

Clinical, Electrical and Therapeutic Aspects of Epilepsies with Centro-Temporal Spikes (EPCT): Before 3 Years Versus EPCT from 3 Years

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Abstract: *Introduction:* Centro-Temporal Spike Epilepsy (CTEP) is one of the idiopathic partial epilepsies of children. However, it can present atypical manifestations such as an early age of onset of seizures before 3 years of age. The objective of this work was to evaluate the clinical, paraclinical and therapeutic factors of EPCT before the age of 3 years versus EPCT from 3 years of age. *Patients and method:* We conducted a retrospective study between January 2005 and January 2021, covering children followed for EPCT at the Albert Royer Children's Hospital and at the Ibrahima Pierre Ndiaye Neuroscience Clinic of the Fann University Hospital Center. *Results:* 189 children were collected, among them, 154 started their seizures at the usual age from 3 years old (EPCTh group) while 35 started their seizures early before the age of 3 (EPCTp group). The average age was 5.22 +/- 3.71 (range 3 months and 12 years). The male gender predominated in both groups. Familial epilepsy was found in 37.5% of patients with EPCTp and in 30.1% of EPCTh patients. Parental consanguinity was 20% in the EPCTp patient group and 17.5% in the EPCTh patients. School difficulties were present in 55.6% of EPCTp patients and in 29% of EPCTh patients. The number of repetitions was 33% among EPCTp and 15.9% among EPCTh. The most frequent types of seizures were hemicorporal CPM (42.4%) in the EPCTp group, and CGTC (38.8%) in the EPCTh. Physical examination was normal in most cases. The majority of EEG abnormalities were Rolandic spikes. Imaging could only be performed in a few patients and came back normal in these cases. The majority of patients were on monotherapy with 69.7% of EPCTp and 52.2% of EPCTh under VPA and 27.3% of EPCTp and 44.2% of EPCTh under PB. The PB had 25% treatment failure and the VPA 33%. Among EPCTp, 5.7% progressed to POCS and 9.7% among EPCTh. *Conclusion:* EPCT is known for its usually favorable evolution, however we note that the more serious the history, the earlier the appearance of the first attacks will be. The challenge lies in the knowledge and proper management of these risk factors in order to avoid the occurrence of early onset crises.

Keywords: Clinical, Electrical, Epilepsies with Centro-Temporal Spikes

1. Introduction

Central-Temporal Spike Epilepsy (CTEP) is common and represents 13 to 23% of benign childhood epilepsies. [5, 8]. It is an epilepsy occurring mainly between 3 and 13 years of age, which is often manifested by brief and infrequent focal seizures [15] occurring mainly during sleep and the existence of an activated centro-temporal spike focus. During sleep on

the electroencephalogram [6, 10]. Age-related focal epilepsies, particularly centrottemporal spike epilepsy, are considered to have excellent prognoses with spontaneous disappearance of seizures and electroencephalographic (EEG) abnormalities during adolescence [14]. The prognosis is generally good but there are rare cases of progression to Continuous Wave Spikes in Sleep Syndrome (POCS). The relative frequency and nosographic situation of typical and atypical forms remain

subjects of controversy [11]. It is in this context that our study takes place, which focuses on patients who developed EPCT before the age of 3 years compared to those who developed it from the age of 3 years. Its objective was to describe the clinical, electrical and therapeutic characteristics of patients under 3 years old and those aged 3 years and over.

2. Patients and Method

This was a retrospective study carried out at the Ibrahima Pierre Ndiaye Neuroscience Clinic and at the Albert Royer Children's Hospital in Dakar from January 2005 to January 2021. We selected the files of children followed in outpatient consultations from neuropsychiatry for an EPCT, having a complete file and meeting our criteria. In these patients, demographic data, history, clinical manifestations, additional examinations, treatment and progressive data were collected on a data collection sheet.

The inclusion criteria were: any child under 16 years of age who presented with epileptic seizures with EPCT-like paroxysms on the electroencephalogram.

Data were analyzed using sphinx statistical software. Descriptive variables were represented by means and percentages. The data was used anonymously to ensure confidentiality in the management of patient information.

3. Results

3.1. General Characteristics

During the study period, 189 children were collected. Among these children, 154 started their seizures at the usual age from 3 years old (EPCTh group) while 35 started their seizures early before the age of 3 years (EPCTp group). The male gender predominated and was found in 22 patients (62.9%) in the EPCTp and in 86 patients (55.8%) in the EPCTh group. The average age of seizure onset was 5.22 ± 3.71 (range 3 months to 12 years), with a median of 5 years. Three patients (10.3%) among the EPCTp patients had a medical history compared to four patients (2.9%) among the EPCTh patients. Undocumented neonatal infections and meningoencephalitis were found in these patients. Parental consanguinity was found in 7 patients (20%) presenting with EPCTp and in 27 patients (17.5%) in the EPCTh group. Nine patients (37.5%) of those with pEPCT had a family history of epilepsy and 37 patients (30.1%) of thEPC patients. In the EPCTp group, 15 patients (42.9%) were enrolled in school compared to 104 patients (67.5%) in the EPCTh. Five patients (55.6%) presented academic difficulties in EPCTp compared to 20 patients (29%) in EPCTh patients. Academic

difficulties were reported as learning difficulties and grade repetition. Among the EPCTp, 2 children (22.2%) were out of school compared to 3 children in the EPCTh group (4.3%).

