Introduction

Diagnosing migraine syndrome (MS) in children represents an everyday clinical problem. Different criteria are suggested as diagnostic of MS in children and adolescents [1, 2]. Sensory, vegetative and affective phenomena, with marked quantitative and qualitative variations among children outline MS [3, 4]. MS clinical features are age-dependent [5]. The younger the child is, the harder it is to diagnose MS [6, 7]. There are no definite reliable principles for safe, accurate and fast diagnosis of MS in children.

This article aims to define those features that would provide easier and more precise diagnosis of MS in children.

Material and methods

The research was carried out in the territory of the northern province of Serbia, Vojvodina, which has a population of 2,031,992 people according to the last census (2002). From 1988 to 2004 participants were selected by a multistage stratified clustered sampling procedure from 23 preschools and 42 grade schools in 9 cities in Vojvodina (Novi Sad, Subotica, Kikinda, Zrenjanin, Vrsac, Bela Crkva, Melenci, Futog and Temerin). 30,636 children aged 3–17 years (mean 9.21, SD 3.16) were surveyed (15,202 girls and 15,434 boys).

A semi-structured questionnaire, developed by the Author, was designed according to the International Headache Society (IHS) criteria. The accuracy of the questionnaire used in this survey was based on the Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain and
International Headache Society-Revised (IHS-R) criteria [8, 9]. We acknowledged all migraine attack characteristics according to the second edition of the International Classification of Headache Disorders. The study was conducted in two phases: completing the questionnaire, and face-to-face interview for those having recurrent headaches. Based on data gathered through the questionnaire, possible migraine sufferers underwent an extended interview and neurological examination.

Canonical discrimination analysis and multiple regression correlation analysis were used to define specific characteristics that can distinguish migraine headaches from primary non-migraine headaches.

Results

Out of 30 636 observed children, 5812 (18.97%) reported primary non-migraine recurrent headaches (2910 male and 2902 female) and 2644 (8.63%) reported migraine headaches (1162 male and 1482 female). Migraine headache is reported for the first time in children aged 5.14 years (range 2.8–14 years). Migraine attacks follow identical patterns in 2509 (94.9%) children: occurring monthly in 2062 (78.0%), occurring in the morning hours in 1547 (58.5%), lasting for several hours in 1192 (45.1%) and ending after sleep in 2028 (76.7%) children.

Migraine-associated photophobia is reported in 2372 (89.7%) children, phonophobia in 2107 (79.7%) children, and other vegetative symptoms (changes in skin colour, sweating, irregular breathing, precordial pain, etc.) in 2610 (98.7%) children. Phonophobia is the dominant symptom in children at average age 11.11 years (range 3–17), phonophobia in children at average age of 11.21 years (range 3–17) and other vegetative symptoms in children aged 9.10 years (range 3–17). Nausea is present in 2607 (98.6%), impulse to vomit in 2583 (97.7%) and vomiting in 2583 (77.2%) children with MS. Nausea, impulse to vomit and vomiting (all together) are dominant in children aged 11.10 years (range 3–17), presenting in 2607 (98.6%) of all children. Recurrent abdominal pain with headache attacks is reported by 1966 (74.4%) children with MS, mostly at age 7.3 years (range 3–17) (Table 1).

Canonical discriminate analysis pointed to the following statistically significant factors (canonical dis-

| Migraine symptom | Migraine and other headaches |
|------------------|----------------------------|
| Vomiting instinct| 0.945                      |
| Relief after sleep| 0.945                    |
| Photophobia      | 0.523                      |
| Nausea           | 0.379                      |
| Phonophobia      | 0.354                      |
| Vomiting         | 0.330                      |
| Vertigo          | 0.165                      |
| Other            | 0.057                      |
| Abdominal pain   | 0.051                      |

