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ORIGINAL ARTICLE

Outcome of Epilepsy Surgery in Pediatrics

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Abstract

Background: **Epilepsy is a brain disorder characterized by recurrent attacks of seizures. A seizure is a sudden change of behavior due to a transient alteration in the electrical pattern of the brain. Since despite appropriate drug treatment, one-third of patients continue to have seizures, other treatment must be considered.**

Aim: **This study aims at emphasizing the importance of epilepsy surgery in pediatrics by assessing surgical outcome as regard seizure freedom and surgical morbidity & mortality at Al-Azhar university hospitals.**

Patients and methods: Prospective study on 27 pediatric patients diagnosed as drug-resistant epilepsy, with 6 months to 1 year follow-up at least. Group A, 14 cases operated by corpus callosotomy, Group B, 10 cases underwent lesionectomy, and Group C, 3 cases underwent MST.

Result: **15 cases become seizure free, and 6 cases have rare disabling seizure. Lesionectomy was better than corpus callosotomy in achieving seizure freedom, In Group A, 4 cases become seizure free in comparison to 9 cases in group B. 11 cases of patients in group A (78.6%) showed increase alertness in comparison to the clinical mentality before surgery. The complications that have occurred were transient and resolved shortly.**

Conclusion: **Epilepsy surgery in childhood is effective & safe and needs must be considered once failed medical treatment to prevent cognitive delay. Even when complete seizure freedom is not achieved, a great decrease in frequency of seizures and number of AEDs is a remarkable result.**

Keywords: Drug-resistant epilepsy, Lesionectomy, Palliative, Seizure outcome

1. Introduction

Drug-resistant epilepsy (DRE) comprises up to 20–30% of childhood epilepsy cases and can be particularly overwhelming and difficult to control.[1]

Addition of extra medication in these cases has a very low success rates, with just 4% reported for the third antiepileptic drug and beyond.[2] As a result, surgical intervention for these patients is sometimes the only viable option, and surgery can often offer substantial seizure management.[3]

The goal of epilepsy surgery is to achieve complete seizure freedom, referred as curative surgery.[4] A significant reduction in seizure frequency will lead to fewer medications and improvement in neurocognition, which is a therapeutic benefit from surgery, but complete seizure remission will remain the main target whenever possible.[5]

Patients with DRE may be especially susceptible to a marked developmental delay due to uncontrolled seizures especially in early age of onset, suggesting that early surgical evaluation could be associated with major cognitive gains.[6]

The ability to define a circumscribed, resectable seizure focus plays a key role in possibility of post-surgical seizure freedom and dictates the surgical strategy. Careful counseling of the patient and family concerning the surgical goals with explaining that surgical techniques for epilepsy comprise a continuum from curative to palliative is also essential both before and after the procedure.[7]

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2. Aim of work

This study aims at emphasizing the importance of epilepsy surgery in pediatrics by assessing surgical outcome as regard seizure freedom and surgical morbidity & mortality at Al-Azhar university hospitals.

3. Patients and methods

From February 2021 to November 2022, this study was conducted on 27 pediatrics patients diagnosed as drug-resistant epilepsy by Epileptology multi-disciplinary team, these patients underwent epilepsy surgery at Al-Azhar university hospitals with 6 months to 1 year follow-up at least.

3.1. Inclusion criteria

Any pediatric patient whose seizures are intractable, and cases that cannot tolerate side effects of antiepileptics.

3.2. Exclusion criteria

All cases in whom the seizures are controlled on two or less antiepileptic drugs without intolerable side effects, and patients other than pediatrics.

All cases were subjected to.

3.3. Preoperative assessment

Clinical history and examination were done for all patients with documentation of the seizure history as regards age of onset, frequency, AEDs used with detailed history of epilepsy types.

Electrophysiological study: Repeated scalp EEG, short or prolonged video EEG.

3.4. Neuroimaging

CT brain and MRI brain epilepsy protocol at least and in some selected cases interictal PET scan was done.

