Original article

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Prescription of emergency antiepileptic medication after a first childhood seizure: analysis of routine administrative data

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ABSTRACT – *Aim*. UK guidelines do not recommend prescribing emergency antiepileptic drugs after first simple febrile seizures or for single afebrile seizures. Non-adherence to the guidelines could result in substantial health service cost. *Methods*. Scottish national hospital discharge records were used to identify children aged one month to 4 years admitted for a first febrile seizures or single afebrile seizures between April 2009 and March 2012. Prescriptions for antiepileptic drugs within 12 months of index admission were identified on the national community prescribing database by matching unique patient identifiers. *Results*. There were 1,978 and 663 children admitted for febrile seizures and single afebrile seizures, respectively. One percent of children admitted with febrile seizures and 1.7% with single afebrile seizures had a subsequent community prescription record for emergency antiepileptic drugs within 12 months of index admission. Total cost of emergency antiepileptic drugs following febrile seizures and single afebrile seizures for the study period was just over £900. *Conclusion*. Health care providers and policy makers can be reassured that emergency antiepileptic drugs are not being inappropriately overprescribed for febrile seizures and single afebrile seizures.

Key words: population-based, febrile seizures, emergency

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When parents witness their child first having a febrile seizure (FS), which affects 2-5% of children under 5 years, many think their child is dying (Fetveit, 2008). Neither prophylactic antipyretics nor diazepam prevent recurrence (Fetveit, 2008). Most seizures are short-lived and long-term neurological, educational and social outcomes are good (Fetveit, 2008).

However, prolonged febrile seizures (PFS), those lasting at least 30 minutes, are associated with

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increased morbidity (Raspall-Chaure *et al.,* 2006; Fetveit, 2008; Martinos *et al.,* 2012; Yoong *et al.*, 2013). With a 40% rate of recurrence of PFS, it would be reasonable to prescribe emergency antiepileptic drugs (AEDs) for the 0.7% of children whose FS are PFS, but not for all children with FS (Fetveit, 2008). Similarly, prolonged afebrile seizures lasting at least 30 minutes are associated not only with increased morbidity, but also with increased mortality (Raspall-Chaure *et al.,* 2006). In a prospective study of new-onset seizures in children, 12% lasted at least 30 minutes (Shinnar *et al.*, 2001) and the risk of recurrence of such seizures is reported to be 17% (Chin *et al.,* 2006). Thus, it would be reasonable to consider prescribing emergency AEDs for such children.

In France, Germany and the Netherlands, there is routine prescription of emergency AEDs for all children with FS (Nabbout R, Bast T, Brouwera O; personal communication). UK guidelines indicate that emergency AEDs should not be routinely given for FS or for single afebrile seizures (SAS) (SIGN, 2005; NICE, 2012).

Benzodiazepines, the preferred emergency AEDs, can cause sedation and respiratory depression. Benefits of their usage must outweigh possible adverse effects. In Europe, rectal diazepam has been the gold standard emergency AED in children, but there has been diffidence towards its use because of the delivery route (McIntyre *et al.,* 2005). Buccal/nasal midazolam is an alternative due to better effectiveness and social acceptability (Klimach, 2009). Since 2005, buccal midazolam has been included in UK guidelines as a preferred emergency AED for seizures, but guidelines are not always adhered to (Chin *et al.,* 2004). Non-adherence by routine prescribing for FS/SAS could result in substantial cost to the health service.

In this retrospective cross-sectional study, we aimed to test the hypothesis that a high proportion of UK children with FS or SAS are prescribed emergency AEDs, with midazolam being prescribed more often than diazepam.

Methods

Scottish national hospital discharge (SMR01) records were used to identify children aged <5 years, admitted to hospital for a first FS or SAS between April 2009 to March 2012. Admissions for FS were defined as records with a diagnosis, either a principal or associated diagnosis, recorded as ICD10 code R56.0 (Febrile convulsions) and for SAS, ICD10 code R56.8 (Other and unspecified convulsions).

Only admission records for children aged ≥28 days were examined in order to exclude neonatal seizures. A first seizure was defined as no prior seizure-related admission with ICD10 codes R56.0, R56.8, G40 (epilepsy and recurrent seizures), or G41 (status epilepticus). A single seizure was defined as no subsequent seizure-related admission within 12 months of index admission. Rectal diazepam and buccal/nasal midazolam (emergency AED) prescriptions within 12 months of index admissions were identified on the national community prescribing (PIS) database by matching children's Community Health Index (CHI) numbers. CHI is the unique patient identifier used on all health records in Scotland. CHI completeness is very high for SMR01 records and is >90% complete for all community prescriptions from 2009 onwards, our chosen study period. All prescriptions included in the PIS database have an associated Gross Ingredient Cost (GIC) recorded. This is the amount (before any discounts) that a pharmacy can expect to receive after dispensing and reflects NHS price as per the British National Formulary or, for generic products, specified price in the Scottish Drug Tariff. Given that medicines for children were exempt from prescription charges in Scotland before the start of our study period, GIC reflects the cost of the prescriptions to the health service.

