

Antiepileptic drug compliance among caregivers of children with epilepsy: An observational cohort study

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Received - 25 September 2018

Initial Review - 07 October 2018

Accepted - 17 October 2018

ABSTRACT

Background: Poor compliance with antiepileptic drugs (AEDs) not only increases morbidity and mortality rates among the children with epilepsy but it also leads to multiple hospital emergency room visits and enhanced health-care costs. **Objective:** The objective of the study was to delineate the prevalence and causes of antiepileptic drug non-compliance among caregivers of children with epilepsy in a tertiary care hospital in North India. **Materials and Methods:** Basic demographic data along with details of AED compliance (method of dispensing, exact dose being dispensed, frequency of administration, missing out on doses, and any side effects noted) were taken from primary caretaker dispensing the medication to the enrolled children with epilepsy on monotherapy with AEDs. **Results:** Wrong dosage of AED dispensed was reported in 20% (overdosing reported in 8% and underdosing in 12%) of the enrolled children. One child among the study participants receiving an overdose of the prescribed AED had emergency room admission with phenytoin toxicity. One child among the study participants was receiving wrong AED while another was receiving the AED in wrong frequency. **Conclusions:** The results from the present study highlight the high level of antiepileptic drug noncompliance among caregivers of children with epilepsy and also the various reasons leading to the wrong administration of AEDs to children with epilepsy. These ground level issues related to poor AED compliance, among caregivers of children with epilepsy, can help devise various methods to address these so as to improve the compliance to AEDs by caregivers of children with epilepsy.

Key words: Antiepileptic drug, Compliance, Epilepsy drug

Poor compliance with antiepileptic drugs (AEDs) not only increases morbidity and mortality rates among the children with epilepsy but it also leads to multiple hospital emergency room visits and enhanced health-care costs [1]. To introspect the aforementioned problem, baseline data as to the magnitude of the problem are required which is the motive of the present study. To devise novel strategies to improve AED compliance among caregivers of children with epilepsy, data on what actually are the ground level reasons leading to such poor compliance are needed.

We know about epilepsy that AEDs noncompliance is a significant problem among caregivers of children with epilepsy and wrong drug dispensing techniques and inadequate counseling about the need for AED compliance is the basic grass root level issues leading to poor compliance. The present study was thus planned with the aim to delineate the prevalence and causes of AED noncompliance among caregivers of children with epilepsy in a tertiary care hospital in North India.

MATERIALS AND METHODS

This was an observational cohort study which was conducted in a tertiary care hospital in North India during March 2017–May 2017.

Consent from concerned caregivers was taken before collecting data on AED compliance. Consecutive first 100 children with epilepsy on single AED, visiting pediatric neurocysticercosis (NCC) clinic and pediatric neurology clinic along with primary caretaker dispensing the AED to the child, were enrolled in the study. All the caregivers who gave their consent for enrollment into the study were checked for their compliance with AED administration to their children.

Basic demographic data along with details of AED compliance (method of dispensing, exact dose being dispensed, frequency of administration, missing out on doses, and any side effects noted) were taken from primary caretaker dispensing the medication to the child. Deviation from the exact prescription was noted as a percentage of children among all those enrolled in the study. The strengthening the reporting of observational studies in epidemiology (STROBE) guidelines for reporting observational studies were followed. All those caretakers whose AED compliance was improper were counseled for the need of proper drug compliance and a detailed demonstration of exact dose, method of dispensing, and its frequency was carried out.

RESULTS

A total of 100 children (males: 54% and females: 46%) with median age (69 months) and age range (6 months–14 years) were enrolled in the present study. Etiology of epilepsy in the majority of the enrolled children was infectious (NCC, 63%) followed by structural (15%) while 22% had unknown etiology. The most common AED prescribed was phenytoin (71%) followed by sodium valproate (15%), levetiracetam (6%), carbamazepine (5%), and phenobarbitone (3%). The majority of children (57%) were prescribed tablet form while 43% children were prescribed liquid preparation of AED. Predominantly mothers (68%) were reported to be the primary caregiver responsible for dispensing of AED to the child followed by father (22%), brother (3%) while self-intake of AED by the child himself was reported in 7% children.