Ethical Considerations: All cases have been informed of the risks and benefits of the intended surgical procedure, other possible surgical or non-surgical alternatives with informed surgical consent.

3.5. Surgical techniques

Group A underwent Corpus Callosotomy, in cases when the epilepsy was generalized with no focus detected, the focus was bilateral or multifocal and when the presentation was in the form of drops attacks. We aimed at splitting the anterior two third of the corpus callosum. In one case splitting extended to the splenium and including the anterior and posterior commissure. In Group B, patients underwent Resective (Lesionectomy) Surgery, in cases when the lesion or the focus detected can be safely removed. It was either, Temporal or extra-temporal as Excision of a lesion (e.g.,cortical dysplasia), or lobectomy. In group C patient underwent Multiple subpial transaction, when the focus is in eloquent area and cannot be safely removed. In this cases brain mapping and intra-operative EEG helped us in deciding the area to be transacted.

3.6. Postoperative assessment

Within 24 h, CT brain was obtained as a routine postoperative follow-up. Clinical examination used to document any neurological deficits using the same scales used preoperatively.

3.7. Follow-up

All patients underwent regular monthly check for at least 6 to 1 year at the outpatient clinic. All the patients kept taking the antiepileptic drugs throughout the follow-up period, Trial of drugs withdrawal, when attempted, has been started 6 months after surgery. Patients were classified based on the Engel classification: class I, seizure free; class II, rare attacks (>90% reduction); class III, 75%–90% reduction; class IV, <75% reduction in seizures. Surgical morbidity and complications were monitored.

4. Results

Table 1.

Table 1. Demographic data and duration of seizures.

Parameters	Studied patients ($N = 27$) N (%)
Sex	
Male	15 (55.6%)
Female	12 (44.4%)
Duration of seizure	
Less than 10 years	22 (81.5%)
More than 10 years	5 (18.5%)
Age (years)	
Mean ± SD	9.76 ± 3.96
Median	10.0
Range	3.0–16.0
Duration of seizure (years)	
Mean ± SD	5.42 ± 4.22
Median	5.0
Range	1.0–15.0

SD, standard deviation.

Table 2. Distribution of the studied cases as regards type of seizures.

Parameters	Studied patients (N = 27) N (%)
Type of seizures	
generalized onset (tonic-clonic)	15 (55.6%)
generalized onset (tonic-clonic, & drops attacks)	3 (11.1%)
focal to bilateral tonic-clonic	3 (11.1%)
focal onset	2 (7.4%)
bilateral focal to bilateral tonic-clonic	2 (7.4%)
Multiforme	2 (7.4%)

There were 15 males and 12 females with male to female ratio 1.25:1. The mean age of children was 9.76 ± 3.96 years, ranged from 3 to 16 years. The mean duration of seizure in the studied cases was 5.42 ± 4.22 years, ranged from one 1–15 years Most children (81.5%) had seizure less than 10 years (Tables 2 and 3).

Anterior corpus callosotomy was done in 13 patients (48.1%) while one case underwent (3.7%) complete callosotomy. MST was done in 3 cases, two of them combined by partial callosotomy. Lesionectomy was performed in 10 cases (Table 4).

All surgical complications were transient and resolved in short time ranged from 5 days to 3 months. The most frequent complication was transient disconnection syndrome that reported in 4 cases (14.8%) all of them underwent corpus callosotomy, followed by transient Urinary incontinence in 2 cases (7.4%), the lesion in one case was frontal while in the other case followed corpus callosotomy. One case had minor CSF leak, one case had emotional liability and one case had transient Left upper limb weakness.

As regard seizure freedom outcome: Engle class I was achieved in 15 cases, 10 cases with IA, 5 cases with IB. Engle class II in 6 cases, 2 cases with IIA, 3 cases with IIB and 2 cases with IID. Engle class III in 1 case, while Engle class IV in 4 cases, 1 case with IVA, 3 cases with IVB (Table 5).

