

Long-term prognosis after childhood convulsive status epilepticus: a prospective cohort study

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Summary

Background The prognosis of convulsive status epilepticus (CSE), a common childhood medical neurological emergency, is not well characterised. We aimed to investigate the long-term outcomes in a cohort of participants who previously had CSE.

Methods In this prospective study, we followed up a population-based childhood CSE cohort from north London, UK (the north London convulsive status epilepticus surveillance study cohort; NLSTEPSS). We collected data from structured clinical neurological assessment, neurocognitive assessment (Wechsler Abbreviated Scale of Intelligence), brain MRI, medical records, and structured interviews with participants and their parents to determine neurological outcomes, with adverse outcome defined as presence of one or more of epilepsy (active or in remission), motor disability, intellectual disability, or statement of special educational needs. We applied multiple imputation to address missing data and performed binary logistic regression analyses on complete-case and imputed datasets to investigate sociodemographic and CSE factors associated with adverse outcomes.

Findings Of 203 survivors (90% of inception cohort), 134 (66%) were assessed at a median follow-up of 8.9 years (IQR 8.2–9.5). The cumulative incidence of epilepsy was 24.7% (95% CI 16.2–35.6), with most (89%) emerging within 18 months after CSE. The cumulative incidence of epilepsy was lower in patients with prolonged febrile seizures (14.3%, 6.3–29.4) and survivors of acute symptomatic CSE (13.3%, 3.7–37.9) than in those of remote symptomatic CSE (45.5%, 21.3–72.0) and unclassified CSE (50.0%, 25.4–74.6). One participant (2.9%, 0.5–14.5) in the prolonged febrile seizures group developed temporal lobe epilepsy with mesial temporal sclerosis. The absence of fever at CSE was the only predictor of incident epilepsy (odds ratio [OR] 7.5, 95% CI 2.25–25.1). Motor and intellectual disability was seen predominantly in participants who had idiopathic and cryptogenic CSE (seven [36.8%, 95% CI 19.1–59.0] and 16 [84.2%, 62.4–94.5] of 19, respectively) and remote symptomatic CSE (33 [62.3%, 48.8–74.1] and 40 [75.5%, 62.4–85.1] of 53), and most of these participants had pre-existing disabilities. Pre-existing epilepsy was the only predictor of intellectual disability (OR 8.0, 95% CI 1.1–59.6). 51.5% (95% CI 43.1–59.8) of those followed up had a statement of special educational needs.

Interpretation Childhood CSE is associated with substantial long-term neurological morbidity, but primarily in those who have epilepsy, neurological abnormalities, or both before the episode of CSE. Survivors without neurological abnormalities before CSE have favourable outcomes.

Funding BUPA Foundation, The Academy of Medical Sciences, Wellcome Trust, National Institute for Health Research, and Young Epilepsy.

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Introduction

Convulsive status epilepticus (CSE), a common childhood medical neurological emergency, is associated with increased mortality and morbidity, but there is considerable variability in reported frequency of adverse outcomes.^{1,2} Between 11% and 45% of patients develop new-onset epilepsy within 5 years after CSE, but most studies do not separate motor and cognitive sequelae. Although some evidence suggests that short-term hippocampal injury and developmental or memory impairments occur after febrile status epilepticus, whether these changes lead to development of mesial temporal sclerosis is uncertain.^{2–5} Most outcome studies are constrained by methodological

shortcomings such as hospital-based or retrospective designs, unclear definition of outcomes, lack of formal neurocognitive assessment and neuroimaging, small sample size, and short follow-up (usually only up to 5 years). Thus, prognosis after childhood CSE is not well characterised.²

We did the first population-based study focused on childhood CSE, the north London convulsive status epilepticus surveillance study (NLSTEPSS), and described incidence, cause, and short-term outcomes.¹ We followed up these participants in this Status Epilepticus Outcomes Study (STEPSOUT). Having previously published data for risk and predictors of death,⁶ we aimed to comprehensively assess this cohort to investigate their

Lancet Child Adolesc Health 2017

Published Online

December 5, 2017

[http://dx.doi.org/10.1016/S2352-4642\(17\)30174-8](http://dx.doi.org/10.1016/S2352-4642(17)30174-8)

