Management of Epilepsy among Children in the Gaza Strip: A Multicenter Clinical Audit

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Keywords

Epilepsy · Child · Clinical audit · Gaza · Neurology

Abstract

Introduction: Seizures are scary phenomena but are quite common especially among children: about 8% will have had at least one seizure by 15 years of age. Most acute seizures in children are brief, terminating spontaneously and do not need any treatment. Seizures that persist beyond 5 min may not stop spontaneously and necessitate comprehensive clinical evaluation and medical care. Seizure control then becomes a matter of urgency for the patient and his family, as the longer the duration of the seizure, the greater the bad effects on body systems especially the brain and the more difficult control is likely to become. **Methods:** A retrospective, multicenter clinical audit was undertaken simultaneously at the three largest centers for epilepsy management in Gaza. A total of 190 medical records were included in our audit from January 1, 2017, to April 30, 2018. **Aims and Objectives:** Our audit aims to evaluate the care provided for patients with epilepsy from diagnosis to treatment and follow-up and to compare it against the latest National Institute for Health and Care Excellence (2017) guidelines and AACC

(American Association for Clinical Chemistry) (January 7, 2018). **Results:** Among 190 reviewed medical records, 61% patients were males and the median age was 9 ranging from 6 to 13 years. 31.5% ($n = 60$) of cases suffered from various comorbidities. The overall adherence of health care professionals to audit standards was moderate. There was severe dearth of information in the medical records. Most records ($n = 147$, 77.4%) did not include the seizure type, frequency, and duration. Drug therapy was inconsistent with seizure type in 16 cases (8.4%). Investigations were underutilized generally. There were marked differences in the practice among health care centers. **Conclusion:** The vast majority of files ($n = 138$, 72.6%) suffered from poor documentation of seizure type, frequency, and duration which needs to be improved. Drug prescription was inconsistent and highly variable and dependent on the treating doctor's memory and diligence. Moreover, electroencephalogram, electrocardiogram, and drug level testing were highly suboptimal. Health professionals should modify and adopt the AACC recommendations to improve diagnostic and therapeutic service and reduce potential complications and sufferings of epileptic patients.

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Introduction

Epilepsy is a common and serious neurological disorder in childhood. In reality it is not a single disease but comprises a range of electroclinical phenotypes that result from many underlying disorders. Children with epilepsy differ from adults not only in the clinical manifestations of their seizures, but also in the presence of unique electroencephalogram (EEG) patterns, etiologies, and response to anti-seizure drugs [1]. They are more prone to seizures, but seizures are more about to disappear as the child grows. The management of the care of children with epilepsy has important implications for all aspects of their daily lives, especially daily activities such as bathing, vocational and leisure pursuits. There are areas of continuing concern with regard to therapy and compliance. Previous studies [2, 3] have shown that there is great potential for improving the management of these children, with particular reference to accurate diagnosis, appropriate therapeutic intervention, and well-documented, careful, ongoing support.

There has been long-standing concern regarding misdiagnosis and quality of management. Thus, this paper reflects on the current practice and further to improve the care delivered in Gaza Strip health care centers.

Additionally, through this work we wanted (I) to document the seizure frequency and appropriateness of daily therapy to aid patient compliance, (II) to ascertain the laboratory tests requested and their frequencies, and (III) to propose strategies to improve these aspects of epileptic care.

Materials and Methods

This study was carried out in the three largest centers for epilepsy management in the Gaza Strip, namely: European Gaza Hospital, Nasser Medical Complex, and Rantisi Pediatric Hospital. The study involved the medical records of 190 children seen at a pediatric neurology department during the period from January 1, 2017, to April 30, 2018.

We chose a clinically representative rather than a randomized controlled sample as the present study aimed to evaluate the performance of the health care professionals.

Medical records with insufficient information on the child, or when laboratory results or prescribed drug lists were missed were excluded from the study since the assessment depends largely on these items.

Principles for the management of these patients were devised from two sources with advice from two neurologists. Validated international standards used for this study were chosen from these principles. Through an audit process, the assessed aspects of care were: (1) seizure documentation, duration and frequency, (2) requested investigations which included imaging studies, blood tests and chemistry, and (3) treatment.

International Standards

The latest National Institute for Health and Care Excellence (NICE) (2018) guidelines and American Association for Clinical Chemistry (AACC) (2017) were followed in this audit [4, 5].

Laboratory and nonlaboratory tests are used to diagnose and monitor epilepsy, to determine what kinds of seizures a child is having, to identify underlying conditions such as toxins, infections or fever in children that may be causing seizures, and to distinguish epilepsy from conditions such as fainting that may cause some of the same symptoms.

