### НАИБОЛЕЕ ЧАСТО ВСТРЕЧАЮЩИЕСЯ ГОЛОВНЫЕ БОЛИ У ДЕТЕЙ: ОСОБЕННОСТИ ДИАГНОСТИКИ И ТЕРАПИИ

Профессор Ахмадеева Лейла Ринатовна www.ufaneuro.org

Подготовлено без финансовой

поддержки со стороны коммерческих

организаций и отражает данные

автора и современной литературы



## ЛЕКЦИЯ В 3 ПРЕДЛОЖЕНИЯХ

- 1. Головные боли у детей встречаются чаще, чем у взрослых
- 2. Диагностика их принципиально такая же, как и у взрослых, но есть ряд особенностей
- 3. В лечении нефармакологические методы могут быть еще более важны, чем для взрослых

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Species Humans Other Animals <u>Clear all</u> Show additional filters	<ul> <li>Management of Episodic Migraine in Children and Adolescents: a Practical Approach.</li> <li>Rastogi RG, Borrero-Mejias C, Hickman C, Lewis KS, Little R. Curr Neurol Neurosci Rep. 2018 Oct 31;18(12):103. doi: 10.1007/s11910-018-0900-0. Review.</li> <li>PMID: 30382405</li> <li>Practice guided</li> </ul>	Download usV your search terms eline update summary: Acute migraine in childr [Neurology. 2020]

#### 5357 статей в PubMed В 2020г – на 26.02.2020 – 31 статья

## ГОЛОВНЫЕ БОЛИ У ДЕТЕЙ ВСТРЕЧАЮТСЯ ЧАЩЕ, ЧЕМ У ВЗРОСЛЫХ:

Частота встречаемости головных болей у 13-15 летних – от **70% до 80%** 

При распределении на все возрастные группы - 12% - 18%

Billie BS (1962) Migraine in school children. a study of the incidence and short-term prognosis, and a clinical, psychological and electroencephalographic comparison between children with migraine and matched controls. Acta Paediatr Suppl 136:1–151

Sillanpää M (1983) Prevalence of headache in prepuberty. Headache 23:10–14

Breslau N, Rasmussen BK (2001) The impact of migraine: Epidemiology, risk

factors, and co-morbidities. Neurology 56:S4–S12

Слайд проф. Осиповой В.В.



#### Международные стандарты диагностики ГБ

Международная классификация расстройств, сопровождающихся головной болью = Международная классификация головных болей (МКГБ)

- -- 1 издание (МКГБ-1, 1988)
- -- 2 издание (МКГБ-2, 2004)
- -- 3 издание (МКГБ-3, 2018)

#### МКГБ-3 (2018) www.headache-society.ru www.paininfo.ru

- Headache Classification Committee of the International Headache Society : classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain. // Cephalalgia. – 1988. - 8 (Suppl 7):1-96.
- 2. Headache Classification Subcommittee of the IHS. The International Classification of Headache Disorders, 2nd ed. Cephalalgia 2004;24(Suppl 1):1-232.
- 3. Headache Classification Subcommittee of the IHS. The International Classification of

Слайд проф. Осиповой В.В.

## МКГБ-3 бета (2018): оглавление

14 разделов (глав), разделенных на формы, типы, подтипы

<u>Часть I:</u> Первичные ГБ (не связанные с заболеваниями мозга и др. структур головы и шеи) (Главы 1-4)

**Часть II:** Вторичные ГБ (связанные с

другими <u>(Главы 5-12)</u>

иложение

заболеваниями)

<u>Часть III:</u> Болевые краниальные невропатии, другие лицевые и головные боли <u>(Главы</u> <u>13-14)</u>

Слайд проф. Осиповой В.В.

# Соотношение первичных и вторичных ГБ



#### Вторичные ГБ

(симптоматические, связаны с другими заболеваниями)

#### Первичные ГБ

(не связаны с другими заболеваниями)

#### NB! Только в 2-4% ГБ является симптомом тяжелого



#### угрожающего жизни заболевания

Rasmussen BK, Jensen R, et al. 1991, Lipton RB, Scher AI, Kolodner K, Liberman J, Steiner TJ, Stewart WF. 2002, European principles of management of common headache disorders in primary care 2007

# Какие виды ГБ встречаются наиболее часто?

- Формы ГБ, наиболее распространенные и значимые для общественного здоровья и экономики
  - Мигрень
    - Головная боль напряжения

- Другие хронические ежедневные ГБ, в т.ч. абузусная ГБ (МИГБ)

> Всемирная кампания против головной боли "Lifting the Burden" (Воспроизведено с разрешения T.Steiner)

Первичные

ГБ

## ВСЕ ОНИ ВСТРЕЧАЮТСЯ НЕ ТОЛЬКО У ВЗРОСЛЫХ, НО И У ДЕТЕЙ!!!



Curr Pain Headache R (2016) 0: 14 DOI 10.1007/s11916-010 0535 z

CHILDHOOD AND ADOLESCENT HEADACHE (S EVERS, SECTION EDITOR)

#### **Chronic Migraine in Children and Adolescents**

Aynur Özge<sup>1</sup> · Osman Özgür Yalın<sup>2</sup>

Хроническая мигрень и ее триггеры у 10-летней девочки

Тяжелая хроническая мигрень у 8-летнего мальчика



Среди детей с хроническими первичными головными болями частота ГБ из-за избыточного употребления медикаментов («абузуса»)- **21–60%** 

#### Среди подростков в США хроническая мигрень встречается у 0.79% (без абузуса) и у 1.75% с абузусным типом

Gelfand AA, Goadsby PJ. **Medication overuse** in children and adolescents. Curr. Pain Headache Rep. 2014; 18(7): 1-6

## В Германии

- 38% у детей младших возрастных групп
- 84% у подростков
  - мигрень: 6% 31%;
    - A tendency for a **global increase** of headaches in the last years/decades was observed. However, this overall picture remains inconsistent.
    - Stress, smoking, caffeine consumption and muscular tension and pain within the neck and shoulder area were confirmed to be risk factors for headache in children and adolescents in all studies.