S2352-4642(17)30174-8

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Research in context

Evidence before this study

A previous systematic review on outcomes of childhood convulsive status epilepticus (CSE) included papers published up to May, 2006. We performed an additional search on PubMed for original articles on outcomes after childhood CSE published between June 1, 2006, and July 31, 2017, with the search terms “status epilepticus” combined with the terms “outcome”, “morbidity”, “prognosis”, “recurrence”, “mesial temporal sclerosis”, “hippocampal sclerosis”, and “cognition”. Searches were repeated with “prolonged febrile convulsion”, “prolonged febrile seizure”, and “lengthy febrile seizure”. Only studies that included patients aged between 1 month and 18 years at the time of status epilepticus were considered. The search identified 32 relevant additional articles. From the results of the systematic review and more recent studies it is clear that childhood CSE is associated with increased mortality and morbidity; however, there is considerable variability in reported frequency of adverse outcomes, primarily because of methodological differences. Also, evidence suggests short-term hippocampal injury and developmental or memory impairments after febrile status epilepticus, but whether these changes lead to development of mesial temporal sclerosis is uncertain. Most previous studies are hospital based or retrospective and have a small sample size or short follow-up (up to 5 years); therefore, whether the existing literature can be generalised to understand the natural history and prognosis following childhood CSE is uncertain.

Added value of this study

After reporting the incidence, cause, and short-term outcomes from children in the north London convulsive status epilepticus surveillance study (NLSTEPSS), we prospectively followed up this cohort to determine their long-term outcomes. To our knowledge, this is the first prospective population-based study to comprehensively describe the natural history and the long-term outlook after childhood CSE due to all causes.

Our results showed that although morbidity is considerable after childhood CSE, this is seen primarily in those with symptomatic causes and pre-existing neurological abnormalities. Previously neurologically normal children have a favourable outcome with low incidence of epilepsy, motor disability, and intellectual disability after CSE. CSE recurrence occurs predominantly in those with previous neurological abnormalities. We also showed that temporal lobe epilepsy and mesial temporal sclerosis can be seen after all forms of childhood CSE, not just prolonged febrile seizures, but are uncommon. Our data suggest that CSE characteristics such as seizure duration are not major predictors of outcome independently of cause.

Implications of all the available evidence

Collectively, the available data are reassuring and suggest favourable outcomes in previously neurologically normal children, and the direct contribution of CSE in the development of neurological sequelae seems less than previously thought. However, whether CSE results in subtle neurocognitive deficits or behavioural difficulties in previously neurologically normal children is uncertain and needs investigation. Studies comparing outcomes after short seizures with seizures lasting 30 min or longer might also help to determine whether early cessation of seizures might improve outcomes. Development of strategies for early identification of those at high risk of neurocognitive sequelae and appropriate support at school and behavioural support might reduce the long-term negative effects of childhood CSE and improve quality of life. In addition to improvements in acute management of seizures, reducing childhood CSE incidence through preventive measures such as universal immunisation and optimal management of epilepsy, particularly in resource-poor settings, offers the best opportunity to reduce the morbidity and mortality associated with childhood CSE.

long-term epilepsy, motor, intellectual, and educational outcomes after CSE.

Methods

Study design and participants

Recruitment for NLSTEPSS has previously been reported.¹ In summary, between May 1, 2002, and April 30, 2004, using a multitiered notification system set up within a collaborative network of 21 hospitals in north London (UK), 226 participants with CSE were enrolled. Clinical and demographic data were shared with the central research team using linked anonymisation.

For STEPSOUT, participants were recruited through their local paediatricians, who used individual unique NLSTEPSS identification to recall patient identifiable information and determine survival status.⁶ All surviving participants from NLSTEPSS were eligible for inclusion.

Local paediatricians sent an invitation letter to these participants or their parents (if participant was still younger than 18 years) on behalf of the research team, with study information and consent forms, asking them to consent for study participation. Non-responders were sent reminders before being considered lost to follow-up.

We obtained written informed consent from all participant’s parents or guardians, and consent or assent from each participant. STEPSOUT was approved by the UCL Institute of Child Health and Great Ormond Street Hospital Research Ethics Committee. We report our study findings according to STROBE guidelines.

Procedures

For each participant, background demographic, medical, and developmental data before CSE, and clinical details about CSE were obtained from the NLSTEPSS database.

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