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Diagnosis and treatment of non-organic enuresis in children: Clinical practice guideline

Luis Guillermo Meave-Cueva[1]
Luisa Díaz-García[2]
Rosalía Garza-Elizondo[3]

[1] Pediatric emergency physician.
[2] Research Methodology.
[3] Head of Continuing Medical Education, Teaching Division.
Instituto Nacional de Pediatría, México, D.F.

ABSTRACT

Background: Bedwetting is an involuntary urination during sleep at the age of 5 years or older. Clinical Practice Guidelines (CPG) have been developed to improve decision-making strategies and standardize medical practice. The Ministry of health in Mexico developed the CPG diagnosis and treatment of non-organic enuresis at the first level of prevention in children. Its evidence is evaluated with the USPSTF (United States Preventive Services Task Force).

Material and methods: Original articles that justify the evidence of Mexican CPG were sought and identified in virtual libraries: Pubmed, Embase, Cochrane Library plus, and then analyzed with the instrument of the USPSTF.

Results: Sixty articles were reviewed. They're the basis for evidence formulation of the Mexican CPG. Only nine articles were level I, adequately powered and well conducted trials and recommendation Grade A, with a substantial net profit. Evidences that were substantial fed by these articles obtained the highest scores.

Discussion: The methodological rigor of the original articles that support the CPG is highly variable. This instrument is meant to evaluate the evidence of the guide but is far from being a reflection of the rigor in the development and applicability of Mexican CPG.

Key words: Bed wetting, level of evidence, Clinical Practice Guidelines, USPSTF.

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Correspondence
Dr. Rosalía Garza Elizondo
Instituto Nacional de Pediatría
Av. Insurgentes Sur 3700-C
04530 Mexico DF
Tel. 10840900 extension 1185

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The International Children's Continence Society 2006[1,2] defines bedwetting as involuntary urination with normal characteristics, which takes place during sleep at an age and with a frequency deemed socially unacceptable, especially at the age of 5 years or more.

There are no national publications that offer precise data on the incidence of this problem, making it necessary to conduct epidemiological studies in our population.[3] Its prevalence diminishes with age, trending toward spontaneous resolution, although not in all cases or at the desired time; in many cases it occurs too late, producing negative emotional impact on the child, and for parents an economic burden and workload, and even problems in their social lives.[4] For that reason it is fundamental to approach diagnosis and treatment of children with enuresis adhering to the available scientific evidence.

Recently, international clinical practice guidelines have been published on epidemiology, management, and treatment of monosymptomatic primary enuresis which differ significantly in their content and methodological quality; also, their applicability in our field is questionable.[5]

High quality clinical practice guidelines are documents that raise specific questions and offer the best scientific evidence, which, in the form of flexible recommendations, can be used in clinical decision making.[6] The methodology used in developing them (in searching the scientific literature and synthesis of evidence to build the final recommendations) is systematic, explicit, and reproducible, following clearly defined steps.[7-10]

In a clinical practice guideline the level of evidence is fundamental in formulating recommendations. Various techniques have been developed for evaluating articles which support the evidence in guidelines. One of the first scales was that formulated in 1979 by the Canadian Task Force on the Periodic Health Examination (www.ctfph.org) for evaluating preventive measures,[11] and adapted in 1984 by the US Preventive Services Task Force (USPSTF). The last edition evaluates the quality of evidence more extensively, taking into account not only the type of design of studies; degrees of recommendation are established based on the quality of the evidence and the net benefit (benefits minus detriments) of the measure evaluated.[12]

With the aim of producing accurate information with a high level of evidence based on a firm methodology, as group of experts at the National Institute of Pediatrics and other institutions in the National Healthcare System under the coordination of the National Center for Technological Excellence in Healthcare, designed and adapted to Mexico the clinical practice guideline: "diagnosis and treatment of non-organic enuresis in pediatric patients at the first tier of healthcare".[3] Grading the evidence for this guideline with a recognized system of evaluation, like the USPSTF's,[12] will help determine its quality at the individual level.

MATERIAL AND METHOD

Transverse evaluation. The clinical practice guideline: diagnosis and treatment of non-organic enuresis in pediatric patients at the first tier of healthcare[3] contains 69 items of evidence divided in: epidemiology, risk factors, diagnostic methods, treatment, relapse, and complications. The evidence was taken from three [13-15] of ten international clinical practice guidelines chosen by means of the model of systematic review of the literature.[5]

For the evidence in the Mexican guideline, the source of the original documents from which it was taken was identified;[16] all these references

were located intentionally by title, author, journal, and year of publication in virtual libraries: Pubmed, Embase, Cochrane plus, and manual identification of gray bibliography (mainly books).

Unit of analysis: the original articles that justify the evidence chosen for the clinical practice guideline: diagnosis and treatment of non-organic enuresis in pediatric patients at the first tier of healthcare.[3]

Inclusion criteria: all articles, references, narrations, reviews, and chapters from which evidence used in the Mexican guideline was taken.

Exclusion criteria: evidence that has no way to be analyzed because the guideline from which it was taken does not specify the literature supporting the evidence. Evidence structurally supported by gray literature was excluded.