## В России

- более 5 тыс. городских школьников в России:
- жалобы на головные боли предъявляли 52,24% детей.
  - чаще беспокоили девочек (57,5%), чем мальчиков (46,69%; р < 0,0001).</li>

-Среди первичных ГБ наиболее распространенными типами были <u>мигрень</u> и <u>ГБН</u>.

> <u>Проф. В.М. ДЕЛЯГИН с соавт.</u>, г.Москва, 2014г. Жур. «Практическая медицина»

## Общая встречаемость – результат анализа 64 кросссекционных исследований

54.4% - головные боли 59.2% среди девочек 49.3% среди мальчиков

«Боль в зоне выше линии, соединяющей орбиту и наружный слуховой проход»

> http://www.uptodate.com/ contents/headache-inchildren-approach-toevaluation-and-generalmanagement-strategies (April, 2016)

**9.1% - мигрени** 10.5% - среди девочек 7.6% - среди мальчиков

Wober-Bingol C(2013) Epidemiology of migraine and headache in children and adolescents. Curr Pain Headache Rep 17:341

## По возрастам

- До 3 лет 3% 8%
- 5 лет 19.5%
- 7 лет 37% 51.5%
- До пубертата чаще у мальчиков
- После пубертата чаще у девочек

Sillanpää M (1983) Changes in the prevalence of migraine and other headaches during the first seven school years. Headache 23:15–19
Sillanpää M, Piekkala P, Kero P (1991) Prevalence of headache at preschool age in an unselected child population. Cephalalgia 11:239–242
Deubner DC (1997) An epidemiologic study of migraine and headache in 10–20 year olds. Headache 17:173–180

## У 73% детей головные боли продолжаются во взрослом возрасте (20-летнее исследование)



Brna P. et al, 2005

## проблемы

- Отсутствие единогласия в мировом сообществе в диагностических критериях для отдельных форм головных болей у детей
- Отсутствие единых международных (и даже отдельных национальных!) стандартов терапии.

В мире опубликованы лишь несколько клинических рекомендаций по лечению острых болей при мигрени у детей.

Winner P, Martinez W, Mate L, Bello L (1995) Classification of pediatric migraine: proposed revisions to the IHS criteria. Headache 35:407–410 Ozge A, Bugdayci R, Sasmaz T, Kaleăgasi H, Kurt O, Karakelle A, Tezcan H, Siva A (2002) The sensitivity and specificity of the case definition criteria in diagnosis of headache: a school-based epidemiological study of 5562 children in Mersin. Cephalalgia 22:791–798 // др.



#### "Бытие определят сознание"

Введение к "Критике политической экономии" К.Маркс (1859)



#### "Диагноз определяет стратегию лечения»"

Special Article



#### CME Practice parameter: Evaluation of children and adolescents with recurrent headaches

#### Report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society

D.W. Lewis, MD; S. Ashwal, MD; G. Dahl, BS; D. Dorbad, MD; D. Hirtz, MD; A. Prensky, MD; and I. Jarjour, MD

Abstract-Objective: The Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society develop practice parameters as strategies for patient management based on analysis of evidence. For this parameter, the authors reviewed available evidence on the evaluation of the child with recurrent headaches and made recommendations based on this evidence. Methods: Relevant literature was reviewed, abstracted, and classified. Recommendations were based on a four-tiered scheme of evidence classification. Results: There is inadequate documentation in the literature to support any recommendation as to the appropriateness of routine laboratory studies or performance of lumbar puncture. EEG is not recommended in the routine evaluation, as it is unlikely to define or determine an etiology or distinguish migraine from other types of headaches. In those children undergoing evaluation for recurrent headache found to have a paroxysmal EEG, the risk for future seizures is negligible; therefore, further investigation for epilepsy or treatments aimed at preventing future seizures is not indicated. Obtaining a neuroimaging study on a routine basis is not indicated in children with recurrent headaches and a normal neurologic examination. Neuroimaging should be considered in children with an abnormal neurologic examination or other physical findings that suggest CNS disease. Variables that predicted the presence of a space-occupying lesion included 1) headache of less than 1-month duration; 2) absence of family history of migraine; 3) abnormal neurologic findings on examination; 4) gait abnormalities; and 5) occurrence of seizures. Conclusions: Recurrent headaches occur commonly in children and are diagnosed on a clinical basis rather than by any testing. The routine use of any diagnostic studies is not indicated when the clinical history has no associated risk factors and the child's examination is normal. NEUROLOGY 2002;59:490-498

Headaches are common in children and become increasingly more frequent during adolescence. In 1962, Bille<sup>1</sup> published his landmark epidemiologic survey of headache among 9,000 school children documenting that more than one third of 7-year-old children and half of 15-year-old children reported having had at least one headache. Data from 5 retrospective studies published between 1977 and 1991 of 27,606 children found the prevalence of any type of headache to range from 37 to 51% in 7 year olds, gradually increasing to 57 to 82% by age 15 years.<sup>24</sup> Prepubertal boys were also found to be more affected with headache than girls, whereas after puberty, headaches were found more commonly in females.

QSS Educational Statement: The Quality Standards Subcommittee (QSS) of the American Academy of Neurology seeks to develop scientifically sound, dimically relevant practice parameters for neurologists for disgnostic procedures, treatment modalities, and clinical disorders. Fractice parameters are strategies for patient management that might include diagnosis, symptom, treatment or procedure evaluation. They consist of one or more specific recommendations based on analysis of evidence.

