

Hypoxia as an etiological factor in epileptic hemiplegic cerebral palsy

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ABSTRACT

Objective: to study hypoxemia as an important etiologic factor in the pathogenesis of epilepsy in hemiplegic's cerebral palsy, the observation that seizures can directly lead to stagnation and regression in early development and affect local connectivity of the cortical zones, so the underlying path physiology of the seizures like hypoxemia had an effect on brain, mental and cognitive development. **Methods:** follow up study 60 hemiplegic's cerebral palsy aged 3-8 years; 30 epileptic and 30 non epileptic patients for 6 months duration to study the mean base line pulse oximetry, arterial blood gases, and tidal CO₂ in during seizure attacks and during rest especially at nocturnal time with regular monthly follow up for at least 6 months. **Results:** 25 epileptic patients showed severe hypoxic manifestation during seizures and at basal standard 35-40 and 40-50 mmHg and oxygen saturation was <60% and 70% respectively, 5 epileptics showed moderate hypoxia PaO₂ 40-50 mmHg and saturation 70-80% during seizures activity but PaO₂ 70-75 mmHg and saturation more than 85% during nocturnal measures without seizures, otherwise the mean baseline arterial oxygen pressure for non epileptic hemiplegic's cerebral palsy showed only nocturnal moderate reduction 50 mmHg in 4 patients and saturation <70%, mild nocturnal hypoxemia of 70mmHg with normal saturation about 85% in 7 patients and within normal limits during normal daily life activity while in the last 19 non epileptic patients showed normal limits at both nocturnal and daily life activity, seizure patients with chronically lowered O₂ tension <40-50 mmHg and associated hypercapnia result in neurological dysfunction. **Conclusion:** as long as the child is making progress, epileptic hemiplegic's patients are often associated with low oxygen saturation as a static developmental disorder in these chronic ill patients. Hypoxemia in hemiplegic's cerebral palsy with epileptic seizure activity play a major role as an underlying pathophysiology. (Int. J. Ch. Neuropsychiatry, 2005, 2(1): 83-88).

INTRODUCTION

Ventilation depends upon stimulation of respiratory muscles, integrated by inputs from the cerebral cortex, reticular formation and the spinal cord to modify automatic ventilatory rhythm^{1,2}. Control of inspiratory time, expiratory time and tidal volume allows fine tuning of mechanical performance to maintain minute ventilation at the lowest possible work of breathing. The simplest technique for assessing drive is to observe end tidal volume CO₂, pulse oximetry and arterial blood gases³. During REM sleep hypoventilation was enhanced by increased resistance and

intermittent obstruction of the upper airways and depression of central respiratory drive, so episodes of severe oxygen desaturation in response to nocturnal hypoventilation are a regular consequence. Originally, an oxygen saturation via pulse oximetry of less than 85% or an arterial oxygen partial pressure of less 55 mmHg while breathing room air, were necessary for reimbursement. In neuropathological studies it has been found that it is not epilepsy even status epilepticus that produces the damage but rather the underlying insult to the brain that causes both status epilepticus and damage, a period of hypoxemia was noticed in many children acutely during a period of their seizures⁴.

The aim of this study is to assess the relationship between epileptic seizures and systemic hypoxemia and hypoventilation in epileptic hemiplegic's cerebral palsy.

SUBJECTS AND METHODS

The current study was carried out in neurological care unit, El-Mataria Teaching Hospital, Cairo; to assess hypoxemia and hypoventilation in 60 hemiplegic's cerebral palsy: 30 epileptics and other 30 non epileptics aged 3-8 years. These two groups were subjected to:

A. Clinical assessment:

1. Detailed medical, peri, pre and post natal history, neurological history taking with special emphasis to establish the presence of metabolic and chromosomal abnormalities.
2. Through general and neurological examination.
3. Assessment of clinical severity, seizure activity, cognitive and motor development.

B. Routine laboratory investigations:

- Complete blood picture.
- Liver function tests
- Kidney function tests.

C. Neuroimaging:

MRI and MRA on brain was done to classify the causes to focal (one structural lesion) or

diffuse abnormality, also to show migrational disorders, small affected hemisphere and also unilateral perisylvian syndrome.

D. Long strip electroencephalogram:

Without and with provocation with emphasis to sleep deprivation and induction as an important tool for seizure provocation.

E. Oxygen and CO₂ measurement:

Mean base line pulse oximetry, respiratory gas measurements and nocturnal end tidal CO₂ during as baseline study and during seizure activity.

Exclusion criteria:

1. Metabolic disorders and syndromes.
2. Symptomatic epilepsy due to other causes like tumor or infection.
3. Other forms of cerebral palsies.