Table 3. MRI findings and pathology in the studied cases.

Parameters	Studied patients (N = 27) N (%)
MRI findings	
No abnormality detected	10 (37.0%)
Frontal encephalomalacia	3 (11.1%)
Brain atrophic changes	3 (11.1%)
Temporal astrocytoma grade II	3 (11.1%)
Temporal ganglioglioma grade I	1 (3.7%)
Temporal DNET	1 (3.7%)
Temporal hippocampal atrophy with abnormal gyral patten and increase intensity	1 (3.7%)
Temporal cystic gliosis	1 (3.7%)
White matter leukodystrophy with pachgyri	1 (3.7%)
Occipital cortical dysplasia with microgyria	1 (3.7%)
Frontal neuroglial cyst	1 (3.7%)
Frontal ganglioglioma grade I	1 (3.7%)

Table 4. Distribution of the cases as regards technique and site of surgery.

Parameters	Studied patients (N = 27) N (%)
Type of surgery	
Callosotomy	
Anterior callosotomy	13 (48.1%)
Complete callosotomy	1 (3.7%)
MST	
MST	1 (3.7%
MST + partial callosotomy	2 (7.4%)
Lesionectomy	
Temporal lobectomy	1 (3.7%)
Excision of temporal lesion	5 (18.5%)
Excision of temporal lesion + Anterior callosotomy	1 (3.7%)
Excision of frontal lesion	2 (7.4%)
Excision of occipital lesion	1 (3.7%)

The postoperative results compared in 3 groups: Group A, 14 cases underwent corpus callosotomy (51.9%). Group B, 10 cases underwent lesionectomy (37.0%). Group C, 3 cases underwent Multiple subpial transaction (11.1%) (Table 6).

In Group A, 4 cases (28.6%) became seizure free (class I), 5 cases (35.7%) with class II, 1 case (7.1%) with class III and 4 cases (28.6%) classify as class VI. In Group B 9 cases (90.0%) became seizure free (class I) and 1 case (10.0%) classified as class II. In Group C, 2 cases (66.7%) became seizure free (class I) and 1 case (33.3%) classified as class II. There was statistically significant relation between seizure outcome in the corpus callosotomy group and the lesionectomy group (p value > 0.05).

Before surgery, there were 14 patients (51.9%) had normal mentality while, 13 patients (48.1%) had subnormal mentality clinically. Regarding clinical cognitive outcome, more than half cases (55.6%) had the same alertness as before surgery, while eleven patients (40.7%) reported increase in alertness and only one case showed deterioration Table 7.

5. Discussion

The International League Against Epilepsy defined Refractory epilepsy as failure to achieve

Table 5. Distribution of the studied cases as regards Seizure freedom outcome.

Parameters	Studied patients (N = 27) N (%)
Engel's Outcome Scale	
I	15 (55.6%)
II	7 (25.9%)
III	1 (3.7%)
IV	4 (14.8%)

Table 6. Seizure outcome in the 3 groups.

Parameters	Studied patients ($N = 24$) N (%)	Chi–Square Test	
		Test value	P value
Engel's Outcome Scale			
Corpus callosotomy Group A			
I	4 (28.6%)		
II	5 (35.7%)		
III	1 (7.1%)	9.18	0.027
IV	4 (28.6%)		
Lesionectomy Group B			
I	9 (90.0%)		
II	1 (10.0%)		
MST Group C			
I	2 (66.7%)		
II	1 (33.3%)		

sustained remission following a trial of two or three appropriate drugs. This is similar to the definition used by several clinicians previously, describing it as failure of two or more antiepileptic drugs (AEDs) and the occurrence of one or more seizures per month over 18 months.[8] However, for routine use, failure of trial of three appropriate AEDs at a maximally tolerated doses should be considered as drug-resistance and is a high indication of failure with trials of subsequent AEDs.[9]

Due to the fact that despite appropriate drug treatment, one-third of patients with epilepsy continue to have seizures, we must consider other treatments.[2] The duration of trial and the number of AEDs used needs to be adjusted once we find a surgical suitable candidate with epileptogenic lesion. In a case of uncontrolled seizure, we may start surgical intervention earlier than two years and before trying a third drug. Excision of this lesion early will Cesate the seizures and protect the child from the undesirable side effect of the AEDs and prevent cognitive delay, and this outweighs the risk of the operation.