From the Department of Pediatrics (Drs. Lewis and Dorbad and G. Dahl), Children's Hospital of the King's Daughters, Eastern Virginia Medical School, Norfolk, VA; the Department of Pediatrics (Dr. Ashwal), Loma Linda University School of Medicine, CA; NINDS (Dr. Hirtz), BetBaseda, MD; Department of Pediatrics (Dr. Prensky), St. Louis Children's Hospital, St. Louis, MO; and MCP-Hahnemann University School of Medicine (Dr. Jarjour), Allegheny General Hospital, Fittsburgh, PA.

Approved by the AAN Standards Subcommittee December 8, 2001. Approved by the AAN Practice Committee April 17, 2002. Approved by the AAN Board of Directors June 8, 2002. Approved by the CNS Practice Committee April 15, 2002. Approved by the CNS Executive Committee April 15, 2002.

Address correspondence and reprint requests to American Academy of Neurology, 1080 Montreal Avenue, St. Paul, MN 55116.

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## Practice Parameter: Pharmacological Treatment of migraine headache in children and adolescents

Report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society

D. Lewis, MD; S. Ashwal, MD; A. Hershey, MD; D. Hirtz, MD; M. Yonker, MD; S. Silberstein, MD

Published in *Neurology* 2004;63:2215-2224

Cephalalgia. 2018 Aug;38(9):1592-1607. doi: 10.1177/0333102417736902. Epub 2017 Oct 16.

Treatment of acute migraine attacks in children with analgesics on the World Health Organization Essential Medicines List: A systematic review and GRADE evidence synthesis. Jeric M1, Surjan N2, Jelicic Kadic A2,3, Riva N4, Puljak L2,5.

Background The World Health Organization Essential Medicines List (WHO EML) contains two analgesics for treatment of acute migraine attacks in children, ibuprofen and paracetamol. Methods The Embase, CDSR, CENTRAL, DARE and MEDLINE databases were searched up to 18 April 2017. We analyzed randomized controlled trials (RCTs) and systematic reviews (SRs) that investigate the efficacy and safety of ibuprofen or paracetamol for treatment of acute migraine attacks in children. We conducted meta-analysis and assessments of evidence with GRADE, Cochrane risk of bias tool, and AMSTAR. <u>Results Three RCTs (201 children) and 10 SRs on ibuprofen and/or paracetamol for acute migraine attacks in children were included</u>. Meta-analysis indicated that ibuprofen was superior to placebo for pain-free at 2 h or pain relief at 2 h, without difference in adverse events. There were no differences between paracetamol and placebo, or ibuprofen and paracetamol. Ten SRs that analyzed various therapies for migraine in children were published between 2004 and 2016, with discordant conclusions. <u>Conclusion</u> Limited data from poor quality RCTs indicate that ibuprofen and paracetamol might be effective analgesics for treating migraine attacks in children in the WHO EML is supported by indirect evidence from studies in adults.

Список ВОЗ содержит два анальгетика для купирования острой мигренозной боли у детей: ибупрофен и парацетамол.

Заключение: Данные ограничены, РКИ плохого качества, говорящие о возможной эффективности этих препаратов. Они включены в список на основании косвенных доказательств в исследованиях на взрослых

# The evaluation and management of paediatric headaches

J.M.Dooley

Published in Paediatr Child Health 2009;14(1):24-30

**NICE** National Institute for Health and Care Excellence

Headaches

Diagnosis and management of headaches in young people and adults

Issued: September 2012

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Abstract -

Cochrane Database Syst Rev. 2016 Apr 19;4:C0005220. doi: 10.1002/14651858.CD005220.pub2.

Drugs for the acute treatment of migraine in children and adolescents.

Richer L<sup>1</sup>, Billinghurst L, Linsdell MA, Russell K, Vandermeer B, Crumley ET, Durec T, Klassen TP, Hartling L.

#### **Review Article**

#### Acute Treatment Therapies for Pediatric Migraine: A Qualitative Systematic Review

Irene R. Patniyot, MD; Amy A. Gelfand, MD

Objective.—We sought to conduct a qualitative systematic review to evaluate the safety and efficacy of available treatments for pediatric patients with migraine or benign primary headache in the emergency department, in an effort to inform future practice.

Methods.—Scopus, Medline, and PubMed databases were searched for randomized controlled trials retrospective reviews, review articles, and case studies discussing migraine or benign primary headache management that were conducted in the emergency room or outpatient acute care setting in pediatric patients (less than 18-years old). Meeting abstracts and cited references within articles were also evaluated. Multiple variables were recorded, including type of treatment, study design, dosing, primary outcome, and side effects. Therapeutic gain was calculated in studies with a placebo arm. Treatments were subjectively assessed based on methodology and number of trials for a particular therapy.

Results.—Thirty-one studies were included in the final analysis. Of these, 17 were randomized controlled trials, 9 were retrospective reviews, and 5 were prospective chart review studies. One pertained to IV fluids, 2 to nonspecific analgesic use, 5 to dopamine receptor antagonists, 2 to valproic acid, 1 to propofol, 1 to magnesium, 1 to bupivicaine, 13 to triptan medications, and 3 to dihydroergotamine (DHE). Treatments considered effective for acute migraine or benign primary headache in the analgesic category include ibuprofen, and to a lesser degree acetaminophen. Ketorolac was not compared to other NSAIDs, but was found to be less effective than prochlorperazine. Of the phenothiazines, prochlorperazine was considered most effective. Of the triptan medications, almotriptan, rizatriptan, zolmitriptan nasal spray, and combination sumatriptan/naproxen are effective agents for acute treatment. Treatments considered probably effective included IV fluids, chlorpromazine, valproate sodium, injectable sumatriptan, and IV DHE. Treatments with oral zolmitriptan showed inconsistent results, while treatments considered ineffective included isolated oral sumatriptan and oral DHE. There is insufficient evidence to comment on propofol, magnesium, and bupivicaine efficacy.