Wrong dosage of AED dispensed was reported in 20% (overdosing reported in 8% and underdosing in 12%) of the enrolled children. One child among the study participants receiving an overdose of prescribed AED had emergency room admission with phenytoin toxicity (serum phenytoin level 29.34 µg/ml; normal 6–14 µg/ml). This child was being dispensed phenytoin in the form of tablet and syrup both leading to double dose being received by the child resulting in phenytoin toxicity. The children receiving the wrong dosage of a liquid formulation of AED were being administered drug through crudely calibrated cap (82%) or spoon (18%). One child was being dispensed a wrong drug (wysolone rather than phenytoin) while in another frequency of AED administration was wrong (OD dose rather than prescribed BD dose) as shown in Table 1.

DISCUSSION

Epilepsy is widely prevalent among children in India. The crude annual incidence rates per 100,000 of epilepsy in India have been reported to range from 25.2 for the urban population of Kolkata to 49.3 for rural population of South India [2,3]. A meta-analysis of previously published and unpublished studies by Sridharan and Murthy reported prevalence per 1000 (and its 95% confidence interval) as 5.33 (4.25–6.41) in urban areas and 5.11 (3.49–6.73) in rural areas with age-specific prevalence of 5.36 and 8.95/1000 in under 10 years and 10–19 years age groups, respectively [4]. The frequency and/or severity of seizures in the majority of the children with epilepsy can be reduced with the appropriate use of AEDs. For achieving the aforesaid objective, in compliance with AED prescription is a major requirement. The present study was thus designed to assess compliance (the

degree to which the caretaker of a child with epilepsy followed the pediatrician's directions on AED dosage and frequency of administration). Such data are of utmost importance to design innovative methods to improve AED compliance so as to have its desired effect.

NCC was reported in nearly one-third of all cases of acute epilepsy in both the urban and rural areas of Vellore [5]. However, higher prevalence rates of NCC have been reported from the northern states of Uttar Pradesh and Bihar [6]. We found NCC to be a predominant cause for epilepsy (54%) in the enrolled participants, of the present study. Such high prevalence among enrolled children resulted because the children with epilepsy were consecutively enrolled from pediatric neurology and pediatric NCC clinics of our institute. Other major etiological causes of epilepsy in the children enrolled in the present study were structural and unknown causes.

In a systematic review of AED utilization in pediatrics by Egunsola *et al.*, sodium valproate was reported to be the most frequently prescribed AED, accounting for up to 66% of prescriptions. Carbamazepine was reported to be the second most frequently prescribed AED in several countries [7]. In our institute, phenytoin is available free of cost to patients through hospital pharmacy. As the majority of the patients visiting our institute are from poor socioeconomic strata, there was a bias (71%) in phenytoin prescription for children with epilepsy. This is also the reason for relatively younger kids too being prescribed tablet form (57%) of phenytoin rather than liquid preparation as the latter is not available free of cost through hospital pharmacy.

For children with epilepsy, caregivers are responsible for adherence to medicines rather than the children themselves [8]. Despite mothers being involved in all household chores, primary caregiver dispensing AED to the enrolled children was mothers (68%) followed by fathers (22%). Despite all enrolled children being under 15 years of age, 7% reported self-dispensing of AEDs. A study on medication non-adherence in children and adolescents with epilepsy by Langer and Goodkin revealed that adherence declined with age [9]. Such self-dispensing of AEDs by minors in the absence of supervision of caregiver can result in numerous issues such as improper dose administration, abuse of drug even after it is stopped by a physician and incorrect reporting of compliance to the physician when checked in follow-up visits.

