary to address previously mentioned several stages of treatment. Enuretic treatment is supposed to be carried out in stages because a certain number of children react to the minimum of treatment and are cured very quickly. The remaining part of children, and CP children especially, need a longterm and more comprehensive treatment. Everybody understands that different patients demand different approaches, to avoid “shooting a mosquito from an elephant gun“ (Chinese saying). The treatment itself consists of one preparatory
stage and three main stages. Preparatory stage requires the elimination of all factors that might influence course of treatment, in the way explained at the beginning of this chapter. Therefore, a preparatory stage enables a detailed diagnostic process, solving problems like opstipation or diabetes, and examining possibilities of starting the treatment. This stage tends to stabilize the family’s psychodynamics.

The first stage of treatment is so called «non-medical stage» when we try to treat children without medications. In this stage the diagnostic process is being fully developed, which makes the clinical image clearer and the treatment process better directed. During this stage patients that do not have deep sleep as basic ethyopathogenic factor are usually cured. The biggest number of patients cured at this stage showed hypersensitivity to certain kinds of food or drinks, or some psychogenic factors that we successfully eliminated.

The second stage of treatment includes introducing medications in the treatment process and performing exercises to treat AHDH syndrome. This is the stage when most patients are cured.

The third stage deals with the number of patients that are not cured during the first two stages. This stage includes deeper and more detailed diagnostics in terms of looking for enuresis causes within factors familiar from the scientific literature on the subject, but which are rarely seen in everyday clinical practice.

In the end we must define the prerequisites that are important for treatment of bedwetting in CP children.

**Firm decision to start the therapy**, made on time, is half the treatment. During our practice of many years, we have convinced ourselves that most parents decide to take a child to treatment from emotional or immediate practical reasons. The most common emotional reasons are child’s tears or relatives’ pressure (grandma, grandpa, etc.) Immediate practical reasons refer to upcoming school trips, curriculum based field trips or sports camps. Therefore, the lowest number of parents decides to treat their child rationally.

**Make sure that the time for starting the treatment is right!** In case there is a newborn child in the family, an illness, a divorce, school pressure or something similar is happening, you should postpone the treatment.

**Make sure that your child wants to be treated!** It is perfectly clear that a child’s motivation presents one of the key factors of successful treatment. You have to be completely sure that your child agrees to your wishes, but to measures and procedures of the therapy during diagnostics and treatment as well.
Make sure you take your child to a qualified specialist! Unfortunately the inefficient system we live in allows for non-qualified experts, even charlatans, deal with problems of bedwetting. Therefore, to emphasise it once again, only a doctor within a specialized team can solve this problem. Your problem can not be solved by separate action of a psychologist, a defectologist, a social worker or some other paramedical experts. If you take your child to a private hospital, feel free to ask for their diploma. Every doctor will be honored to present it to you. Most doctors start a treatment the moment the patient enters his office. It’s a mistake. We have to wait for the right moment, no matter when, because the treatment is by far more successful, and the number of patients that give up the treatment is lower if the doctor starts treatment at the right time. Within this context, it is of highest importance to doctors to evaluate psychodynamics of the family and the motivation of a child to be cured. If all these parameters are favourable, the doctor can start the treatment with classic medical procedures.

Make a plan of the treatment according to causes of enuresis nocturna found during diagnostic process. Parents must be aware that they are the means by which the doctor can successfully treat their child. Only the complete cooperation between parents and the doctor is the guarantee of the right treatment plan. General advice to parents is: ask, make agreements and be consistent in what you have agreed to!

CONCLUSION

In the end, we can state that the most efficient enuresis treatment in CP children is medical therapy unlike integral treatment of this condition in children of ordinary population which implies hygienic-diet system of living, following the rules of treatment and performing exercises for CNS maturation, relaxation, enhancing attention stability, developing imagination etc.

REFERENCES