Conclusions.—Of the available evidence, ibuprofen, prochlorperazine, and certain triptan medications are the most effective and safe agents for acute management of migraine and other benign headache disorders in the pediatric population. Additional studies in this population are needed, and should take into consideration variables such as dosing, coadministered medications, treatment duration, and length of treatment effect.

Key words: pediatric headache, emergency room headache treatment, acute pediatric migraine

Abbreviations: DHE dihydroergotamine, ED emergency department, NSAIDs non-steroidal anti-inflammatory drugs, RCT randomized controlled trial, VPA valproic acid Н.Н. Заваденко, Ю.Е. Нестеровский, Г.Ш. Хондкарян, Е.М. Шипилова, А.А. Холин

#### ПЕРВИЧНЫЕ ГОЛОВНЫЕ БОЛИ У ДЕТЕЙ И ПОДРОСТКОВ

Учебнометодическое пособие

Москва 2015

(Headache 2016;56:49-70)

## АНАМНЕЗ КРАЙНЕ ВАЖЕН

Исследование – 150 детей

Хорошо собранный анамнез – в 100% случаев правильный диагноз и правильное лечение

Dooley JM, et al, 2009

## СПРАШИВАТЬ У <u>ДЕТЕЙ</u>, А НЕ У РОДИТЕЛЕЙ!

# **36%** родителей не знают о головных болях у своих детей

•Sasmaz T, Bugdayci R, Ozge A, Karakelle A, Kurt O, Kaleagasi H (2004) Are parents aware of their schoolchildren's headaches? Eur J Public Health 14:366–368

- Мигрени чаще от 30 мин. до 120 мин., ГБН – «целый день», кластерные – короткие
- Ночные головные боли часто из-за ВЧГ (хотя 25% мигреней у детей ночные), дети с ГБН часто говорят о пробуждении с головной болью (но не о том, что они проснулись ИЗ-ЗА головной боли)



Figure. Headache patterns. (Adapted with permission from Rothner AD. The evaluation of headaches in children and adolescents. Semin Pediatr Neurol. 1995;2[2]:109-118.)

ppt.com

 У детей с хроническими утренними головными болями и бруксзмом – обратить внимание на возмость дисфункции височнонижечелюстного сустава

Локализация при мигрени – лобная билатеральная (55%), более диффузная при ГБН



Необходимо основываться не только на жалобах и клинических симптомах, но и на **«поведении»** и других дополнительных диагностических особенностях (например, уход ребенка в темное помещение, выключение света, сворачивание «калачиком» или сидение на корточках, боли в животе, обострение ощущения запахов и др.)

> Headache Classification Subcommittee of the International Headache Society (2004) The International Classification of Headache Disorders, 2nd edition, vol 24. Cephalalgia, pp 9–160 Headache Classification Committee of the International Headache Society (IHS) (2013) The International Classification of Headache Disorders, 3rd edition, vol 33. Cephalalgia, pp 629–808

 Что делает ребенок, если головная боль появилась во время игры (не в школе) – при мигрени чаще уходит домой в спокойное темное помещение, при ГБН в основном смотрят ТВ, играют в компьютерные игры

## Как выглядит ребенок: больным при мигрени, обычно – при ГБН



- Задайте вопрос о том, что с точки зрения ребенка вызывает боль (часто дети называют фактор, о котором родители даже не догадываются)
- Хронические синуситы обычно
   не вызывают хронические
   головные боли

## ПОПРОСИТЕ РЕБЕНКА НАРИСОВАТЬ ЕГО ГОЛОВНУЮ БОЛЬ:

Carl Stafstrom – 10 лет, коллекция рисунков >700 детей (111 – повторные визиты)

В 90% случаев рисунки позволяли отличить мигренозную головную боль от немигренозной

C.Stafstrom et al, 2002, 2005










ПОПРОСИТЕ РЕБЕНКА НАРИСОВАТЬ ЕГО ГОЛОВНУЮ БОЛЬ:

Серии рисунков – корреляция с динамикой клинического статуса (Se=0.825, Sp=0.91, PPV=0.946)

C.Stafstrom et al, 2002, 2005

«жук, прогрызающий дырки в голове, животе, руках и ногах»



Аскар, 7 лет (собственное наблюдение) фрагмент рисунка



fppt.com



# НЕВРОЛОГИЧЕСКИЙ СТАТУС

Lewis and Qureshi – исследование – 150 детей, доставленных по «скорой»:

18% - вторичные,

ВСЕ из них сопровождались неврологическими объективными симптомами при осмотре

# НЕВРОЛОГИЧЕСКИЙ СТАТУС

В 85% опухолей мозга – отчетливые неврологические знаки в течение 8 недель от начала головных болей

При осмотре у 98% детей с опухолями есть хотя бы один объективный неврологическим симптом

Sobri: для интракраниальной патологии наиболее значимы три «находки»: отек диска зрительного нерва (гл.дно), парез, какое-либо нарушение сознания

# ФИЗИКАЛЬНЫЙ СТАТУС

Измерить температуру тела (30% острых головных болей – из-за инфекционных заболеваний)

Осмотреть кожу (нейрофиброматоз I типа – связь с головными болями)

Измерить окружность головы (гидроцефалия)

Аускультация артерий головы

# ПАРАКЛИНИЧЕСКИЕ МЕТОДЫ

# Крайне редко требуются!!!

Слайд проф. Осиповой В.В.

