کارگاه‌های آموزشی مرکز اطلاعات علمی

مقاله نویسی علوم انسانی

اصول تنظیم قراردادها

آموزش مهارت های کاربردی در تدوین و چاپ مقاله
Febrile Seizures: Etiology, Prevalence, and Geographical Variation

How to Cite This Article: Delpisheh A, Veisani Y, Sayehmiri K, Fayyazi A. Febrile Seizures: Etiology, Prevalence, and Geographical Variation. Iran J Child Neurol. 2014 Summer; 8(3):30-37.

Abstract

Objective

Febrile seizures (FSs) are the most common neurological disorder observed in the pediatric age group. The present study provides information about epidemiological and clinical characteristics as well as risk factors associated with FS among Iranian children.

Materials & Methods

On the computerized literature valid databases, the FS prevalence and 95% confidence intervals were calculated using a random effects model. A meta-regression analysis was introduced to explore heterogeneity between studies. Data manipulation and statistical analyses were performed using Stata10.

Results

The important viral or bacterial infection causes of FSs were; recent upper respiratory infection 42.3% (95% CI: 37.2%–47.4%), gastroenteritis 21.5% (95% CI: 13.6%–29.4%), and otitis media infections 15.2% (95% CI: 9.8%–20.7%) respectively. The pooled prevalence rate of FS among other childhood convulsions was 47.9% (95% CI: 38.8–59.9%). The meta–regression analysis showed that the sample size does not significantly affect heterogeneity for the factor 'prevalence FS'.

Conclusion

Almost half of all childhood convulsions among Iranian children are associated with Febrile seizure.

Keywords: Febrile seizure; Iran; Meta–analysis; Pediatrics

Introduction

Febrile seizure (FS) is the most common neurological disorder observed in the pediatric age group. It has been reported that one in every 25 children in the population will experience at least one FS during their childhood (1). The International League against Epilepsy (ILAE) has defined FS as seizure events in infancy or childhood are featured with temperatures over 38°C without any evidence of acute electrolyte imbalances in CNS infection or history. A child with FS often loses consciousness, shakes, and moves limbs on both sides of the body. Most FSs occur during the first day of a child’s fever (2).

The direct cause of FS is unknown, but the most important associated factors are fever, epilepsy, hypoglycemia, hypocalcaemia, head injury, poisoning and drug overuse, respiratory infection, or gastroenteritis (3–5). The association between seizure and bacterial infection is conventional (6, 7). Although, FS may cause great
AND Iran [Affiliation])

Selection and quality assessment of articles
All identified papers were critically appraised independently by two independent reviewers. Disagreements were resolved through discussion. Appraisal was guided by a checklist assessing clarity of aims and research questions. The inclusion criteria were as follows: 1. Studies in the mentioned databases with full text, despite the language of original text; 2. Hospital-based data; 3. Reporting among Iranian children; and 4. Studies with overlapping time and sample collection from the same origin. The following exclusion criteria were also applied: 1. inappropriate design; 2. inadequate reporting of results, i.e., studies not reporting prevalence data for relevant outcomes.

Data extraction
Data were extracted using a standardized and pre-piloted data extraction form. Data extraction was undertaken by the first reviewer and checked by a second reviewer. However, the process was discussed and piloted by both reviewers. All identified papers were critically appraised independently by both reviewers. Disagreements were resolved through discussion. Appraisal was guided by a checklist assessing clarity of aims and research questions. Information was extracted from author, title, year, setting of study, sample selection, sample size, study type, seizure types, age, and prevalence. Therefore, risk of bias for inadequate reporting was reduced. All data abstraction forms were reviewed and eligible papers were entered into the meta-analysis.

Statistical analysis
The random effects model was used for combining results of studies in meta-analysis. Variance for each study was calculated using the binomial distribution formula. The presence of heterogeneity was determined by the Der Simonian–Laird (DL) approach (14). Significance level was <0.1 and I² statistic for estimates of inconsistency within the meta-analyses. The I² statistic estimates the percent of observed between-study variability due to heterogeneity rather than to chance and ranges from 0 to 100% (values of 25%, 50% and 75% were considered representing low, medium, and high
Febrile Seizures: Etiology, Prevalence, and Geographical Variation

Results
Overall, 115 studies (1 study in Pub Med, 114 studies in other databases) were identified. Of them, 94 studies were excluded based on the inclusion and exclusion criteria (Figure 1). Finally, 21 articles including one in English (10) and 20 in Persian (11–13, 16–32) were adopted (Figure 1). On a whole 4599 children with FS including 2734 males and 1865 females included in Meta analysis. Prevalence of FS according to the age of children under 2 years and 2 to 6 years were 55.8% (95% CI: 50.4–61.2%) and 44.1% (95% CI: 38.8–62.2%), respectively (Table 1).