This study included 27 children with DRE, most of the cases were in early and middle childhood. Most children (81.5%) had seizure less than 10 years.

It is to be noted that male predominance was common in most studies done to pediatrics with DRE which is coincide with our study and there is in general male predominance in epilepsy.[10]

Table 7. Distribution of the studied cases as regards number of antiepileptic drugs in the pre and postoperative follow-up.

Parameters	Studied patients ($N = 27$)	
	Preoperative	Postoperative
Numbers of antiepileptic drugs		
Mean ± SD	3.44 ± 1.5	2.33 ± 1.3
Median	4.0	3.0
Range	1.0–7.0	0.0–4.0

SD, standard deviation.

In our study we found no relationship between the seizure outcome and age of the patient at surgery or the duration of epilepsy before surgery (<10 or >10 years). It is never too late to do surgery for pediatrics with DRE whatever the time elapsed between onset of epilepsy and surgery.

As regard type of seizures in our study; generalized onset seizures were the most common type of seizure in 18 cases (66.7%). Focal onset seizures were found in 2 cases (7.4%). On Repeated EEG, generalized epileptogenic activity was predominant. Till this moment we depend on surface EEG due to lack of availability of advanced other measures like stereotactic EEG.

In the study of **Tan et al.,**[11] focal epilepsy was the most common in 24 cases (73%). Eight (24%) had LennoxGastaut syndrome (LGS) and two (6%) had West Syndrome (WS) (Combined generalized and focal epileptogenic activity). Whereas in the study of **Kim et al.,**[12] complex partial seizure (focal onset) was the most common type of seizure (97 cases).

In analyzing the history of the patients in our study, the type of seizures was of focal onset at first then changed over years and become generalized. The predominance of generalized seizure in our study may be due to the delay in the referral from pediatric neurologist. We think that the cause of this delay is the practice of trial of large number of antiepileptic drugs (AEDs), reaching 7 drugs in some cases, before referring the patient for further intervention. This may lead to some sort of brain encephalopathy causing generalized epileptic discharge.

The mean number of (AEDs) in the present study was 3.44 ± 1.5 with range from one drug to 7 drugs, this decrease in the postoperative follow-up to a mean of 2.33 ± 1.3 with range from no drug to 4 drugs, which was significant (Parametric test, r (25) = 0.73, p (2-tailed)=<0.001) (Table 7).

While, in the study of **Helmstaedter et al.,**[13] antiepileptic drugs reduced from 1.8 at baseline to 1.4 after 1 year of follow-up.

Also, **Jenny et al.,**[14] The AEDs were reduced in 67.9% of cases by one agent at least, 19.2% had no change, and 5.1% needed a reinforcement of drugs taken.

It is to be mentioned that in our study AEDs have been reduced (by at least 1 AEDs) in 77.8% of the cases (3 of them have stopped all medications), while 22.2% had no change.

Vagal nerve stimulator is an available palliative option in our country, however because it is expensive and due to insurance issue, we did not practice it at al-Azhar hospitals. Hemispherectomy either anatomical or functional not done in our

study due to lack of cases with complete hemispheric pathology and due to refusal of the operations by parents.

To avoid disconnection syndrome, we do anterior callosotomy and defers complete callosotomy if the seizure outcome was not satisfactory and after discussion with parents. Only in one case (3.7%), complete callosotomy was done accompanied by anterior and posterior commissurotomy, this patient was mentally retarded and most of the multiple focus that was detected were bilaterally temporal located.