## Два «золотых правила» диагностики первичных ГБ

Диагностика <u>первичных</u> ГБ является <u>исключительно</u> <u>клинической,</u> т.е. базируется на жалобах, данных анамнеза и объективного осмотра и <u>не</u> <u>требует дополнительных</u> <u>исследований</u> Дополнительные обследования проводятся только <u>при наличии</u> <u>показаний</u>

European principles of management of common headache disorders in primary care, J Headache Pain 2007; 8 (supplement 1), МКГБ-2, 2004

# ПАРАКЛИНИЧЕСКИЕ МЕТОДЫ

ЭЭГ не рекомендована в связи с отсутствием возможности в помощи для диагностики мигрени и др.ГБ

# ПАРАКЛИНИЧЕСКИЕ МЕТОДЫ

Нейровизуализационные методы показаны ТОЛЬКО если есть очаговая неврологическая симптоматика (в т.ч. эпилепсия)

У 25% школьников – хронические головные боли, опухоли – у 3 из 100 000, «доброкачественные находки» на МРТ – у 20%

Со слайда проф. Осиповой В.В.

## Головная боль: диагностический

## алгоритм



# ЛЕЧЕНИЕ

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На первом месте для большинства, включая хронические ежедневные

- Нефармакологические методы терапии и профилактики:
  - ДНЕВНИК ГОЛОВНОЙ БОЛИ (ведет ребенок, НЕ родители)
  - Гигиена сна
  - Регулярная физическая активность
  - Методики релаксации, «само-гипноза»
  - Биологическая обратная связь
  - Уменьшение употребления кофеина



## МЕДИКАМЕНТОЗНЫЕ МЕТОДЫ

- Крайне мало исследований
- ОЧЕНЬ высок эффект плацебо (60-70%)
- Большинство головных болей купируются в течение 2 часов
- Основные принципы:
  - Лечить с минимумом побочных эффектов
  - Фармако-экономическая эффективность
  - Минимум самолечения
  - Приступ мигрени лечить в самом его начале

## ОСТРАЯ ГОЛОВНАЯ БОЛЬ: снять!

S NCBI Resources	🖸 How To 🗹	
Pub Med.gov	PubMed	r
US National Library of Medicine National Institutes of Health		Advanced

Abstract -

Cochrane Database Syst Rev. 2016 Apr 19;4:CD005220. doi: 10.1002/14651858.CD005220.pub2.

#### Drugs for the acute treatment of migraine in children and adolescents.

Richer L<sup>1</sup>, Billinghurst L, Linsdell MA, Russell K, Vandermeer B, Crumley ET, Durec T, Klassen TP, Hartling L.

- 27 рандомизированных контр. исследований (РКИ)
  - в 26 из них были данные о побочных эффектах
- 9158 детей и подростков включены, в т.ч.
- 7630 (сред.возраст 8.2-14.7л.) получали
  - лек.препараты
  - 70% (19) РКИ проведены на средства фармкомпаний

30% РКИ про интраназальный путь введения, 70% - про оральный

24 РКИ по препаратам класса ТРИПТАНЫ, включая sumatriptan (50% исследований!) zolmitriptan по 4 исследования rizatriptan sumatriptan + naproxen sodium almotriptan 1 исследованию ПО eletriptan naratriptan

Другие исследования: paracetamol (acetaminophen) ibuprofen dihydroergotamine (DHE)

## РЕЗУЛЬТАТЫ

- Ибупрофен был в 1.9 раз более эффективен, чем плацебо по уменьшению боли в течение 2 часов после приема в 2 РКИ (CI 1.15-3.04)
- Парацетамол не был эффективнее, чем плацебо (1 РКИ 80 детей)

Figure 5. Forest plot of comparison: 2 Ibuprofen vs placebo in Children, outcome: 2.1 Pain-free.

	Ibupro	fen	Place	bo		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year	M-H, Random, 95% Cl
Hämäläisen 1997e	12	20	8	- 21	40.1%	2.10 [0.98, 4.51]	1997	
Lewia 2002	20	45	10	- 39	59,9%	1.73 (0.93, 3.24)	2002	+
Total (95% CI)		65		60	100.0%	1.87 [1.15, 3.04]		-
Total events	32		16					
Heterogeneity: Tau <sup>a</sup> =	:0.00; Chi	<sup>a</sup> = 0.11	5, df = 1.0	P = 0.7	$0); 1^{a} = 0.9$	6		
Testfor overall effect	Z = 2.641	P = 0.0	n)					Favours Placebo Favours Ibuorofen

Ibuprofen compared with placebo in children with migraine

Patient or population: acute treatment of migraine in children	
Setting: ambulatory	
Intervention: ibuprofen	
Comparison: placebo	

Outcomes	Anticipated absolute effect	sª (95% CI)	Relative effect (95% Cl)	No of participants (studies)	Quality of the evidence (GRADE)
	Response with placebo	Response with Ibuprofen			
Pain freedom at 2 h	Study population		RR 1.87	125 (0.00Te)	an be
	267 per 1000	499 per 1000 (307 to 811)	(1.15 to 3.04)	(2 RCTs)	Low
Adverse events	100 per 1000	0 per 1000 ( 13 to 13)	RD 0.00 (- 0.13 to 0.13)	80 (1 RCT)	-

•			
Author,	Class	Drug: (NSAIDs and non- opiate analgesics )	Efficacy
Year			
Hamalainen,	1	Ibuprofen	Active: 68%
et al., 1997		ИБУПРОФЕН	Placebo: 37%
•		10 мг/кг	P-value: <.05*
Lewis, et al.,	1		Active: 76%
2002			Placebo: 53%
•			P-value: .006
Hamalainen,	1	Acetaminophen	Active: 54%
et al., 1997		АЦЕТАМИНОФЕН	Placebo: 37%
		10-15 мг/кг	Exact p-values not
			provided <.05

