

prescribed in 72.4% of infants, followed by ibuprofen (34.6%). The antipyretic most frequently prescribed in combination was ibuprofen (48.4%) (Fig. 1).

We found that antipyretics were used very frequently prior to visiting the emergency department. Although the use of paracetamol or ibuprofen (alone or in combination) was most prevalent,⁶ we also found combinations of up to three agents for which the efficiency and safety have not been demonstrated. The use of physical methods, as recommended in different GCPGs, predominated in the emergency room;^{2,3} however, prescription of antipyretics not previously used and of agents like metamizole (banned in developed countries) to schoolchildren and adolescents was also common. The current recommendations are the use of monotherapy by the oral route and educating parents on the benefits of fever and its adequate control.^{1,2} The major finding in our study was the change in the prescription of antipyretics at discharge to the home. Contrary to what we expected, at discharge most patients were prescribed an additional antipyretic or an antipyretic other than the one that had been used to control the fever. This may be interpreted as anxiety on the part of both parents and doctors, so better communication and education on warning signs, and not only on the control of body temperature, would be advisable. Our results need to be confirmed by studies performed in other locations and under different conditions.

References

1. Sullivan EJ, Farrar CH. Fever and antipyretic use in children. *Pediatrics*. 2011;127:580–7.
 2. Chiappini E, Principi N, Longhi R, Tovo P-A, Becherucci P, Bon-signori F, et al. Management of fever in children: summary of the Italian pediatric society guidelines. *Clin Ther*. 2009;31:1826–43.
 3. National Institute of Health and Clinical Excellence. Understanding NICE guidance. Feverish illness in children. London: NICE; 2013 [accessed 01.03.14]. Available from: www.nmc-uk.org/publications
 4. Demir F, Sekreter O. Knowledge attitudes and misconceptions of primary regarding fever in children: a cross sectional study. *Ital J Pediatr*. 2012;38:40 [accessed 05.05.14]. Available from: <http://www.ijponline.neet/38/1/40>
 5. Lava SAG, Simonetti GD, Ramelli GP, Tschumi S, Bianchetti MG. Symptomatic management of fever by Swiss board-certified pediatricians: results from a cross-sectional, web-based survey. *Clin Ther*. 2012;34:250–6.
 6. Purssell E. Systematic review of studies comparing combined treatment with paracetamol and ibuprofen, with either drug alone. *Arch Dis Child*. 2011;96:1175–9.
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Narcolepsy-cataplexy, a disease of autoimmune origin☆☆☆



Narcolepsia-cataplejía, una enfermedad de etiología autoinmune

To the Editor:

The current International Classification of Sleep Disorders includes two different types of narcolepsy: narcolepsy type 1 (with hypocretin deficiency or cataplexy) and narcolepsy type 2 (without hypocretin deficiency).^{1,2}

Narcolepsy type 1 was traditionally known as narcolepsy-cataplexy and is a chronic disease with symptoms that include excessive daytime sleepiness, sleep attacks, sudden episodes of loss of muscle tone when awake, hypnagogic hallucinations, sleep paralysis and disrupted nocturnal sleep.^{2,3}

It has an autoimmune aetiology, the target of which is the secretion of the hypothalamic neuropeptide hypocretin-1,⁴ and it is strongly associated with HLA-DQB1*0602.⁵

We present the case of a 9-year-old boy that was previously healthy. There was no family history of neurologic disease.

The child sought care for attention deficit with a decline in academic performance lasting 3 months. He also reported chronic daytime hypersomnia punctuated with sleep attacks during which the patient dreamed. In the last 2 months the patient had experienced 4–5 episodes a day of sudden and brief loss of muscle tone in the neck and lower extremities with no clear trigger and associated, as we later found, to tongue protrusion. In the past few weeks he had been eating more than usual.

The clinical examination was normal, although the child reported sleepiness.

The awake electroencephalogram and the head and hypothalamus MRIs were normal.

The modified Epworth sleepiness scale was completed to assess the degree of daytime sleepiness, and the patient scored within the severe range (20/24).