3.2. Clinical Aspects

For the EPCTp group, the most frequent seizures were hemicorporal CPM (partial motor seizures) in 14 patients (42.4%) followed by CGTC in 12 patients (36.4%) then BF CPM (brachiofacial) in 6 patients (18.2%). Secondary generalized CPMs were found in 1 patient (3%). For the EPCTh group, they were dominated by CGTC in 59 patients (38.8%), then by hemicorporal CPM in 56 patients (36.8%), followed by BF CPM in 31 patients (20.4%). and secondarily generalized CPM in 6 patients (3.9%). In patients with pEPCT, seizures occurred exclusively during sleep in 20 patients (66.7%) and during wakefulness in 2 patients (6.7%); 8 patients (26.7%) presented seizures invariably during wakefulness and sleep. In EPCTh, the attacks were nocturnal in the majority of patients (81.5%), diurnal in 13 patients (10.9%) and mixed in 9 children (7.6%). The physical examination was normal in the majority of cases, in 28 patients (90.3%) in the pEPCT group and in 132 patients (94.3%) in the ThEPC group.

3.3. EEG and Brain Imaging Abnormalities

The abnormalities found were spikes in 1 patient in the EPCTp group (100%) and in 7 patients in the EPCTh group (87.5%). The predominant locations were the Rolandic regions in 15 patients (51.7%) in EPCTp and in 69 patients (59%) in EPCTh followed by CFT locations (centro-fronto-temporal) in 6 patients (20.7%) in EPCTp and 18 patients (15.4%) in EPCTh. CPT locations were observed in 5 patients (17.2%) of EPCTp and in 16 patients (13.7%) of EPCTh. Brain imaging was only done in 3 patients (9.1%) in EPCTp and in 11 patients (7.2%) in EPCTh. Either way, it was unremarkable.

3.4. Treatment

The majority of patients took monotherapy, 33 patients (97.1%) in the pEPCT group and 138 patients (90.2%) in the ThEPC group (table 1). Concerning the initiation of dual therapy, 1 patient from EPCTp benefited (2.9%) and 15 patients (9.8%) from EPCTh. In patients who experienced pEPCT, 23 (69.7%) were on VPA (Sodium Valproate), 9 (27.3%) on PB (Phenobarbital) and 1 (3%) on CBZ (Carbamazepine). Among EPCTh, 72 (52.2%) took VPA, 61 (44.2%) PB and 5 (3.6%) CBZ. The CBZ had 100% success, the PB 67.2% success, 25% failure and 7.8% regression, the VPA 63.8% success, 33% failure and 3.2 % regression (Table 2).

Table 1. Type of monotherapy taken according to the age of the patients.

| Age of seizure onset | | Monotherapy (1st Treatment taken) | | | |
|-----------------------|-------------|-----------------------------------|-------|-------|--------|
| | | CBZ | PB | VPA | Total |
| Less than 3 years old | Workforce | 1 | 9 | 23 | 33 |
| | Percentages | 3.0% | 27.3% | 69.7% | 100.0% |
| 3 years and over | Workforce | 5 | 61 | 72 | 138 |
| | Percentages | 3.6% | 44.2% | 52.2% | 100.0% |

| Age of seizure onset | | Monotherapy (1st Treatment taken) | | | |
|----------------------|-------------|-----------------------------------|-------|-------|--------|
| | | CBZ | PB | VPA | Total |
| Total | Workforce | | 70 | 95 | 171 |
| | Percentages | 3.5% | 40.9% | 55.6% | 100.0% |

Table 2. Evolution of monotherapy according to the age of the patients.

| Monotherapy (1st Treatment taken) | | Follow-up of the first treatment | | | |
|-----------------------------------|-------------|----------------------------------|---------|------------|--------|
| | | Stop | Failure | Regression | Total |
| CBZ | Workforce | 5 | 0 | 0 | 5 |
| | Percentages | 100.0% | 0.0% | 0.0% | 100.0% |
| P.B. | Workforce | 43 | 16 | 5 | 64 |
| | Percentages | 67.2% | 25.0% | 7.8% | 100.0% |
| VPA | Workforce | 60 | 31 | 3 | 94 |
| | Percentages | 63.8% | 33.0% | 3.2% | 100.0% |
| Total | Workforce | 108 | 47 | 8 | 163 |
| | Percentages | 66.3% | 28.8% | 4.9% | 100.0% |