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## РЕЗУЛЬТАТЫ

- *Триптаны* были эффективнее, чем плацебо для снятия боли
  - 3 РКИ, 273 ребенка, RR 1.67, 95% CI 1.06-2.62, NNTB 13)
  - 21 РКИ, 7026 подростков (RR 1.32, 95% CI 1.19-1.47, NNTB 6)

Triptans compared with placebo in children with migraine

Patient or population: acute treatment of migraine in children Setting: ambulatory Intervention: triptans Comparison: placebo

Outcomes	Anticipated absolute e	ffe ctsª (95% CI)	Relative effect (95% Cl)	No of participants (studies)	Quality of the evidence (GRADE)	Comments	•
	Response with placebo	Response with triptans					•
Pain freedom at 2 h	Study population		RR 1.67	345	., b,c	Includes rizatriptan oral	
	276 per 1000	461 per 1000 (292 to 723)	(1.06 to 2.62)	(3 RCTs)	MODERATE	(1 study) and sumatrip- tan by nasal spray (2 studies)	
Adverse events	176 per 1000	11 per 1000 (7 to 30)	RD 0.06 (- 0.04 to 0.17)	420 (3 RCTs)	-		•

Triptans compared with placebo in adolescents with migraine

Patient or population: acute treatment of migraine in adolescents Setting: ambulatory Intervention: Triptans Comparison: placebo

	Outcomes	Anticipated absolute ef	fectsª (95% CI)	Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
1		Response with placebo	Response with Trip- tans				
	Pain freedom at 2 h			RR 1.32	6761	, <i>b,c</i>	Includes almotriptan
		230 per 1000	303 per 1000 (273 to 338)	(1.19 to 1.47)	(21 RCTs)	MODERATE	(1 study), eletriptan (1 study), naratriptan (1 study), rizatriptan (1 study), rizatriptan
	Adverse events	184 per 1000	24 per 1000 (15 to 33)	RD 0.13 (0.08 to 0.18)	7876 (21 RCTs)	-	(4 studies), sumatrip- tan (10 studies), and zolmitriptan (4 studies)

#### Figure 6. Forest plot of comparison: 7 Triptans vs placebo in Adolescents, outcome: 7.1 Pain-free.

	rigare o. Torest	piece	i con	ipans		mpa	ans vs placebo i		dolescents, outcome: 7.1 Pain-free.		
• • • •		Tripia		Placel			Risk Ratio		Risk Ratio		
	Study or Subgroup 3.1.1 Almotriptan	Events	Total	Events	Total	Weight	M-H, Random, 95% CI		M-H, Random, 95% Cl		
	Linder 2008	212		60	170	10.6%	1.10 (0.88, 1.39)				
	Subtotal (95% CI)		544		170	10.6%	1.10 (0.88, 1.39)		*		
	Total events Heterogeneity: Not as	212		60						•	
	Testfor overall effect		P = 0.40	n							
	3.1.2 Eletriptan										
	Vilnner 2007 Subtotal (95% CI)	51	141 141	20	133	3.6% 306%	1.46 (0.88, 2.43) 1.46 (0.88, 2.43)		-		
	Total events	31		20							
	Heterogeneity: Not ap										
	Testfor overall effect	Z = 1.46 (	)P = 0.14	Ð							
	3.1.3 Maratriptan										
	Rothner 1997	52		16	74	3.8%	1.06 [0.65, 1.75]				
	Subtotal (95% CI) Total events	52	226	16	74	3,8%	1.06 (0.65, 1.75)		<b>—</b>		
	Heterogeneity: Not ap			10							
	Testfor overall effect		P=0.81	0							
	3.1.4 Rizatriptan										
	Ahonen 2006	34	96	17	96	3.7%	2.00 (1.20, 3.33)				
	'Afinner 2002	4B	149	40	142	6.4%	1.14 (0.81, 1.62)				
	Ho 2012 Visser 2004a	87	284	62 75	286 240	8.5% 9.6%	1.41 (1.07, 1.87) 1.25 (0.98, 1.60)				
	Subtotal (95% CI)	91	233 762	15	764		1.34 [1.13, 1.60]		•		
	Total events	280		194							
	Heterogeneity: Tau <sup>2</sup> = Test for overall effect				P = 0.3	1); P= 179	6				
	restror overall effect	Z = 3.28 (	)= = 0.01	10							
	3.1.5 Sumatriptan										
	Hämäläinen 1997b Rofiner 1999b	5	23 62	2 3	23 30	0.5%	2.50 [0.54, 11.60]				
	Rothner 1999c	11	66	5	36	1.1%	1.45 (0.42, 4.98) 1.20 (0.45, 3.18)				
	Callenbach 2007	12	46	9	46	1.8%	1.33 (0.62, 2.66)				
	Rothner 1999a Fuilta 2014	43 18	208 74	10 20	35 70	2.9% 3.0%	0.72 [0.40, 1.30]				
	Ahonen 2004	26	83	17	83	3.4%	0.76 (0.43, 1.34) 1.53 (0.90, 2.60)				
	Winner 1997	58	222	14	78	3.5%	1.42 [0.84, 2.39]				
	10inner 2000	118	377	32	130	6.8%	1.26 [0.99, 1.75]				
	Winner 2006 Subtobal (95% CI)	191	483 1644	68	242 771		1.41 [1.12, 1.77] 1.27 [1.10, 1.48]		•		
	Total events	4B7		180							
	Heterogeneity: Tau* = Tertifer moral effect				P = 0.44	4); I* = 0%					
	Testfor overall effect	£ = 3.19 (	P - 0.01	14)							
	3.1.6 Zolmitriptan										
	Evers 2006	6	14	1	14	0.3%	6.00 (0.83, 43.59)		+		
	Lewis 2007 Rothner 2006	58 108	148 483	24 32	127 162	5.1% 6.4%	2.07 (1.37, 3.13) 1.13 (0.80, 1.61)				
	NCT01211145	88	299	60	298	7.8%	1.77 [1.30, 2.41]				
	Subtotal (95% CI)	050	933	100	599	19.3%	1.66 [1.16, 2.38]		-		
	Total events Heterogeneity: Tau*=	258 : 0.07: Chi	r = 7.34	107 . df = 3 iF	P = 0.06	8): <b>1* = 6</b> 93	6				
	Testfor merall effect				- 6.0		*				
	Tabul (BSN: Ch		4350		36.44	100.02	1 33 1 40 1 43				
	Total (95% CI) Total events	1300	4250	577	2011	100.0%	1.32 [1.19, 1.47]		•	•	
	Heterogeneity: Tau <sup>a</sup> –		F= 27.1		1 (P = 0	0.13); P = 2	6%	1			
	Test for overall effect	Z = 5.11 (	)P < 0.00	0001)	7			U.1	0.2 0.5 i 2 5 10 Favours Placebo Favours Triptan	• • • • fppt.c	com
	Tent for submous off	fernalias i	Ch <sup>a</sup> e 4	72 iffe	5/P = 0	0.461 P=1	195			ipplic	