Table 1 Age-dependent symptoms in migraine headache

| Symptoms                  | Headache/symptoms presence | Children with migraine | Arithmetical mean | Standard deviation | Pearson’s coefficient of correlation | Statistical significance of correlation coefficient |
|---------------------------|-----------------------------|------------------------|-------------------|--------------------|--------------------------------------|------------------------------------------------------|
| Phonophobia               | Minimal                     | 1081                   | 11.21             | 2.90               | 0.09                                 | –                                                   |
|                           | Maximal                     | 1563                   | 11.00             | 3.16               | 0.1                                 |                                                     |
|                           | Medium                      | 2644                   | 11.11             | 3.04               | 0.07                                 |                                                     |
| Photophobia               | Minimal                     | 1166                   | 11.34             | 2.80               | 0.08                                 | –                                                   |
|                           | Maximal                     | 1478                   | 11.12             | 3.16               | 0.1                                 |                                                     |
|                           | Medium                      | 2644                   | 11.21             | 3.06               | 0.05                                 |                                                     |
| Other vegetative symptoms | Minimal                     | 975                    | 11.73             | 2.93               | 0.11                                 | 0.01                                                |
|                           | Maximal                     | 1769                   | 10.76             | 3.04               | 0.08                                 |                                                     |
|                           | Medium                      | 2644                   | 11.10             | 3.04               | 0.07                                 |                                                     |
| Nausea, impulse to vomit  | Minimal                     | 297                    | 6.48              | 1.31               | 0.25                                 | 0.01                                                |
|                           | Maximal                     | 2347                   | 10.17             | 3.00               | 0.07                                 |                                                     |
|                           | Medium                      | 2644                   | 11.10             | 3.04               | 0.07                                 |                                                     |
| Abdominal pain            | Minimal                     | 678                    | 12.27             | 2.15               | 0.06                                 | 0.001                                               |
|                           | Maximal                     | 1966                   | 6.23              | 2.22               | 0.11                                 |                                                     |
|                           | Medium                      | 2644                   | 7.33              | 2.21               | 0.05                                 |                                                     |

\* Test of independent samples: F 33.315, t 6.6222, DF 6595, Sig 0.0001
\* Test of independent samples: F 24370, t 9.088, DF 3072, Sig 0.0001
\* Test of independent samples: F 70074, DF 1, Sig 0.0001
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criminant coefficient >0.3) to distinguish migraine from non-migraine headaches in children: vomiting impulse (0.945), relief after sleep (0.945), photophobia (0.523), nausea (0.379), phonophobia (0.354) and vomiting (Table 2).

Multiple analysis with multiple regression showed a very high (canonical discriminant coefficient >0.75) correlation for relief after sleep, vomiting impulse, photophobia, vomiting and photophobia with MS in children. Nausea and phonophobia have high correlation with migraine in children (0.75). Other analysed symptoms did not present a significant correlation with MS in children (Table 3).

| Migraine symptom/migraine headache | $r_{12}$ | $r_{12}^2$ (%) |
|-----------------------------------|--------|-------------|
| Relief after sleep                | 0.96   | 93.17       |
| Vomiting instinct                 | 0.94   | 89.72       |
| Vomiting                          | 0.90   | 81.00       |
| Photophobia                       | 0.84   | 71.89       |
| Nausea                            | 0.75   | 55.71       |
| Phonophobia                       | 0.75   | 55.71       |
| Vertigo                           | 0.23   | 5.13        |
| Other                             | 0.19   | 3.66        |
| Abdominal pain                    | 0.18   | 3.35        |

Discussion

In the northern province of Serbia, MS appears in 8.36% (43.95% m: 56.05% f) of children aged 3–17. Our findings are comparable to the conclusions of other studies. Sillanpaa and Anttila found a headache prevalence of 37% in 2941 children in Finland aged 7–14 years. In 2.7% children aged 7 years and 10.6% children aged 14 years he defined migraine using Vahlquist’s criteria [10]. Wöber-Bingöl et al.’s population study of migraine in children and adolescents [11] encountered migraine prevalence of 1.1%–5% in children and 3%–17.6% in adolescents. Zencir et al. [12] found overall migraine prevalence was 8.8%; it was 6.7% in boys and 11.0% in girls (OR: 1.7; 95% CI: 1.3–2.3). Balottin et al. [13] reports a mean age at onset of 4 years and 2 months, and a range of 10 months to 6 years presenting with headache symptomatology. In our group the first migraine headache attack is reported at a median age of 5.14 years (range 2.8–14 years).

Children with migraine headaches describe their attacks as identical even four times more often than children with non-migraine headaches. Migraine headache is mostly unilateral. Distinct pain location in migraine headaches is ($p<0.0001$) connected with the age of the children and their ability to interpret it [14]. Wöber-Bingöl et al. [15] found in 260 consecutive patients aged 3–69 that headache duration and the prevalence of unilateral, pulsating pain, photophobia and phonophobia increased in females, whereas the prevalence of aggravation by physical activity decreased with age.

Migraine headaches that affect younger children last significantly shorter: a few minutes at an average age of 4.5 years, up to 1 h at an average age of 5.37 years, and more than 2 h beyond 12.32 years. Analysing 409 children, Wöber-Bingöl et al. [16] found the duration of migraine attacks was less than 2 h in 19.0% of migraine patients.

Migraine headaches often occur early in the morning, with a clear prevalence in the group with rare attacks (several times a year – 78.0% : 22.7%; $p=0.0001$). The frequencies of migraine attacks, as well as other characteristics of childhood MS, depend on children’s age. Most migraine attacks occur several times a year in children with an average age of 11.11 years and onset at the age of 5.11 years. Sleeping off the pain (76.6%) and absence of spontaneous pain relief (2.6%) are also among the characteristics of migraine headaches in children [14]. Senbil et al. [17] described relief of headache with sleeping or lying down in a dark, quiet room was found to be the highest specific and sensitive factor of migraine headache not included in diagnostic criteria.