A medical history, input from the patient, and input from family members who have witnessed the seizures are important parts of the diagnostic process. Someone with epilepsy may remember a strange smell, an aura, and/or sensations that precede a seizure but may not remember what has happened during the seizure itself. Depending upon the signs and frequency of a child's seizures, it may take some time to determine the proper diagnosis. Table 1 demonstrates the best available recommendations for practice.

Data Collection

Five medical students were trained for 1 week on study protocol, tools and data collection techniques of the study. Data were collected using a self-designed questionnaire based on the NICE and AACC guidelines. The survey tool encompassed questions related to demography and socioeconomic, presence of comorbidities, diagnostic information and treatment prescribed for the case. The data collection sheet was revised after conducting a pilot survey among 15 medical records. The data were collected retrospectively choosing the first completed files, which contained the adequate information we needed. The study focused on all known children with epilepsy in the three centers.

Definitions of Variables

Children were selected for this study as younger than 15 years old. Medical records were chosen as they had the ICD number G40 which indicates the diagnosis of epilepsy.

Statistical Analysis

The collected data were initially entered to Microsoft Excel. Then, data were analyzed by SPSS version 23. Frequency distributions and percentages were computed for all the variables.

Ethical Consideration

Ethical clearance was obtained from the Directorate General of Human Resources Development at the Ministry of Health, State of Palestine. Written and verbal consents were gained from health care centers' heads to enable us to review medical records. Study objectives, data collection procedures, benefits and risks of the study, confidentiality, and anticipated use of the results were explained to the research committee in the ministry in detail before executing our work.

Results

Baseline Characteristics

Our study included the revision of medical records of 190 children diagnosed with epilepsy in three hospi-

Table 1. Key recommendations for practice [6–16]

Specifics addressed	Basis of recommendations	Key recommendations
Management of pediatric status epilepticus	Expert opinion; not systematic review	First-line treatment benzodiazepines (either diazepam or lorazepam) Second-line treatment phenytoin or fosphenytoin OR phenobarbital OR valproate (intravenous) with intensive-care unit care including ventilation $\pm$ EEG monitoring $\pm$ invasive hemodynamic monitoring
Seizures including partial seizures (simple complex and secondarily generalized), and generalized tonic and/or clonic seizures	Italian League against Epilepsy systematic evidence-based review	History and examination warranted though only observational studies support this Investigations recommended: Complete blood count Glucose Urea Electrolytes Calcium Creatinine Alanine and aspartate aminotransferases Creatine kinase/prolactin Urine analysis Toxicological tests With evidence in case-control and cohort studies For infants, assessing for hyponatremia has high-level evidence from meta-analysis studies Imaging with CT or MRI and EEG recommended based upon level 1 evidence with prospective cohort studies, clinical trials or meta-analysis
Diagnostic assessment of child with status epilepticus	Evidence-based review by American Academy of Neurology and Child Neurology Society	Insufficient data to support blood cultures or lumbar puncture unless there is clinical suspicion of systemic or CNS infection and insufficient data to routinely recommend neuroimaging Checking AED levels in child on an AED was considered “probably effective” The following were determined to be “possibly effective”: toxicology studies, metabolic studies for inborn errors of metabolism, EEG for nonconvulsive status epilepticus
Treatment of status	Finnish Neurologic Society	First line: buccal midazolam, rectal diazepam, or intravenous diazepam or lorazepam Second line: phenobarbital Third line: suppressive anesthesia with continuous EEG
Generalized convulsive status epilepticus in children	Canadian Paediatric Society providing care guidelines while acknowledging there are insufficient data to guide care. Pragmatic expert advice	Check glucose then ABCs including positioning, suctioning, oxygen, and low threshold for ventilation First line with intravenous treatment is lorazepam, diazepam or midazolam; if no intravenous line, then buccal lorazepam, buccal or intranasal lorazepam, or rectal diazepam Second line intravenous fosphenytoin, phenytoin or phenobarbital; if IO then fosphenytoin, phenytoin, or paraldehyde Refractory status with intravenous midazolam or pentobarbital
Generalized convulsive status epilepticus	Expert opinion noting there are no nationally recognized specific protocols in North America	Initially check glucose and ABCs; intubation and ventilation; ceftriaxone or vancomycin pending head CT and LP; electrolytes and chemistries needed. EEG if nonconvulsive status epilepticus of concern Treatment with intravenous diazepam or lorazepam immediately; then phenytoin or fosphenytoin; if further treatment is needed, phenobarbital or valproate For refractory status, continuous infusion with midazolam or propofol
Treatment of convulsive status epilepticus	Italian League against Epilepsy systematic evidence-based review	First line preferred via intravenous lorazepam or diazepam; if no intravenous access, then intramuscular or buccal midazolam or buccal lorazepam based upon RCT or meta-analysis of RCT Second line phenytoin or phenobarbital or valproate based upon at least one RCT For refractory status epilepticus, they recommend thiopental or propofol or midazolam based upon expert opinion
	Multi-Disciplinary Group for the Management of Status Epilepticus in Children in India	Diagnostics to include total and ionized calcium in those <2 years old, sodium in those <6 months old, and complete blood count and LP if febrile; second-line diagnostics to include EEG and imaging ABC with oxygen and continuous positive airway pressure or invasive ventilation if needed First-line treatment intravenous lorazepam, diazepam or midazolam. If no intravenous treatment, then intramuscular/intranasal/buccal midazolam or rectal diazepam Second-line treatment phenytoin, fosphenytoin, phenobarbital or valproate. If this fails, pyridoxine in <2 years old; otherwise, levetiracetam Refractory status midazolam or thiopental