Statistical analysis:

Comparison between two groups was made using the unpaired student t test for numeric variables and X² test for difference among proportions. Multivariate logistic analyses was performed to determine the independent effect of hypoxemia on seizure activity in hemiplegic's cerebral palsy. Differences was considered statistically significant at P<0.05. Data were analyzed using Epi-Info version 0.1 for the year 2000.

RESULTS

Table 1. Shows degrees of hypoxemia in epileptic and non-epileptic patients.

	Total patients	Hypoxemia	mild hypoxic	Non hypoxic
Epileptic patients	30	25	5	0
Non epileptic patients	30	3	8	19
Number of patients	60	28	13	19
percentage	100%	46.6%	21.6%	31.6%

Table 2. Shows PaO₂ degrees in epileptic and non-epileptic patients.

mmHg	Epileptics		Non epileptics		p-value
	Basal	Seizure	Basal	Seizure	
PaO ₂ (30-40)	0	25	0	0	< 0.05
PaO ₂ (40-50)	25	5	4	0	< 0.05
PaO ₂ (60-70)	0	0	7	0	0.5
PaO ₂ (70-85)	0	0	19	0	< 0.05

Table 3. Shows Saturation % in epileptic and non-epileptic patients.

Saturation%	epileptic	Non-epileptic	total	p-value
60-70%	25	4	29	<0.05
70-80%	5	7	12	0.68
>80%	0	19	19	0.5

Table 4. Shows mean and SD of EtCO₂, PaO₂, Saturation % in epileptic and non-epileptic patients.

	Epileptics (Basal Levels)	Epileptics (Seizure Level)	Non Epileptics (Basal Levels)
EtCO ₂	6.8±37.4	9.4±46.3	5.9±32.6
PaO ₂	8.9±46.3	7.7±37.6	11.4±71.6
Saturation %	10.4±67.3	9.3±61.2	12.1±84.2

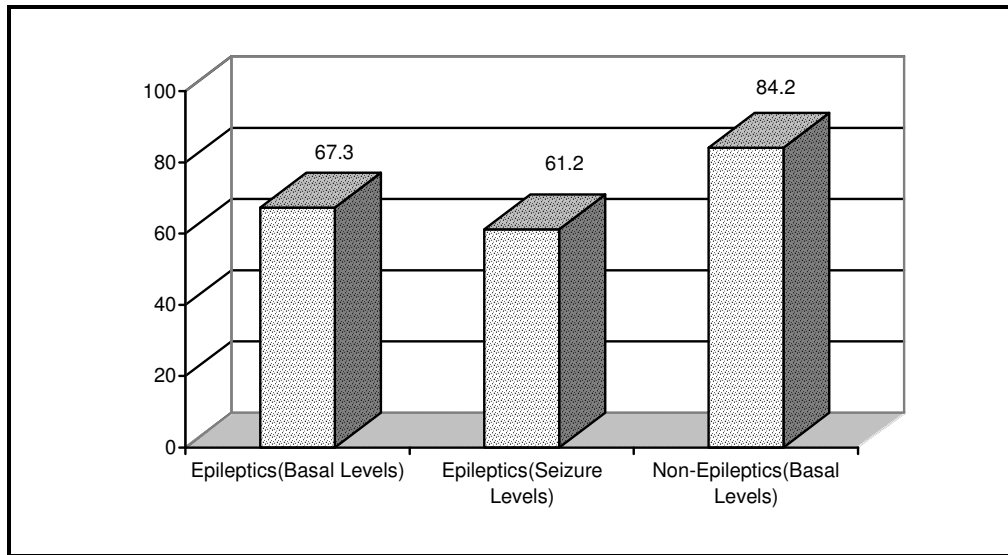


Fig. (1): Shows Saturation % in epileptic and non-epileptic patients.

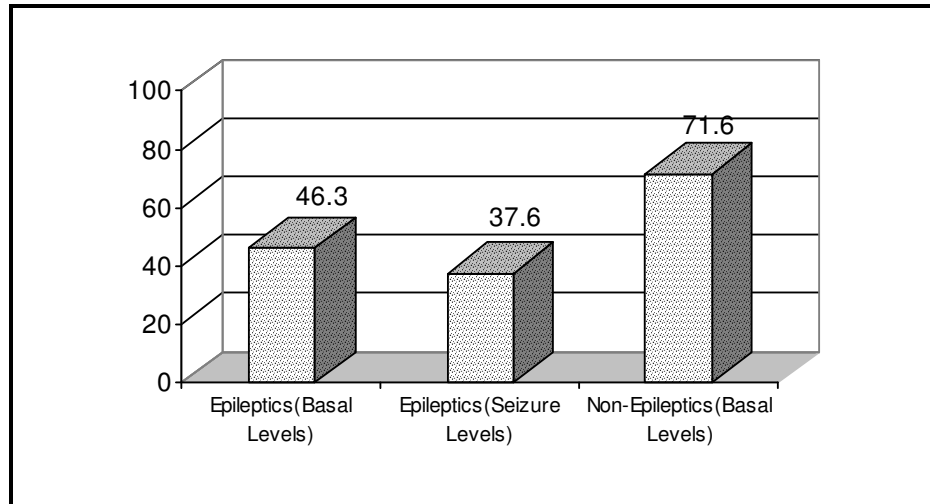


Fig. (2): Shows PaO₂ in epileptic and non-epileptic patients.