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•••	Author,	Class	Drug: (Triptrans)	Efficacy	
	Year				•••
•••	Ueberall, 1999	1	Sumatriptan, Nasal	Active: 85.7%	
•••			СУМАТРИПТАН	Placebo: 42.8%	••••
•••			<u>НАЗАЛЬНЫЙ</u>	P-value: .03	
	Winner, et al.,	I	5-20 мг	Active: 66%	
	2000			Placebo: 53%	•••
•••				Exact p-values not	
				provided (~.05)	
Ó	Ahonen, et al.,	1		Active: 64%	
	2004			Placebo: 39%	
				P-value: .003	
0		•	•		•••
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## **Class I Evidence**

					•
	Author,	Class	Drug: (Triptrans)	Efficacy	
	Year				•••
	Hamalainen,	I	Sumatriptan, Oral	Active: 30%	
	et			Placebo: 22%	
	al., 1997			P-value: non-	
				significant	•
	Winner, et al.,	I	Oral Triptans,	Active: 66%	•••
(/	2002		Rizatriptan	Placebo: 56%	
	)))			P-value: non-	
11				significant	•
Ý					
•					
					•

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## РЕКОМЕНДАЦИИ ААN (2002г.)

актуальны, подтверждены в июле 2013г.

- Суматриптан (назальный спрей) эффективен и должен применяться для лечения острого приступа мигрени у подростков (Класс I, уровень А)
- Нет данных об эффективности оральных форм триптанов у детей или подростков (Класс IV, уровень U)
  - Неоднозначны данные для принятия решения об эффективности подкожного введения суматритана (Класс IV, уровень U)

Many children and adolescents use and benefit from nonprescription oral analgesics like acetaminophen, ibuprofen, and naproxen.

Triptans are <u>less commonly</u> prescribed in children than in adults, and only almotriptan (for patients aged 12 years and older), rizatriptan (for patients aged 6–17 years), sumatriptan/ naproxen (for patients aged 12 years and older), and zolmitriptan NS (for patients aged 12 years and older) are approved by the Food and Drug Administration (FDA) for use in children.

Ergots and oral naproxen alone have not been studied in children.

Данные с сайта Американской Академии неврологии от 26/02/2020г.

https://www.aan.com/Guidelines/home/GuidelineDetail/966

Level	Recommendation
Level B	Clinicians should counsel that acute migraine treatments are more likely to be effective when used earlier in the migraine attack, when pain is still mild.
Level B	Clinicians should prescribe ibuprofen oral solution (OS) (10 mg/kg) as an initial treatment option to reduce pain in children and adolescents with migraine.
Level B	For adolescents with migraine, clinicians should prescribe sumatriptan/naproxen oral tablet (OT) (10/60 mg, 30/180 mg, 85/500 mg), zolmitriptan nasal spray (NS) (5 mg), sumatriptan NS (20 mg), rizatriptan oral disintegrating tablet (ODT) (5 mg or 10 mg), or almotriptan OT (6.25 mg or 12.5 mg) to reduce headache pain.

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## РЕЗУЛЬТАТЫ: побочные явления триптанов

Триптаны при применении у подростков увеличивают риск малых (не серьезных) побочных эффектов (NNTH 8), но ни в одном из исследований не выявлены серьезные побочные явления

Риск незначительных побочных явлений у детей не был значительным (NNTH 17).

## РЕЗУЛЬТАТЫ

Sumatriptan plus naproxen sodium – **лучше снимает боль**, чем плацебо:

1 РКИ, 490 подростков (RR 3.25, 95% CI 1.78 - 5.94, NNTB 6)

Дигидроэрготамин (Per os) не снимал боль лучше, чем плацебо – 1 РКИ, 13 детей.

# Только топирамат одобрен FDA для детей старше 12 лет для профилактики мигрени

Paediatr Drugs. 2015 Jun;17(3):217-26. doi: 10.1007/s40272-015-0125-5.

#### Prophylaxis of migraine in children and adolescents.

Kacperski J<sup>1</sup>.

#### Author information

Division of Neurology, Cincinnati Children's Hospital Medical Center, 3333 Burnet Ave-MLC 2015, Cincinnati, OH, 45229-3039, USA, Joanne.Kacperski@cchmc.org.