Table 1 (continued)

Specifics addressed	Basis of recommendations	Key recommendations
Monitoring oxygen saturations, providing supplemental oxygen, evaluation and treatment of acute seizures	World Health Organization's Paediatric Emergency Triage, Assessment and Treatment Group	<p>Re: monitoring oxygenation – strong recommendation with low quality of evidence for monitoring given low risk</p> <p>Re: oxygen use – conditional recommendation with low quality of evidence for use of oxygen with judicious use and lower threshold for discontinuation where supplemental oxygen is a rare resource</p> <p>Re: diagnostic assessments with acute seizures – strong recommendation with low quality of evidence for checking glucose, sodium if there is dehydration or diarrhea; also for LP if febrile particularly for those <18 months old, those with complex seizures, prior antibiotic use or not vaccinated for <i>Haemophilus influenzae</i> and/or streptococcal meningitis; LP deferral if unstable; image if new focal findings or comatose</p> <p>First-line treatment with intravenous access has strong recommendation based on low-quality evidence for treatment with benzodiazepine but condition recommendation on choice of agent with these being midazolam, lorazepam or diazepam, where intravenous access; where there is no established intravenous access, there are strong recommendations based upon low evidence for rectal diazepam, oral or intranasal midazolam, rectal or intranasal lorazepam, or intramuscular lorazepam or midazolam</p> <p>Second-line treatment is a conditional recommendation based upon low-quality evidence for phenytoin or phenobarbital or valproate</p>
Compared anticonvulsant treatments for convulsive status epilepticus	Evidence-based guidelines from American Epilepsy Society	<p>Of 38 studies and RCTs, only 4 provided level 1 evidence (“established as effective”) based upon blinded RCT; 2 studies provided evidence “established as probably effective” from one or more unblinded or otherwise limited RCT; the remainder of the RCTs or observational studies provided evidence of “possible” effectiveness</p> <p>Established as effective included intravenous lorazepam or intravenous diazepam for acute seizure management; there was insufficient evidence for superiority of lorazepam vs. diazepam</p> <p>Established as possibly effective was rectal diazepam, intramuscular midazolam, intravenous midazolam, buccal midazolam</p> <p>For second-line treatment, fosphenytoin is better tolerated than phenytoin</p>
Management of status epilepticus	Expert panel developed consensus; no evidence ratings given	<p>ABC with high concentration oxygen; check glucose and establish intravenous access</p> <p>First line with intravenous access is lorazepam; if lorazepam is not available then diazepam; if no intravenous access, then buccal midazolam</p> <p>Second line phenobarbital or phenytoin</p> <p>Refractory status with midazolam or thiopental</p>
AED, antiepileptic drugs; ABC, airway, breathing and circulation; LP, lumbar puncture; RCT, randomized controlled trial; IO, intraosseous.		

tals in the Gaza Strip. Based on the analysis of the whole cohort, 60.5% ($n = 115$) were males, and the median age was 9 ranging from 6 to 13 years old; however, the median age at which the first seizure appeared was 5 years. The children involved in the study suffered from many comorbidities, 54% ($n = 103$) of cases suffered from pneumonia, asthma and other etiological conditions of epilepsy. Regarding seizure type, 12.5% of cases ($n = 24$) had tonic-clonic seizure, 3.5% ($n = 7$) had febrile seizure, 2.5% ($n = 5$) had generalized tonic seizure, and 3.5% ($n = 7$) had other types. On the other hand, 77.5% of cases ($n = 147$) had no documentation regarding seizure type. Furthermore, the seizure frequency was not documented at all. Table 2 summarizes the results for each center.