In the group of children with headache who experience nausea, 83.8% have migraine and 16.1% non-migraine headaches. Among children who experience vomiting impulse, 98.7% have migraine and 1.3% have non-migraine headaches. In the group of children who experience vomiting, 99.4% have migraine headaches and 0.6% non-migraine headaches. In the group of children with headache-associated nausea and/or vomiting impulse and/or photophobia, 83.7% have migraine headache and only 16.3% have non-migraine headaches. In the group of children who have neither nausea nor vomiting impulse, only 0.7% have migraine headaches, and 99.3% have non-migraine headaches [14]. Our results clearly define nausea, vomiting impulse and vomiting as elements of MS attacks in children, much more frequent in younger children. Only 1.3% of children with migraine headaches at average age of 6.45 years have no nausea, vomiting impulse or vomiting. Zambrino et al. [18] report that with the exception of the presence of vomiting in migraine patients, the age at onset was not found to be a factor influencing the characteristics of the headache.

A percentage of 74.46 children at average age of 6.23 years reported recurrent abdominal pain during MS headache attacks. A percentage of 75.44 children at average age of 12.27 years had no recurrent abdominal pain during...
MS headache attacks. Among children who experience bowel movement disorders or changes in stool consistency, 97.4% have migraine and 2.6% non-migraine headaches. Considering the fact that only a small number of children have headache-associated bowel movement disorders, this symptom has a low significance, but a very high specificity [14]. Numerous authors write about abdominal migraine as one of the variants of migraine headache that typically occurred in children within the group (coded as 1.3.2 in the revised edition of IHS classification – ‘Childhood periodic syndromes that are commonly precursors of migraine’). The affected children frequently develop typical migraine later [19]. Vomiting and abdominal pain are symptoms that may arise from a number of different causes. Both are noted for the absence of pathognomonic clinical features but also for the large number of other conditions to be considered in their differential diagnoses. It is important to carefully evaluate these patients, as well-being between vomiting episodes does not guarantee the absence of organic disease [20].

A percentage of 99.3 children with headache-associated phonophobia suffer from migraine headaches and only 0.7% from non-migraine headaches. Migraine-associated photophobia is reported in 89.7% of children with migraine headaches, and only in 0.2% of children with non-migraine headaches. Other vegetative symptoms (changes in skin colour, sweating, irregular breathing, precordial pain) are associated with migraine headache in 98.7% of children and in 8.8% with non-migraine headaches [14]. Migraine-associated skin pallor is found in 96.1% and dark circles under the eyes in 70.2% of children with migraine headaches ($p=0.000001$) [14]. There is a high specificity of vegetative symptoms in migraine headaches (97.5%) ($p=0.0001$), which allows inclusion of various vegetative symptoms collectively into the diagnostic criteria of MS in children [14]. No age-dependent correlation was present with photophobia and phonophobia presence during MS headaches in our study group. Nausea, vomiting impulse and vomiting are basic elements of migraine attacks in children. Vegetative symptoms seem to be age dependent, with higher expression in younger children.

Highly statistically significant (>0.3) discrimination factors between migraine headaches and non-migraine headaches in children, established by canonical discriminate analysis, which should be included into the definition of children MS, are as follows: relief after sleep, vomiting impulse, photophobia, nausea, phonophobia and vomiting. Wöber-Bingöl [15] found that intensity of pain, aggravation of headache by physical activity, nausea and vomiting were the most important features, and the quality of pain, photo- and phonophobia were less helpful in the differential diagnosis of migraine and tension-type headache.

Multiple analyses with multiple regressions show the strongest connection of relief after sleep, vomiting impulse, vomiting and photophobia with MS in children. Nausea and phonophobia also show slightly lower connections with migraine in children. Other analysed symptoms did not present significant correlations with childhood MS.

**Conclusions**

This study pointed to certain specific features of migraine headaches in children: identical signs and symptoms during individual migraine attacks, onset in early morning hours, lasting several hours and monthly migraine episode frequency, specific migraine-associated symptoms (nausea; impulse to vomit; vomiting; nausea, impulse to vomit and vomiting all together; pallor; phonophobia; photophobia; dark circles under the eyes), and cessation of symptoms after sleep. The strongest connection with MS in children had the following factors: relief after sleep, vomiting impulse, vomiting and photophobia present during MS headache. Slightly lower but still high connections are found with nausea and phonophobia. MS headache in children can be distinguished from primary non-migraine headache in children by relief after sleep, vomiting impulse, photophobia, nausea, phonophobia and vomiting.

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