#### Abstract

While it has been established that headaches in the pediatric age group are relatively common, the characterization of headache disorders and their treatment in this group has historically been limited. Due to the paucity of controlled studies on prophylaxis of the primary headache disorders in children, the diagnosis of migraine often rests on criteria similar to those used in adults. Data from adult studies are often extrapolated and applied to the pediatric patient. Although it appears that many prophylactic agents are safe, well tolerated and efficacious in children, currently only topiramate is FDA-approved for use in patients 12 years and over. As a result, despite often experiencing significant disability, many children who present to their physician with migraines do not receive preventive therapy. One-third of adolescents meet the criteria for warranting prophylactic therapy, yet few are offered a preventative medication. Moreover, controlled clinical trials investigating the use of both abortive and prophylactic medications in children have suffered from high placebo response rates. A diverse group of medications are used to prevent migraine attacks, including antidepressants, antiepileptics, antihistamines and antihypertensive agents, yet there still remains a serious lack of controlled studies on the pharmacological treatment of pediatric migraine.

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### Paediatric migraine: evidence-based management and future directions.

Orr SL<sup>1</sup>, Kabbouche MA<sup>2,3</sup>, O'Brien HL<sup>2,3</sup>, Kacperski J<sup>2,3</sup>, Powers SW<sup>3,4</sup>, Hershey AD<sup>2,3</sup>.

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- 4 Division of Behavioral Medicine and Clinical Psychology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA.

#### Abstract

Migraine is prevalent in children and adolescents and constitutes an important cause of disability in this population. Early, effective treatment of paediatric migraine is likely to result in improved outcomes. Findings from the past few years suggest that a biopsychosocial approach that uses interdisciplinary multimodal care is most effective for treatment of migraine in the paediatric population. Key elements of this management include effective and timely acute pharmacological interventions (such as NSAIDs and/or triptans), education of patients regarding self-management techniques, and psychological interventions such as biofeedback, relaxation and cognitive-behavioural therapy. The efficacy of current pharmacological or nutraceutical interventions for migraine prevention in children and adolescents is unclear, although reported placebo response patterns suggest that the effect of pill-taking behaviour is positive. As such, clinicians can consider adding a preventive intervention that involves a daily pill-taking behaviour to evidence-based non-pharmacological first-line preventive interventions (such as cognitive-behavioural therapy). More rigorous research is needed to delineate the role of pharmacological and nutraceutical interventions, the mechanisms of the clinically relevant placebo response, and interventions that enhance this response for migraine prevention in this population. Given the prevalence of migraine, cost-effective and efficacious strategies are needed for the large-scale delivery of interdisciplinary multimodal paediatric migraine care.

JAMA Pediatr. 2020 Feb 10. doi: 10.1001/jamapediatrics.2019.5856. [Epub ahead of print]

Efficacy, Safety, and Acceptability of Pharmacologic Treatments for Pediatric Migraine Prophylaxis: A Systematic Review and Network Meta-analysis.

Locher C<sup>1,2,3</sup>, Kossowsky J<sup>2,3</sup>, Koechlin H<sup>2,3</sup>, Lam TL<sup>4</sup>, Barthel J<sup>4</sup>, Berde CB<sup>3</sup>, Gaab J<sup>2</sup>, Schwarzer G<sup>5</sup>, Linde K<sup>6</sup>, Meissner K<sup>4,7</sup>.

#### **RESULTS:**

 Twenty-three studies (2217 patients) were eligible for inclusion. Prophylactic pharmacologic treatments included antiepileptics, antidepressants, calcium channel blockers, antihypertensive agents, and food supplements. In the short term (<5 months), propranolol (standard mean difference, 0.60; 95% CI, 0.03-1.17) and topiramate (standard mean difference, 0.59; 95% CI, 0.03-1.15) were significantly more effective than placebo. However, the 95% prediction intervals for these medications contained the null effect. No significant long-term effects for migraine prophylaxis relative to placebo were found for any intervention.

#### Journal of Pain Research 2019:12 3437-3459

#### Journal of Pain Research

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REVIEW

Nonpharmacological Interventions Addressing Pain, Sleep, and Quality of Life in Children and Adolescents with Primary Headache: A Systematic Review

> This article was published in the following Dove Press journal: Journal of Pain Research

Susanne Hwiid Klausen (D)<sup>1</sup> Gitte Rønde<sup>1</sup> Birte Tornøe (D<sup>2</sup> Lene Bjerregaard (D<sup>3</sup>

<sup>1</sup>Department of Pediatrics, Zealand University Hospital, Roskilde, Denmark; <sup>2</sup>Department of Health Sciences, Lund University, Lund, Sweden; <sup>3</sup>Open Patient **Purpose:** Children and adolescents with primary headache are at risk of persistent somatic symptoms and reduced quality of life (Qol) due to pain and pain-related behaviors, such as avoiding school and activities. Sleep is essential to health, and children and adolescents with primary headaches have more sleep complaints than do healthy controls. A treatment approach that addresses multifactorial causes is likely important. Nonpharmacological interventions seem promising. However, knowledge about effective strategies is limited. The objective of this review is to assess the effect of nonpharmacological interventions in randomized controlled trials (RCTs) among children and adolescents with primary headache in order to identify useful strategies.



## НЕОБХОДИМЫ ДАЛЬНЕЙШИЕ ИССЛЕДОВАНИЯ С КАЧЕСТВЕННЫМ ДИЗАЙНОМ



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The WOrld Children and Adolescent Headache project



Headache and Migraine in Children and Adolescents are in fact commonly associated with other several comorbidities which contribute to the disability and the worsen of the **quality of life** of the affected children.