Investigations

EEG, the primary diagnostic tool for epilepsy, was done in 49 out of 190 patients (25.7%). NICE guidelines recommend doing EEG for all epileptic patients to determine the type of seizure. An electrocardiogram (ECG) was investigated in 7% of patients ($n = 13$) only; the NICE guideline recommends that a standard 12-lead ECG should be done in all patients presenting with suspected seizure. Drug levels have been monitored in only 19.5% of cases ($n = 37$). According to the AACC guideline, clotting tests must be studied in patients on valproic acid. In spite of that, only 14 (7.4%) patients had been tested. Figure 1 shows how frequently investigations were requested in the actual practice.

Table 2. Characteristics of study subjects and distribution of comorbidities

Study variables	EGH, % (n)	NMC, % (n)	RPH, % (n)	Total, % (n)
Total number of cases	23.5 (45)	34 (65)	42.5 (80)	100.0 (190)
<i>Seizure type</i>				
Generalized tonic	4.5 (2)		3.75 (3)	2.5 (5)
Tonic-clonic	18 (8)	23 (15)	1.25 (1)	12.5 (24)
Myoclonic		1.5 (1)	1.25 (1)	1.05 (2)
Febrile seizure	2 (1)	9 (6)		3.5 (7)
Focal seizure	4.5 (2)			1.05 (2)
Absence seizure	2 (1)			0.5 (1)
Status epilepticus		3 (2)		1.05 (2)
Not documented	69 (31)	63 (41)	93.75 (75)	77.5 (147)
<i>Comorbidities and etiological conditions</i>				
Pneumonia	29 (13)		18.75 (15)	15.0 (28)
Sanjad-Sakadi syndrome	4.5 (2)			1.05 (2)
Cerebral palsy	82 (37)	1.5 (1)	1.25 (1)	20.5 (39)
Celiac disease	2 (1)			0.5 (1)
Asthma	4.5 (2)		3.75 (3)	2.5 (5)
Angelman syndrome	2 (1)			0.5 (1)
Brain atrophy	11% (5)	6% (4)		4.5 (9)
Hepatitis A	2 (1)			0.5 (1)
Familial Mediterranean fever	2 (1)			0.5 (1)
Cystic fibrosis	2 (1)			0.5 (1)
Acute bronchiolitis		5 (3)	1.2 (1)	2.0 (4)
Down syndrome			2.5 (2)	1.05 (2)
Immunodeficiency			1.25 (1)	1.05 (2)
Neurodegenerative disease			1.25 (1)	0.5 (1)

One child may have more than one comorbidity. Empty cells mean none or zero. EGH, European Gaza Hospital; NMC, Nasser Medical Complex; RPH, Rantisi Pediatric Hospital. For percentages presented in the field under each hospital, the number is divided by the total of the hospital. For percentages in the total column, the numbers are divided by 190.

Drug Therapy

Interestingly, 25% of cases ($n = 48$) were under no therapy. However, 42.5% ($n = 81$) were under polytherapy and 32% ($n = 61$) were under monotherapy (Fig. 2). Valproic acid was the most prescribed drug. It was prescribed in 36% of cases ($n = 67$), followed by phenobarbital, phenytoin, and diazepam; they were collectively prescribed in 62% of cases ($n = 118$). By contrast, the drug was not matched with the type of seizure in 8.5% of cases as compared to the NICE guidelines. Drug levels are of important concern in epilepsy patients. However, only 19.5% of cases ($n = 37$) had their drug level being monitored during therapy. In summary, Figure 3 demonstrates the number of

drug prescriptions in the practice. It is well observed in Figure 2 that health care providers depended largely on a combination between antiepileptic drugs. Most of these combinations were between phenobarbital and valproic acid in 31.5% of cases ($n = 60$) and between clonazepam and diazepam in 11% of patients. As previously mentioned, as most children suffered from various comorbidities, they were admitted several times to the hospital. As a result, they were also prescribed drugs for their conditions. Antibiotics were on the top of the list followed by ranitidine and nonsteroidal anti-inflammatory drugs.

Fig. 1. Percentages of requested tests.

Adherence to Guidelines

It is clearly observed that the practice of health care providers in Gaza Strip centers is not highly committed to the guidelines. The practice varied among the three centers in almost all categories of the standards. However, there were some mutual deficits in the practice in all centers. For example, all files suffered from poor documentation of basic information such as seizure type, seizure frequency, and duration. On the other hand, the centers differed in drug prescriptions and combinations. Overall, their adherence to the adopted standards was found only in 29% of cases ($n = 55$).