A polysomnography (PSG) was performed, showing a disrupted sleep architecture with fragmented but efficient sleep with onset in REM sleep and with a higher than expected proportion of REM sleep for his age. The

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multiple sleep latency test (MSLT) comprised 4 naps; REM sleep at sleep onset occurred in 3 of the naps, and the mean sleep latency was less than one minute. All of these results were compatible with narcolepsy-cataplexy, so more specific studies were conducted: the immunochemical assay was positive for HLA-DQB1*0602, and the measurement of hypocretin-1 in cerebrospinal fluid (CSF) revealed a concentration below 10 pg/mL, confirming the clinical diagnosis.

We finally initiated symptomatic treatment for narcolepsy, stressing the importance of proper sleep hygiene. We prescribed immediate release methylphenidate at breakfast and following each of two 30-min naps after lunch and the afternoon snack, and imipramine before bedtime. The patient reported a substantial improvement in his quality of life.

Narcolepsy-cataplexy has an autoimmune origin that targets the secretion of hypocretin-1,⁴ a neurotransmitter produced in the dorsal and lateral hypothalamus that promotes wakefulness and inhibits REM sleep. The measurement of hypocretin is a definitive diagnostic test, albeit one that must be interpreted within the appropriate clinical context.³

When there is suspicion of persistent hypersomnia compatible with narcolepsy, it is important to determine its severity by means of validated scales, such as the modified Epworth Sleepiness Scale or the Paediatric Daytime Sleepiness Scale, and to confirm the diagnosis by means of specific complementary tests: a PSG followed by a MSLT, an immunogenetic examination, and measurement of the CSF hypocretin-1 concentration.³

Although a specific treatment for narcolepsy-cataplexy in children has yet to be established, there are two different and complementary approaches to its management: a cognitive-behavioural approach, and a pharmacological-symptomatic approach.²

Key elements of management include proper sleep hygiene practices, avoidance of substances that promote a lethargic state or increase wakefulness, and adequate psychosocial support.²

The first-line treatment of daytime hypersomnia in adults is modafinil, but its administration in children younger than 16 years has not been approved, even though clinical experience suggests that it is an effective, safe and commonly used drug to manage narcolepsy in the paediatric age group.⁶ The drug that has been used most commonly in children has been methylphenidate, which stimulates the central nervous system and promotes wakefulness.

Treatment with sodium oxybate has been introduced to treat hypersomnia and cataplexy in adults, but its use in

children has yet to be approved.² Traditionally, drugs that inhibit REM sleep, such as tricyclic antidepressants, have been used for this purpose. In this case, we chose imipramine due to its extensive use in the paediatric age group.

Given the autoimmune aetiology of this disease, it has been suggested that early treatment with intravenous immunoglobulin could prevent the loss of hypocretin-producing neurons, although there is no objective evidence of this beneficial effect.²

Since it is clear that this disease has an autoimmune origin, we believe it is necessary to perform new studies with the aim of finding a replacement therapy to address the neuropeptide deficiency.

References

1. American Academy of Sleep Medicine. The international classification of sleep disorders. Diagnostic and coding manual electronic version. 3rd ed. Westchester: American Academy of Sleep Medicine; 2014. The new classification distinguishes between two basic forms of narcolepsy: narcolepsy type 1 (with hcrt-1 deficiency) and narcolepsy type 2 (without hcrt-1 deficiency).
2. Nevsimalova S. The diagnosis and treatment of pediatric narcolepsy. *Curr Neurol Neurosci Rep.* 2014;14:469.
3. Peraita-Adrados R, García-Peñas JJ, Ruiz-Falcó L, Gutiérrez-Solana L, López-Esteban P, Vicario JL, et al. Clinical, polysomnographic and laboratory characteristics of narcolepsy-cataplexy in a sample of children and adolescents. *Sleep Med.* 2011;12:24–7.
4. de Lecea L, Sutcliffe JG. The hypocretins and sleep. *FEBS J.* 2005;272:5675–88.
5. Mignot E, Lin L, Rogers W, Honda Y, Qiu X, Lin X, et al. Complex HLA-DR and DQ interactions confer risk of narcolepsy-cataplexy in three ethnic groups. *Am J Hum Genet.* 2001;68:686–99.
6. Lecendreau M, Bruni O, Franco P, Gringras P, Konofal E, Nevsimalova S, et al. Clinical experience suggests that modafinil is an effective and safe treatment for paediatric narcolepsy. *J Sleep Res.* 2012;21:481–3.

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