In the present study, poor compliance to AEDs was detected in 20% of the enrolled children which is definitely a significant percentage. A review on medication adherence in people with epilepsy by Malek *et al.* reported the prevalence of significant medication non-adherence in epilepsy to vary between 26% and 79% [10]. In a population-based study of adherence to AEDs in children (<16 years) by Shetty *et al.*, only 30.9% of the total 320 children adhered to recommended AED treatment across a year of treatment [11]. Thus, the problem of poor compliance with AED is a widely prevalent issue and calls for the urgent need to devise steps to improve the same. It is well known that therapeutic drug levels of AEDs, which can be achieved by proper drug compliance, are the cornerstones of suppression of seizures in children with epilepsy [12].

Table 1: AED compliance among caregivers of enrolled children

Compliance	Number of children
Correct dosing and frequency	78
Wrong drug	1
Over dosing	8
Under dosing	12
Wrong frequency of drug administration	1

AED: Antiepileptic drug

Furthermore, overdosing of AEDs was reported in 8% children, which is a serious issue that needs to be addressed due to devastating effects of antiepileptic drug overdosing [13]. In fact, one of the enrolled children had an emergency room visit due to phenytoin toxicity. The cause for such overdosing was the fact that the child was prescribed liquid formulation of phenytoin at discharge from emergency and later in follow-up was prescribed tablet form of phenytoin. However, both the preparations of the drug were administered to the child by the primary caregiver resulting in drug toxicity. Of the children being dispensed the wrong dose of AED 55% were on liquid formulation while 45% were on tablet formulation of the AED. The children, receiving wrong dosage of liquid formulation of AED, were being administered drug through crudely calibrated cap (82%) or spoon (18%). The exact drug dosage to be dispensed was not mentioned on the crudely calibrated cap in 66% children and was being dispensed the drug by estimation (using nearest calibrated mark as guide) by the caregiver. No specific spoon was used to dispense the AED to the two enrolled children by the caretakers instead any handy spoon was used for the purpose. Of the children receiving wrong dosage of tablet form of AED, 89% were being dispensed tablet not as per prescribed number/fraction while one child was being dispensed tablet phenytoin available in two packaging forms: Bottle and strip leading to double dose being dispensed.

Introspecting the ground realities mentioned above leading to poor drug compliance of caregivers of children with epilepsy to AEDs, various methods have been adopted in our pediatric neurology and pediatric NCC clinics: Repeated counseling about proper AED compliance at each follow-up visit, compulsory attendance of primary AED dispenser at each follow-up visit, advise to use finely calibrated syringes rather than crudely calibrated caps or spoons for drug dispensing and compulsory demonstration of AED dosage and method adopted by caregiver at each follow-up visit to the nursing staff.

The present study has various limitations: Being a pilot study to figure out whether noncompliance with AED is a significant problem in our institute, no baseline data as to the prevalence of noncompliance with AEDs to calculate estimated sample size were available. The scope of the present study was to check for the magnitude of noncompliance with AEDs among caregivers of children with epilepsy in our institute and look for ground-level issues leading to such noncompliance. Larger studies are needed to correlate the poor compliance to demographic and health sector related variables and to check for effectiveness and cost-benefit analysis of steps to improve the poor compliance with AEDs, as noted in the present study.

CONCLUSIONS

The results from the present study bring out ground level issues related to poor antiepileptic drug compliance among caregivers of children with epilepsy. Various methods to address these issues are suggested so as to improve the compliance to antiepileptic drugs by caregivers of children with epilepsy. Such steps can go a long way in improving seizure control on antiepileptic drug therapy, thereby reducing mortality and morbidity associated with both epilepsy and side effects of AEDs and reduce health-care costs as well.

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Funding: None; Conflict of Interest: None Stated.

How to cite this article: Aulakh R. Antiepileptic drug compliance among caregivers of children with epilepsy: An observational cohort study. *Indian J Child Health*. 2018; 5(10):619-621.

Doi: 10.32677/IJCH.2018.v05.i10.004