Etiology and prevalence of febrile seizures
The important viral or bacterial infection causes of FSs were recent upper respiratory infection 42.3% (95% CI: 37.2%–47.4%), gastroenteritis 21.5% (95% CI: 13.6%–29.4%), otitis media infections 15.2% (95% CI: 9.8%–20.7%), pneumonia 8.7% (95% CI: 5.4%–11.9%), urinary infections 3.2% (95% CI: 1.3%–5.0%), rosella 2.0% (95% CI: 0.02%–3.8%), and other infections 12.8% (9.8%–15.8%). The pooled prevalence rate of childhood febrile seizure compared to other childhood seizures in Iran was 47.9% (95% CI 12.3–29.5%) (Figure 2).
Prevalence of simple and complex febrile seizure were 69.3% (95% CI: 19.6–31.0) and 28.3% (95% CI: 59.5–79.0), respectively. Generalized seizures are classified into a number of categories depending on their behavioral effects. Tonic–colonic seizures the prevalence rate among other types of generalized seizures was 78.9% (95% CI: 68.8%–89.2%).

**Geographical variation of febrile seizures**

A significant geographic discrepancy on prevalence of

**Table 1. Feature of childhood febrile seizure at different regions of Iran**

| Study location (city) | First Author (year) | Study period | No. of patients | Gender (Male) No (%) | Data collection procedure |
|-----------------------|----------------------|--------------|-----------------|----------------------|--------------------------|
| Yazd                  | Fallah (2008)        | 2004–2005    | 139             | 63 (0.55)            | Hospital                 |
| Yazd                  | Golestani (2008)     | 2002–2005    | 100             | 59 (0.59)            | Hospital                 |
| Kerman               | Hosseininasab (2006) | 2000–2002    | 115             | 68 (0.59)            | Hospital                 |
| Mashhad            | Ashrafzadeh (2002)   | 2001–2002    | 50              | 35 (0.70)            | Hospital                 |
| Zahedan             | Khazai (2007)        | 2005–2006    | 178             | 94 (0.53)            | Hospital                 |
| Birjand            | Namakin (2011)       | 2006–2007    | 145             | 84 (0.61)            | Hospital                 |
| Bandar Abbas      | Moayedi (2001)       | 2001–2002    | 181             | 112 (0.62)           | Hospital                 |
| Sanandaj          | Ghotbi (2002)        | 2000–2001    | 115             | 70 (0.61)            | Hospital                 |
| Isfahan          | Amini (2008)         | 2005–2007    | 1486            | 892 (0.60)           | Hospital                 |
| Zanjan            | Kazemi (2001)        | 2000–2001    | 50              | 33 (0.66)            | Hospital                 |
| Kashan             | Talebian (2006)      | 2001–2002    | 120             | 72 (0.60)            | Hospital                 |
| Tehran            | Khodapananahande (2001) | 2007–2008 | 107             | 64 (0.60)            | Hospital                 |
| Tabriz            | Barzegar (2006)      | 2001–2003    | 582             | 321 (0.55)           | Hospital                 |
| Bushehr           | Sanaidashti (2006)   | 2005–2006    | 102             | 64 (0.65)            | Hospital                 |
| Bandar Abbas      | Ahmadian (1996)      | 1996–1997    | 211             | 127 (0.60)           | Hospital                 |
| Tehran            | Hassanpoor (2009)    | 2003–2005    | 103             | 64 (0.62)            | Hospital                 |
| Babel             | Rasholi (1999)       | 1999–2000    | 230             | 138 (0.60)           | Hospital                 |
| Zanjan            | Sadeghzadeh (2011)   | 2005–2006    | 117             | 64 (0.55)            | Hospital                 |
| Tehran            | Ehsanypoor (2004)    | 1997–2007    | 245             | 140 (0.57)           | Hospital                 |
| Ilam              | Mohammadi (2008)     | 2007–2008    | 172             | 98 (0.57)            | Hospital                 |
| Ahvaz             | Dehdashtian (2008)   | 2003–2008    | 94              | 54 (0.57)            | Hospital                 |
that year conducted of the studies significantly affects heterogeneity for the factor ‘prevalence rate FS’ (Reg Coef = .00030, p= 0.026). Publication bias is the term for what occurs whenever the research that appears in the published literature is systematically unrepresentative of the population of completed studies. There was no evidence of publication bias (Egger’s test β0: 0.04; p=0.96) so we tried considered the most of published articles in this subject.