Anterior corpus callosotomy is effective in seizure control in cases of generalized tonic-clonic and multiform seizures with bilateral discharges. It is inexpensive procedure which does not require special resources. It is of major value in countries with low resources. Disconnection syndrome usually complicates complete callosotomy, hence it is reserved only for the cases which need more extensive splitting of the corpus callosum.[15]

As regard surgical complications in our study, 33.3% of the cases had surgical complications, all the complications were transient and resolved shortly. The surgical morbidity of the operations done in our study were transient and minor if compared to the benefit of the surgery. No postoperative mortality has occurred.

In the study of **Hosoyama et al.,**[16] there were no surgical deaths. At their most recent follow-up, all but one of the 85 patients indicated that their morbidities had no strong negative effect on their activities of the daily life.

In the study of **Kim et al.,**[12] there was no postoperative mortality. After temporal resection, visual field defect was one of the most frequent complications and was not disabling. In extratemporal resection, the commonest complication was hemiparesis, which was transient in most cases. Three patients suffering dysphasia. Complication was minor following corpus callosotomy.

In cases of temporal lobe epilepsy whether we do anterior temporal lobectomy or, selective mesial structure resection, we depend on suction in a subpial manner with preservation of the arachnoid intact, this helped us in avoid complication related to the medial structures. The intraoperative mapping and EEG helps us a lot while working in eloquent area to avoid complication related to motor deficit.

As regard seizure freedom in our study, Engle class I was achieved by 15 cases (55.6%) (become seizure free). 6 cases (25.9%) showed rare disabling seizure (Engle class II). Engle class III was achieved by 1 case (3.7%), while Engle class IV was achieved by 4 cases (14.8%) (no improvement).

Lesionectomy was better in achieving seizure freedom more than corpus callosotomy, In Group A, 4 cases become seizure free in comparison to 9 cases in group B (Chi2 = 9.18, P value > 0.05). So, we have learned to exert a lot of work in correlation between patient semiology, repeated EEG and MR imaging hoping to find a lesion or focus which cause this secondary epilepsy. All patients that underwent temporal surgery (7 cases) 100% become seizure free.

Furthermore, **Kim et al.,**[12] stated that 100 patients (75%) achieved Overall, favorable outcome: 93 (69%) were seizure free (Engel Class I) and 7 had rare seizures (Engel Class II). 88% of patient become seizure free following temporal resection, were seizure free, and 90% had favorable seizure outcome.

In group A, 11 cases (78.6%) showed increase alertness in comparison to the clinical mental status before surgery, even when seizures freedom not happened, which was significant (Chi2 = 6.51, P value > 0.05). We depended on parents' observation and questionnaires in assessment of cognitive outcome, however further tests in the future needs to be done.

In accordance with our results study of **Helmstaedter et al.,**[13] as they reported that all functions except for verbal memory, figural memory, and IQ significantly improved as compared to measures before surgery.

In our study we found no relationship between the seizure outcome and age of the patient at surgery or the duration of epilepsy before surgery (< 10 or > 10 years), particularly in the corpus callosotomy group. It is never too late to do surgery for pediatrics with DRE whatever the time elapsed between onset of epilepsy and surgery, However, this conclusion needs further longterm studies and more studied cases.

Our study is limited by small number of cases due to limited resources and limited referral specialists. Follow-up studies of longer-term seizure control and neuropsychological and social outcomes would also be desirable. The issue of whether to do surgery early or late need further studies.

5.1. Conclusion and summary

Surgical interference for pediatrics with drug-resistant epilepsy is safe, effective, and improve the cognitive outcome. Seizure freedom after palliative surgery is not high as lesionectomy, but even when seizure freedom is not achieved in all cases, a great decrease in the frequency of attacks of seizures and

the number of AEDs is a remarkable result. This markedly improve the patient quality of life, cognitive and psychological outcome.

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Conflicts of interest

There are no conflicts of interest.

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