All data were analysed by NHS National Services Scotland, Information Services Division (ISD); the organisation managing routine data generated by NHS Scotland. Although it would have been ideal to be able to assess duration of seizures within our analysis, such data are not included in routine data collated by ISD. No individual level/identifiable data were made available to the authors and no new data were generated. The study was an audit of prescription practices for children with first seizures; ethical approval was not required.

Results

Tables 1 and 2 show the key findings. In total, 1,978 children aged <5 years admitted for a first, single FS were identified. FS was most common in the 12-23-month age group. A community prescription record of emergency AEDs within 12 months of admission was reported for 0.9% (18/1978). Total cost of emergency AED medication for FS was £570. Most prescriptions (15/18) were for rectal diazepam; midazolam prescriptions were uncommon. All children who received prescriptions for midazolam were 2 years or older, suggesting a particular preference for midazolam in older children compared to diazepam.

There were 663 children with a first SAS identified. Emergency AED prescriptions within 12 months of admission were reported for 1.7% (11/663); 8/11 (72%) were for rectal diazepam. Total AED cost was £340.

Table 1. Prescription of emergency AEDs in children following a first simple single febrile seizure, by age group.

Age group (months)	Admitted for first, single febrile seizure Apr 2009-Mar 2012	Prescription of emergency AEDs (rectal diazepam, buccal or nasal midazolam) within 12 months of seizure admission	
	n	***n***	**% (95%CI)**
1-11	232	3	1.3 (0.4-3.7)
12-23	999	5	0.5 (0.2-1.2)
24-35	431	5	1.2 (0.5-2.7)
36-47	210	2	1.0 (0.3-3.4)
48-59	106	3	2.8 (1.0-8.0)
All	1,978	18	0.9 (0.6-1.4)

Source: ISD Scotland.

Table 2. Prescription of emergency AEDs in children following a first afebrile seizure, by age group.

Age group (months)	Admitted for first, single afebrile seizure Apr 2009-Mar 2012	Prescription of emergency AEDs (rectal diazepam, buccal or nasal midazolam) within 12 months of seizure admission	
	n	***n***	**% (95% CI)**
1-11	165	0	0.0 (0.0-2.3)
12-23	224	7	3.1 (1.5-2.3)
24-35	118	2	1.7 (0.5-6.3)
36-47	89	1	1.1 (0.2-5.9)
48-59	67	1	1.5 (0.3-7.9)
All	663	11	1.7 (1.0-2.9)

Source: ISD Scotland.

Discussion

There is high level of adherence to current guidance in order to avoid prescribing emergency AEDs for FS/SAS. Our findings are consistent with those of a recent national audit of management of childhood epilepsy that showed throughout the UK, but particularly in Scotland, a high level of adherence to 12 key areas of the guideline (RCPCH, 2012). It could be argued that since 12% of children with SAS have a prolonged seizure (Shinnar *et al.*, 2001), then perhaps more children should be prescribed emergency AEDs rather than the 1.7% observed. However, individual social and medical circumstances, particularly the aetiology and duration of seizures, need to be considered before prescribing. The nature of our study did not allow us access to such data. Further study is needed in this population.

In general, adherence to clinical guidelines is not common. It can, however, be enhanced by clear evidence-based guidelines that are simple (and cheap) to implement in practice, and if the guidelines are supported by integrated networks comprising policy makers, managers, clinicians, health workers and service users (Lugtenberg *et al.*, 2009; Garliardi *et al.*, 2011). These features are evident in the high quality of guidance provided for the management of seizures in children (SIGN, 2005; NICE, 2012) and the training and monitoring activities of the Scottish Paediatric Epilepsy Network (SPEN) set up in 2007 to improve service provision and patient outcomes (National Services Division of NHS, 2010). We hypothesize that our finding of good adherence is at least partly attributable to the work of SPEN.

It was surprising, overall, that more prescriptions were for rectal diazepam even though midazolam is more

effective, has fewer side effects, and is more socially acceptable (Fetveit, 2008; Klimach, 2009). Children were exempt from prescription charges; relative AED costs were unlikely to influence parental choice. However, midazolam incurs a substantially higher cost (up to 20 times more) to the NHS than diazepam, so this may have influenced prescribers' choices. A licensed form of buccal midazolam only became available in 2012. Thus, prior to 2012, doctors may have preferred prescribing the more well-known and licensed rectal diazepam.

Our study demonstrates the utility of using routine administrative data in order to answer clinically relevant questions. However, it is not without its limitations. Only children admitted and assigned a relevant ICD10 diagnostic code were included. We acknowledge that not all children with first afebrile or febrile seizures may be admitted to hospital, despite national UK guidelines (https://www.nice.org.uk/guidance/cg160/chapter/1-recommendations#management-by-the-paediatric-specialist-2). If this were the case, our finding of a low inappropriate prescription rate would be an over-estimate and strengthens the conclusion that inappropriate overprescribing does not represent a major issue or NHS cost. It is possible though that clinicians are being conservative in prescribing emergency AEDS for children with prolonged SAS. Prescriptions dispensed from hospital pharmacies (*e.g.* given to patients at the point of discharge) are not recorded on the PIS database. However, in view of the shelf life of emergency AEDs, community-initiated repeat prescriptions would have been expected within a year and hence, picked up in our analysis.