Table 3. Type of dual therapy taken according to the age of the patients.

| Age of seizure onset | | Dual therapy (1st treatment taken) | | | | | Total |
|----------------------|-------------|------------------------------------|--------|--------|---------|---------|--------|
| | | Other | PB+CBZ | PB+VPA | VPA+CBZ | VPA+RVT | |
| < 3 years | Workforce | 1 | 0 | 0 | 0 | 0 | 1 |
| | Percentages | 100.0% | 0.0% | 0.0% | 0.0% | 0.0% | 100.0% |
| ≥ 3 years | Workforce | 4 | 6 | 2 | 2 | 1 | 15 |
| | Percentages | 26.7% | 40.0% | 13.3% | 13.3% | 6.7% | 100.0% |
| Total | Workforce | 5 | 6 | 2 | 2 | 1 | 16 |
| | Percentages | 31.3% | 37.5% | 12.5% | 12.5% | 6.3% | 100.0% |

Dual therapy (table 3) mainly concerned the EPCTh group. Six children (40%) benefited from the PB+CBZ association, 4 children (26.7%) benefited from another treatment, 2 children (13.3%) were on VPA+CBZ, 2 children (13.3%) under PB+VPA and 1 child (6.7%) under VPA+RVT (Rivortril). The other treatments were PB+Temesta, VPA+BZD (Benzodiazepines) and PB+CT (Corticotherapy).

The VPA+RVT association had experienced 100% success in one child. Failure was observed in 2 children respectively on PB+VPA and VPA+CBZ. PB+CBZ dual therapy had 3

failures and 3 successes.

In the EPCTp group, 27 children (77.1%) did not have treatment failure, 6 patients (17.1%) had one failure, 1 child had 2 failures (2.9%) and another had 3 failures (2.9%). In the EPCTh group, 121 children (78.6%) did not have treatment failure, 27 patients (17.5%) had one failure, 4 children had 2 failures (1.9%), 3 children had 3 failures (1.3%) and 1 child (0.6%) had 4 failures. Among EPCTp, 5.7% progressed to epilepsy with continuous spike waves of sleep (POCS) and 9.7% among EPCTTh (table 4).

Table 4. Evolution of dual therapy according to patient age.

| Dual therapy (1st treatment taken) | | Follow-up of the first treatment taken | | |
|------------------------------------|-------------|--|---------|--------|
| | | Stop | Failure | Total |
| Other | Workforce | 2 | 2 | 4 |
| | Percentages | 50.0% | 50.0% | 100.0% |
| PB+CBZ | Workforce | 3 | 3 | 6 |
| | Percentages | 50.0% | 50.0% | 100.0% |
| PB+VPA | Workforce | 0 | 2 | 2 |
| | Percentages | 0.0% | 100.0% | 100.0% |
| VPA+CBZ | Workforce | 0 | 2 | 2 |
| | Percentages | 0.0% | 100.0% | 100.0% |
| VPA+RVT | Workforce | 1 | 0 | 1 |
| | Percentages | 100.0% | 0.0% | 100.0% |
| Total | Workforce | 6 | 9 | 15 |
| | Percentages | 40.0% | 60.0% | 100.0% |

4. Discussion

The average age of seizure onset for our patients was 5.22 \pm 3.71 years (range 3 months to 12 years) and a median of 5 years. The age group under 3 years old represented 18.5% and those aged 3 years and over 81.5%. Our figures are similar to Basse's study [1] where the average age was 5.83 \pm

2.83 years, twenty-three children (21.8%) had started seizures before the age of 2. and 57 other children (54.1%) before the age of 4. Bourrous found extreme ages of 1 and 16 years, with an average of 8 years [12] and Blom of 1 and 13 years, with a maximum between 5 and 9 years [3]. In other studies, the age of the first attacks was later with extremes of 18 months to 13 years in Loiseau [9] and from 2 to 12 years in 98% of cases, from 4 to 10 years in 80% of patients with a

maximum at 7-10 years for Marc [2].

The male gender predominated among EPCTp and EPCTh with respectively 62.9% and 55.8% of cases. These data are also found in Jaouad with 54% boys [13]. Another study by Marc [2] found similar results (60%). These figures are not very different from Loiseau [9] which found 55.3% and in a study carried out in Morocco where boys represented 53% [12].