Discussion

This systematic review aimed to provide epidemiological characteristics of FSs based on 21 separate samples (from 115 publications) based on 4599 neonates. The pooled prevalence of childhood febrile seizures (among other convulsions) in Iran was 47.9% (95% CI; 38.8–59.9%). Complex FSs was seen in 28.3% (95% CI: 59.5–79.0) of patients in this study, although other studies have reported a range of prevalence 6.7%–35% (33, 34). This difference in findings may be due to a variety of reasons, including ethnic and geographic differences, better diagnosis of partial seizures and improved methods of FS was also observed in different parts of the country. Subgroup analysis based on the type of climate showed no interaction with prevalent of FS. Prevalence rate of FS among other childhood convulsions in central Iran was 40.03% (95% CI: 37.09%–42.07%), in the east it was 59.4% (95%CI: 38.2%–80.7%), 44.1% (95% CI: 37.4%–50.8%) in the south, and 57.5% (95% CI: 49.1%–65.9%) in western of Iran. According to the data, the lowest prevalence was observed in north of the country 33.0% (95% CI: 24.5%–41.5%).

Meta-regression analysis

Meta-regression, thus, helps explore several possible reasons for the observed heterogeneity among the studies Meta–regression showed an association between year of study and prevalence rate of FS as well as it shows causes of the variability in the results of studies. Meta-regression showed variability in prevalence of FS a non significant effect for sample (Reg Coef = 0.017, p= 0.11). Therefore studies with large sample size show prevalence rate of FS high in comparison with studies with small sample size. Meta-regression analysis found that year conducted of the studies significantly affects heterogeneity for the factor ‘prevalence rate FS’ (Reg Coef = .00030, p= 0.026). Publication bias is the term for what occurs whenever the research that appears in the published literature is systematically unrepresentative of the population of completed studies. There was no evidence of publication bias (Egger’s test β0: 0.04; p=0.96) so we tried considered the most of published articles in this subject.

**Fig 2.** Forest plots of recurrent FS for random effects meta–analyses (Squares represent effect estimates of individual studies with their 95% confidence intervals of prevalence FS with size of squares proportional to the weight assigned to the study in the meta–analysis. The diamond represents the overall result and 95% confidence interval of the random–effects meta–analysis).
According to the national epidemiological survey, the prevalence rate of FSs rate has been decreasing from childhood to adulthood in community trials. This is consistent with the findings in the present study, that FS in children under 2-years is higher than for 2- and 6-years of age, 58.8% as well as 41.2%, respectively.

Tonic-colonic seizures the prevalence rate among other types of generalized seizures was 78.9% (95%CI: 68.8%–89.2%). Generalized seizures are classified into a number of categories depending on their behavioral effects. Tonic-colonic seizures are most commonly associated with epilepsy and seizures in general (36, 37). In children between the ages of 6 and 60 months, a simple FS is a benign and common event, and nearly all children have an excellent prognosis. Generalized seizure more associated with susceptibility to epilepsy (38). As epilepsy is most likely due to genetic predisposition rather than structural damage to the brain caused by recurrent simple FSs, there is no evidence that prophylactic treatment of children with simple FS would reduce the risk (39). However, no study has shown that successful treatment of simple FSs can prevent the later development of epilepsy. Further, there is no evidence to date that simple febrile seizures can cause structural damage to the brain (5).

Our study is the first systematic review and meta-analysis that preformed to measure the risk of bacterial infection causes in children with FSs in fewer than for six-year age group. According to the results, urinary infections were 3.2% (95% CI: 1.3%–5.0%) in the previous study conducted by Lee et al (1991) and Bauchner (1987). There were some considerations for bacterial infection playing a role in incidence of FSs, frequency of urinary tract infection was 5%, and 1.7%, respectively (6, 7). Bacterial meningitis was very uncommon in children diagnosed with FSs inconsistent with our results. Results in this systematic review showed that 8.7% (95% CI: 5.4%–11.9%) were positive, for Streptococcus pneumonia in comparison with Teach et al (1999) whom reported 2.9% (95%CI 0.6–5.2) in children with FSs (40).