Although, overall, CHI completeness on PIS records has been >90% since 2009, CHI completeness varies between specific medications and between areas. CHI completeness for rectal diazepam prescriptions from 2009 is around 55% and for midazolam prescriptions is around 86%. Since most prescriptions were for diazepam, this suggests that subsequent prescribing rates may be up to 2% rather than the 1% presented here for FS, and 3.5% rather than 1.7% for SAS, as prescriptions lacking a CHI number will not have been matched for the analysis. Finally, the PIS database records dispensed prescriptions, thus written prescriptions that were never cashed were excluded.

In summary, NHS Boards and policy makers in Scotland can be reassured that emergency AEDs are not being inappropriately overprescribed for FS and SAS. It would be of interest to compare and contrast results on adherence with other countries where there are nationally agreed guidelines for prescribing emergency AEDs. □

Supplementary Data.

The STROBE checklist for this observational study and summary didactic slides are available on the www.epilepticdisorders.com website.

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References

Chin RFM, Verhulst L, Neville BG, Peters MJ, Scott RC. Inappropriate emergency management of status epilepticus in children contributes to need for intensive care. *J Neurol Neurosurg Psychiatry* 2004; 75(11): 1584-8.

Chin RFM, Neville BGR, Peckam C, Bedford H, Wade A, Scott RC. Incidence, cause and short-term outcome of convulsive status epilepticus in childhood: prospective population-based study. *Lancet* 2006; 368: 222-9.

Fetveit A. Assessment of febrile seizures in children. *Eur J Pediatr* 2008; 167: 17-27.

Garliardi AR, Brouwers M, Palda VA, Lemieux-Charles L, Grimshaw JM. How can we improve guideline use? A conceptual framework of implementability. *Implement Sci* 2011; 6: 26.

Klimach VJ. The community use of rescue medication for prolonged epileptic seizures in children. *Seizure* 2009; 18: 343-6.

Lugtenberg M, Zegers-van Schaick JM, Westert GP, Burgers JS. Why don't physicians adhere to guideline recommendations in practice? An analysis of barriers among Dutch general practitioners. *Implement Sci* 2009; 4: 54.

Martinos MM, Yoong M, Patil S, *et al*. Recognition memory is impaired in children after prolonged febrile seizures. *Brain* 2012; 135(10): 3153-64.

McIntryre J, Robertson S, Norris E, *et al*. Safety and efficacy of buccal midazolam versus rectal diazepam for emergency treatment of seizures in children: a randomized controlled trial. *Lancet* 2005; 366(9481): 205-10.

National Institute for Health and Care Excellence (NICE). *The epilepsies: the diagnosis and management of the epilepsies in adults and children in primary and secondary care*. Published Guidelines CG137. 2012. http://guidance.nice.org.uk/CG137/NICEGuidance/pdf/English.

National Services Division of NHS, National Services Scotland. Review of nine managed clinical networks. *Report by the National Services Division NHS, National Services*

Scotland. *2010* http://www.nsd.scot.nhs.uk/publications/servicereviews/nmcn_review.pdf (accessed July 2014).

Raspall-Chaure M, Chin RFM, Neville BG, Scott RC. Outcome of pediatric convulsive status epilepticus: a systemic review. *Lancet Neurol* 2006; 5(9): 769-79.

Royal College of Paediatrics and Child Health (RCPCH). Epilepsy 12 United Kingdom collaborative clinical audit of healthcare for children and young people with suspected epileptic seizures. National Report (http://www.rcpch.ac.uk/system/files/protected/page/Epilepsy_web.pdf (accessed October 2012).

Scottish Intercollegiate Guidelines Network SIGN. *Diagnosis and management of epilepsies in children and young people*, 2005, http://sign.ac.uk/guidelines/fulltext/81/index.html.

Shinnar S, Berg AT, Moshe MD, Shinnar R. How long do new-onset seizures in children last? *Annal Neurol* 2001; 49(5): 659-64.

Yoong M, Martinos MM, Chin RF, Clark CA, Scott RC. Hippocampal volume loss following childhood convulsive status epilepticus is not limited to prolonged febrile seizures. *Epilepsia* 2013; 54(12): 2108-15.

TEST YOURSELF

(1) How often are children prescribed emergency antiepileptic drugs after first-ever hospital admission for febrile/afebrile seizures?

(2) How well does prescribing of emergency antiepileptic drugs in children after first-ever hospital admission for febrile/afebrile seizures comply with national guidelines?

Note: Reading the manuscript provides an answer to all questions. Correct answers may be accessed on the website, www.epilepticdisorders.com, under the section "The EpiCentre".