Three patients (10.3%) among the EPCTp patients had a medical history compared to 4 children (2.9%) among the EPCTp patients. Mark [2] found in 13% of patients a history of neonatal anoxia. Loiseau, for his part, found only 5.4% of neonatal difficulties [9]. Parental consanguinity was found in 20% of EPCTp and in 17.5% of EPCTh. It was estimated that 37.5% of those with pEPCT had a family history of epilepsy and 30.1% had thEPC. Similar results were found in Basse [1] where familial epilepsy and parental consanguinity were found respectively in 36.2% and 14.3% of patients. On the other hand, in a study carried out in Marrakech, out of 37 cases of benign Rolandic epilepsy, consanguinity was found in 10.8% of cases and the notion of familial epilepsy was only found in 19% of patients. [13] In Marc, family history of epilepsy was only 13% [2]. Concerning academic difficulties, 55.6% of EPCTp patients presented them while only 29% had them in EPCTh patients. These figures were found at Bourrous [4] where academic difficulties were reported in 42% of children. The data is different for Blom [3] where none of them had experienced any difficulties at school.

For the EPCTp group, the most frequent attacks were hemicorporal CPM in 42.4% followed by CGTC in 36.4% then BF CPM in 18.2%. Secondary generalized CPMs were found in 1 patient (3%). In Loiseau [9], the majority 119 patients also presented CP and 49 generalized seizures, with or without partial seizures. For the EPCTh group, they were dominated by CGTC in 38.8%, then by hemicorporal CPM in 36.8%, followed by BF CPM in 20.4% and secondarily generalized CPM in 3.9%. Blom [3] also found the three most frequent types of seizures with 12 cases of CP, 15 cases of CGTC and 12 cases of secondarily generalized partial seizures.

The majority of abnormalities found were spikes in 100% in the EPCTp and in 87.5% in the EPCTh group. The predominant locations were Rolandic regions in 51.7% among EPCTp and in 59% among EPCTh followed by CFT locations in 20.7% patients among EPCTp and in 15.4% among EPCTh and CPT locations in 17.2% cases among EPCTp and in 13.7% among EPCTh. The literature data found somewhat the same electrical anomalies. Jaouad reported spikes or spike waves in the centro-temporal [13] Marc found spikes located in the lower central region in 75% of patients, in the upper central region in 8% or in both in 17%, 36 patients had a temporal or parietal focus [2].

In other studies the locations were all Rolandic, such as Bourrous [4] who reported Rolandic discharges in 100% of cases, as well as Blom [3] in whom the EEGs of the 40 children in the study showed spikes or sharp waves with maximum amplitude in the centrottemporal region.

The majority of patients were on monotherapy, 97.1% in the EPCTp group and 90.2% in the EPCTh group. Concerning the initiation of dual therapy, 2.9% of EPCTp benefited from it and 9.8% of EPCTh. In another Senegalese study, 87.6% were on monotherapy compared to 12.4% on dual therapy [1] In our patients who presented with EPCTp 69.7% were on VPA, 27.3% on PB and 3% on CBZ. Among EPCTh, 52.2% took VPA, 44.2% PB and 3.6% CBZ. The same molecules are found in Basse [1] with sodium Valproate as first-line treatment (44.8%) followed by Phenobarbital (31.4%) and Carbamazepine (9.5%). At Bourrous [4], Sodium Valproate was also used as first-line treatment (84.2%) before Carbamazepine (15.8%). Among our patients who received dual therapy, the majority (40%) benefited from the PB+CBZ combination, 13.3% took VPA+CBZ dual therapy, 13.3% PB+VPA and 6.7% VPA+RVT. At Basse, the same dual therapies were found and combined either PB+CBZ (9 patients) or VPA+CBZ (4 patients) [1].

In the EPCTp group, 77.1% did not have treatment failure and in that of EPCTh, 78.6% of cases. The evolution at Jaouad was also marked by complete control of seizures in 71.4%. [13] and in 85.93% at Basse [1]. The same data were also found in Marc where 65% did not recur after the start of treatment [2]. On the other hand, in other studies, the success rate was higher with 92% complete remission of attacks beyond 2 years in Bourrous [4] and 95% in Blom [3] in Loiseau [9], approximately at what we find in our study, remission was earlier in patients with an onset at the age of 4-9 years than in patients who started before the age of 4 years and even earlier in patients with a start after 10 years. In our study, the CBZ had 100% success, the PB 67.2% and the VPA 63.8%. However, in a study by Kamoun [7] which reported the case of a 16-year-old child placed on CBZ, the outcome progressed towards myoclonus which ceased with the cessation of the treatment and electrical worsening.

5. Conclusion

Centro-Temporal Spike Epilepsy is included in the international classification of epilepsies and epileptic syndromes among idiopathic partial epilepsies of children; it is the most common form. However, it can present atypical manifestations such as an early age of onset of seizures before 3 years of age. Its evolution is usually favorable, however we note that the more serious the history, the earlier the appearance of the first crises will be. The challenge lies in the knowledge and good management of these risk factors in order to avoid the occurrence of early-onset Centro-Temporal Spike Epilepsy.

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