Some limitations in the present study need to be addressed. It was an observational study and patients were not randomly selected. Therefore, selection bias and confounding seems to be expected. Meanwhile, the authors’ ability to assess the quality of studies was limited by the fact that many studies failed to offer detailed information of selected subjects or valid data on important factors. Our analysis also suggests the need for large population-based incidence studies of febrile seizure, particularly in children under six year age, to generate more accurate estimates as well as provide a reasonably robust assessment of heterogeneity.

Acknowledgements

The cooperation and financial assistance of the Research Deputy, Ilam University of Medical Sciences is gratefully appreciated.

Author’s contribution

Ali Delpisheh: Study design
Yosef Veisani: Main investigator and corresponding author
Koroush Sayehmiri: Statistical analysis
Afshin Fayazzi: Scientific consultant

References

1. Felipe L, Siqueira M. Febrile seizures: update on diagnosis and management. Siqueira LFM. 2010;56 (4):489–92.
2. Oka E, Ishida S, Ohtsuka Y, Ohtahara S. Neuroepidemiological Study of Childhood Epilepsy by Application of International Classification of Epilepsies and Epileptic Syndromes (ILAE, 1989). Epilepsia. 1995;36 (7):658–61.
3. Shi X, Lin Z, Ye X, Hu Y, Zheng F, Hu H. An epidemiological survey of febrile convulsions among pupils in the Wenzhou region. Zhongguo Dang Dai Er Ke Za Zhi. 2012 Feb;14 (2):128–30.
4. Waruiru C, Appleton R. Febrile seizures: an update. Arch Dis Child. 2004;89 (8):751–6.
5. Bettis DB, Ater SB. Febrile seizures: Emergency department diagnosis and treatment. The Journal of Emergency Medicine. 1985;2 (5):341–8.
6. Bauchner H, Philipp B, Dashefsky B, Klein J. Prevalence of bacteriuria in febrile children. Pediatr Infect Dis J. 1987;6 (3):239–42.
7. Lee P, Verrier Jones K. Urinary tract infection in febrile convulsions. Arch Dis Child. 1991;66 (11):1287–90.
8. Fukuyama Y, Seki T, Ohtsuka C, Miura H, Hara M. Practical guidelines for physicians in the management of febrile seizures. Brain and Development. 1996;18 (6):479–84.

9. Mohebbi M, Holden KR. Febrile and afebrile or provoked and unprovoked seizures? Pediatric Neurology. 2005;32 (4):291.

10. Fallah R, Karbasi S. Recurrence of febrile seizure in Yazd, Iran. Turk J Pediatr ;52 (6):618–22. 2010 Nov–Dec;52 (6):618–22.

11. Ghotbi N, Soleimani S. Causes of seizures in children 1 month to 12 years. Journal Of Medical Sciences Kurdistan. 2002;7 (25):32–6.

12. Golestani M, Fallah R, Akhavan Krbsi S. Hundred cases of cerebrospinal fluid in children hospitalized due to febrile seizures. Journal of Yazd Medical Sciences 2008;16 (5):3–7.

13. Hassanpoor H, Ghofrani M, Taheri N, Ziaee A. Risk factors in the recurrence of seizures with fever. Journal of Iran Medical Sciences 2009;16 (65):46–54.

14. Grossman P, Niemann L, Schmidt S, Walach H. Mindfulness–based stress reduction and health benefits: A meta–analysis. Journal of Psychosomatic Research. 2004;57 (1):35–43.

15. Ades AE, Lu G, Higgins JP. The Interpretation of Random–Effects Meta–Analysis in Decision Models. Medical Decision Making. 2005;25 (6):646–54.

16. Ahmadian M, Javadi N. Etiologic factors and risk factors in 211 patients with seizure. Hormozgan Med J. 1996;12 (2):145–8.

17. Amini A, Kazemi A, Ghorbani A. Causes of Seizures in Children. Iran J Neurol. 2008;7 (24):355–60.

18. Ashrafzadeh F, hashemzadeheh A, Malek A. Febrile seizure in children six months to six years. Iranian Journal of Otorhinolaryngology. 2001;16 (1 (35)):33–9.

19. Barzegar M, karegar mahem,Kivancheh N. Epidemiologic and clinical characteristics of seizures in children with first febrile attack. Med J Tabriz Univ Med Sci. 2006;28 (1):17–21.