Discussion

To the best of our knowledge, this is the first audit in Palestine concerned with epilepsy in children. However, there is no reliable statistics regarding the incidence of epilepsy among children. Here, our work had some criteria for selecting the medical records, and we did not include every single record of epileptic patients. The information we sought to evaluate in the medical records was half-heartedly demonstrated. This was the barrier as we did not include all patient files.

It is well recognized that documentation of seizure type, frequency, and duration is poor. The absence of documentation suggests that epilepsy was not the focus of the consultation. The reasons for this are likely to have been that the patients were consulting for reasons other than epilepsy, that their condition was stable, or that there was not enough time available during the consultation. It may be that neither patients nor doctors wish to draw attention to this stigmatized condition.

As mentioned above, most patients suffered from other comorbidities. Moreover, investigations are underutilized, and appropriate laboratory tests as well as imaging studies were not requested occasionally. In addition, the unavailability of some lab tests and lab technicians had a great impact on utilization of these facilities.

Drug prescription was inconsistent and highly variable and dependent on the treating doctor's memory and diligence. There is large dependence on some medications due to their availability. On the other hand, some medications should be prescribed, but the health system lack them, or the family of the child cannot afford them.

As the diagnosis of the epilepsy type is not accurate, the treatment plan will not be convenient. And the treatment period is prolonged without noticeable development in the case condition. However, health care provid-

Fig. 2. Distribution of drug therapy.

Fig. 3. Number of antiepileptic drug prescriptions. One patient may be prescribed more than one drug.

ers were aware enough in changing the medication and about drug combination. Thus, we did not record any complicated condition.

It is clearly obvious that the practice in Gaza Strip centers is suboptimal. So, as a result of this audit, further developments are planned. Successive audits and close monitoring of the practice will dramatically lead to better documentation and proper use of investigations. This in turn will fulfill the gap of incorrect diagnosis. This eventually will aid in suitable drug prescriptions.

During our work, we observed marked variation in the practice among the centers and this is due to the lack of agreement between health care providers on the best standards to follow. However, the measures in the previous paragraph could remedy this gap.

Studies on children with epilepsy in regional countries have provided some useful statistics. A study in Saudi Arabia [17] found the prevalence rate of epilepsy in children is 6.54/1,000 in 2001 by door-to-door survey. The study also reported that perinatal and inherited factors

are the predominant causes of symptomatic epilepsy. Another study conducted in Sudan as a low-resource country as the Gaza strip concluded that epilepsy continues to be a major public health problem with a considerable gap in its treatment. The study also added there is a need for rational use of investigation when required. Furthermore, the study addressed the importance of public knowledge and attitude improvement [18]. The previous recommendations are similar to those of our study.

This study shows that annual review and seizure frequency documentation are required in order to improve the medical records, but alterations in drug therapy are more difficult. Barriers to change exist, but it is proposed that they can be overcome by successive audits based on a primary care team approach with close collaboration with a neurologist. Health professionals should modify and adopt the AACC recommendations to improve diagnostic and therapeutic service and reduce potential complications and sufferings of epileptic patients.

Conclusion

Epilepsy management in Gaza Strip centers is clearly suboptimal compared to internationally validated practices particularly in the fields of completing documentation and the proper use of investigations and medications. A specialized epilepsy clinic should be the focal point for acute and follow-up care. Traditionally, the main player in this care is the epilepsy experts; however, overall care improvement requires better collaboration between neurologists and other general practitioners who can make a considerable contribution to continued patients care. The authors suggest that a local protocol of management of epilepsy should be drafted based on vali-

dated guidelines. It is also suggested that local epilepsy registers should be created to enable long-term surveillance and research.

Finally, a refreshing course on the management of epilepsy has to be conducted for concerned staff followed by a successive audit to measure improvements.

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Statement of Ethics

Ethical clearance was obtained from the Directorate General of Human Resources Development at the Ministry of Health, State of Palestine. Written consent was gained from health care centers' heads to enable us to review medical records. Study objectives, data collection procedures, benefits and risks of the study, confidentiality, and anticipated use of the results were explained to the research committee in the ministry in detail before executing our work.

Disclosure Statement

The authors declare that they have no competing interests.

Author Contributions

T.A. and K.E. designed the study questionnaire. T.A., A.A., H.A.E., A.A.L., and M.S. collected the data. Data analysis was done by M.S. and T.A. T.A. wrote the first draft of the manuscript. K.E. revised it for grammatical mistakes and reviewed the statistics and figures. K.E. supervised the overall process and reviewed the final draft. All authors approved the final version of the manuscript.

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