Measuring instrument: the articles included were analyzed and evaluated using the classification proposed by the USPSTF (US Preventive Services Task Force), a system that balances simplicity, feasibility, and adequate quality in rating evidence and grading recommendations.[12]

After analyzing each article individually, the evidence (supported by the sum of several of these articles) was analyzed. Interventional studies were graded depending on the net benefit (benefit-detriment) of their results.[12]

RESULTS

All the original articles, updates, and chapters taken as sources in developing the clinical practice guideline: diagnosis and treatment of non-organic enuresis in pediatric patients at the first tier of healthcare[3] were enumerated, classified, and graded with the USPSTF instrument.[16] This publication describes the findings of that work and cites the articles with the highest level of evidence and greatest strength in their recommendations.

The section *Epidemiology* in the clinical practice guideline: diagnosis and treatment of non-organic enuresis in pediatric patients at the first tier of healthcare[3] contains four items of evidence supported by five original articles, three of them transverse (the expected design for studies of epidemiology of a pathology), a book chapter, and an interventional cohort[17] (level of evidence II-2).

The section *risk factors* contains 16 items of evidence. The articles supporting them are eight transverse studies which are not considered the study of choice for this section, which impoverishes it. We also analyze cohort studies[18] and cases and controls[19-22] (level of evidence II-2, II-3), an expected situation given that such designs allow for monitoring over time of healthy children who may subsequently suffer from the disorder. We also observed a non-randomized clinical trial[23] with a small net benefit (recommendation grade C).

The section *diagnostic methods* has 18 items of evidence. Those taken from the clinical practice guideline by Ubeda Sansano MI et al.[13] are based on another clinical practice guideline with level of evidence I and recommendation grade A[15] (highly recommendable), a cohort and a clinical trial with level of evidence C and a small net benefit, and on six transverse studios. The evidence taken from the other two clinical practice guidelines are based only on transverse studies and on book chapters.

In the section *Treatment* (21 items of evidence) 29 articles were analyzed, including two systematic reviews of the Cochrane literature, which are the fundamental basis for the recommendations established by international guidelines.[24,25] Only seven articles were classified with level of evi-

dence I and recommendation grade A;[24-30] most support the evidence taken from the guideline by Ubeda Sansano MI et al.[13] The evidence taken from the other two guidelines, based on our analysis, do not offer an optimum level that could lend strength to their recommendations.

The section *Relapse* contains six items of evidence and its primary support is from three systematic reviews with a substantial recommendation grade.[24,25,31]

Finally, the section *Complications* (four items of evidence) analyzed two articles: a systematic review[32] level of evidence I and recommendation grade B, and a clinical case with level of evidence III.

Thirty-three percent (23) of the items of evidence in the Mexican guideline were not evaluated because the international guidelines[13-15] do not specify the original articles on which they base some of their claims, which subsequently were taken as evidence in the Mexican guideline.

DISCUSSION AND CONCLUSIONS

The articles graded best by the instrument used support the following evidence contained in the Mexican guideline:[3]

The prevalence of bedwetting varies at different ages due to inconsistencies in its definition, differences in data collection methods, and the characteristics of the study population. Bedwetting has a rate of spontaneous resolution of 14% per annum between five and nine years, 16% between 10 and 14 years, and 16% between 15 and 19 years. In persons over 20 years it persists even in 3%.

Retardation in motor and speech development, and alterations in secretion of the antidiuretic hormone, have been observed in children with enuresis. Also, bedwetting has been associated with functional alterations of the bladder, detrusor instability, and evacuatory dysfunction.

In addition to physical examination and complete clinical history, which includes history of attention deficit disorder and hyperactivity, chronic headaches, constipation, or sleep apnea, it is essential that the patient and his/her family keep a urination record (daily urine volumes, urine leaks, urinary urgency, situations of holding to the limit, etc.).

As regards treatment, moisture alarms (not available in Mexico) are effective to reduce symptoms of enuresis. Motivational therapy increases the number of dry nights. Associating desmopressin with the alarm offers no long-term advantage, although initially it may increase the number of dry nights.

Abrupt withdrawal of desmopressin therapy raises the likelihood of relapse. The alarm offers advantages over desmopressin; the percentage of relapse with alarm varies from 30 to 50%.

Finally, bedwetting may have negative consequences, with impact on social life and isolation, physical aggression, low self-esteem, alteration in personal relationships, high cost of laundry, and parental anxiety. Notwithstanding, 20% of physicians offer no treatment for the condition.

The process of classifying and evaluating the literature that supports the clinical practice guideline: diagnosis and treatment of non-organic enuresis in pediatric patients at the first tier of healthcare[3] shows that not all evidence has equal methodological force, despite having been taken from clinical practice guidelines developed with high methodological rigor.

This investigation classified only articles that provided the evidence offered by the Mexican

clinical practice guideline[3] and on that basis attempted to evaluate its contents. The results are far from being a reflection of rigor in the development, applicability, or presentation of international clinical practice guidelines, which are the basis for the Mexican clinical practice guideline,[3] and therefore the evaluation of source documents which individually supported the different international clinical practice guidelines reviewed in developing the Mexican guideline does not reflect the methodological quality of those clinical practice guidelines.

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