20. Dehdashtian M, Momen AA, Ziae T, Moradkhani SH. Evaluation of seizure etiology in convulsive neonates admitted to Imam Khomeini and Abozar hospitals of Ahvaz 2004–2007. Jundishapur Sci Med J. 2009;8 (2):163–7.

21. Ehsanypoor F, Khadapnahndh F, Aslani Z. The frequency of meningitis in children hospitalized with febrile seizures. Iran J Med Sci. 2004;11 (44):907–12.

22. Fallah R, Akhavan Krbsi S, Mir–Nasseri F. Demographic and clinical characteristic children with first febrile seizure. Journal of Yazd Medical Sciences 2008;16 (5):65–1

23. Hosseininasab A, Daiparizzi M–H, Alidosti K. Demographic characteristics and risk factors of febrile seizure. J Med Counc IR Iran. 2006;24 (2):107–12.

24. Kazemi A, Mousavi Nasab N, Fatemi K. Cerebrospinal fluid examination in children hospitalized. Journal Of Medical Sciences Zanjan. 2001;9 (35):32–6.

25. Khazai T, Hossein Zadeh A, Javadzadeh M. Causes of seizures in children. Journal of Birjand Medical Sciences 2007;14 (4):45–52.

26. Khodapanahhandeh F. Studied 107 children with febrile seizures. Journal ofIran Medical Sciences. 2001;8 (25):175–8.

27. Moayedi AR, Nazemi Qshmy A, Safdarian F. Epidemiology and etiology of seizures and fever in children. Hormozgan M J. 2005;9 (3):153–6.

28. Mohammadi J. Biochemical Disorders in Children with Febrile Seizure. Scientific Jour of Ilam Med University. 2008;16 (4):1–6.

29. Namakin K, Shryfzadh G, Rezaei S. Demographic and clinical features febrile seizures. Journal of Birjand Medical Sciences 2010;17 (4):281–7.

30. Rasoli M, Moghimian A. Causes of fever in children with febrile seizures in children’s hospital. Journal of Babol University of Medical Sciences. 1999;10 (3):131–7.

31. Sadeghzadeh M, Asl P, Mousavi–Nasab N, kosha A, Pakdel M. Relationship between serum zinc levels and febrile seizure. Journal of Medical Science Zanjan. 2011;19 (74):17–24.

32. Talebian A, Momtazmanesh N, Mousavi GH, Khojesteh M. Relationship between febrile seizure and anemia. Iran J Pediatr. Mar 2006;16 (1):79–86.

33. Najaf–Zadeh A, Dubos F, Hue V, Pruvost I, Bennour A, Martinot A. Risk of bacterial meningitis in young children with a first seizure in the context of fever: a systematic review and meta–analysis. PLoS One. 2013;8 (1):1–8.
34. Eseigbe E, Eseigbe P, Adama S. Febrile seizures in Kaduna, north western Nigeria. Niger Med J. 2012;53 (3):140–4.

35. Offringa M, Bossuyt PMM, Lubsen J, Ellenberg JH, Nelson KB, Knudsen FU, et al. Risk factors for seizure recurrence in children with febrile seizures: A pooled analysis of individual patient data from five studies. The Journal of Pediatrics. 1994;124 (4):574–84.

36. Sampaio LP, Caboclo LO, Kuramoto K, Reche A, Yacubian EM, Manreza M. Prevalence of Epilepsy in Children From a Brazilian Area of High Deprivation. Pediatr Neurol. 2010 Feb;42 (2):111–7.

37. van Zeijl JH, Mullaart RA, Borm GF, Galama JMD. Recurrence of febrile seizures in the respiratory season is associated with influenza A. The Journal of Pediatrics. 2004;145 (6):800–5.

38. Berg A, Shinnar S, Hauser W, Leventhal J. Predictors of recurrent febrile seizures: a metaanalytic review. J Pediatr. 1990 Mar;116 (3):329–37.

39. Berg AT. Risk of recurrence after a first unprovoked seizure. Epilepsia. 2008;49 (Suppl 1):13–8.

40. Teach S, Geil P. Incidence of bacteremia, urinary tract infections, and unsuspected bacterial meningitis in children with febrile seizures. Pediatr Emerg Care. 1999;15 (1):9–12.
کارگاه‌های آموزشی مرکز اطلاعات علمی

مقاله نویسی علوم انسانی

اصول تنظیم قراردادها

آموزش مهارت های کاربردی در تدوین و چاپ مقاله