DISCUSSION

Infantile hemiplegia may not be perceived until the age of 4-6 months of life. Grigoris and Murphy¹ found that maternal mentality, birth weight <2000 gram and fatal malformation were among the leading predictors of static structural problem from birth, hemiplegic's cerebral palsy comprises several pathological entities and are often associated with oxygen desaturation (table 1), this current study came in the view of many studies which showed that blood gases, partial O₂ pressure, tidal CO₂, were affected up to 1-4 hours of seizure activity⁵, as the child is making progress, even if the pace is very slow, the additional effect of ongoing seizures, the interruption of activities at crucial stages of development; prospective longitudinal studies of cases in which regression or catch up in several areas of development (or only in a selective one) can be clearly correlated with the epileptic activity is the best demonstration of the direct role of epilepsy. It requires systematic and prolonged studies of babies even appeared normal initially, and at the other extreme of severely retarded ones who may nevertheless significantly improve if the epilepsy is

kept under control⁶. As a role, epilepsy is more common when infantile hemiplegia is caused by congenital anomalies rather than vascular stroke.

Epileptic discharges in developing brain areas particularly implicated in cognitive functions and behavior have important effects. The areas which support them have prolonged developmental periods, as opposed to those that mature more quickly, such as motor areas or primary sensory areas. If the brain systems involved are intermittently unavailable because of seizure activity, learning from experience and practice cannot take place. If the epileptic activity is maximal at the time of the normally occurring programmed development of these areas, the consequences will be greater because the stabilization of connections necessary for the consolidation of emerging cognitive functions cannot take place this came in our view (tables 2 and 3) which showed marked reduction in oxygen tension and saturation in epileptic hemiplegics patients of statistically significant difference ($p < 0.05$). Experimentally, it has been shown that local development and connectivity of the cortical zones affected by epileptic discharges in a

developing animal can be significantly disturbed. Thus, in addition to the intermittent interruption of cognitive activity and learning during discharges, permanent structural brain changes can occur⁷.

All these reasons explain why early epilepsy can be so detrimental to development, more so than even major fixed non-epileptic lesions. A cortical epileptogenic lesion can now be recognized with functional studies in most cases of this syndrome and the pathology can be situated in any location. The onset of the epilepsy probably occurs at a younger age if the pathology affects cortical areas which have normally an early rate of maturation i.e. occipital areas⁸. The importance for cognitive development of the cortical zones implicated in the epileptic process, its age of onset and duration will, among other factors, determine the long-term cognitive and behavioral sequelae.

A particularly dramatic example of the influence of the location and spread of the epileptic focus on behavior and development is seen in the syndrome of gelastic seizures with hypothalamic hamartomas. This dysplasia is intrinsically epileptogenic and hypoxia play an important role in the pathogenesis of epileptic attacks⁹. The severe behavioral disturbances of young children with this syndrome and the progressive intellectual decline are very probably related to the strategic posture of this malformation and the spread of the epileptic discharges by hypothalamic-amygdala connexions¹⁰.

The earlier the onset of epilepsy, the more restricted will be the repertoire of cognitive and behavioral performances that the baby will have achieved and the more difficult it is to evaluate the effect of epilepsy per se on development. As long as the child is making progress, even if the pace is very slow, the additional effect of ongoing seizures, the interruption of activities at crucial stages of learning, can pass unnoticed clear-cut episodic regressions with visible seizure activity are recognized, hypoxemia play an important effect which also had proved during our current study (Table 3).

Another possible but probably important situation is that of baby with early intractable epilepsy from the first days or weeks of life who shows no or minimal development¹¹. If epilepsy

stops spontaneously or finally becomes under control, some unexpected partial catch-up becomes possible even after a few months with its underlying pathology affect life style, prospective longitudinal studies of cases in which regression or catch-up in several areas of development (or only in a selective one) can be clearly correlated with the epileptic activity is the best demonstration of the direct role of epilepsy¹⁶. It requires systematic and prolonged studies of babies even if they appear normal initially, and at other extreme of severely retarded ones who may nevertheless significantly improve if the epilepsy is kept under control¹². The best examples are the cerebral hemiplegic patients. There are several reports of early surgery for young children with major dysplasias and intractable epilepsy who sometimes make rapid and remarkable progress after successful surgery¹³. However, these babies are now studied systematically with neuro-psychological methods and detailed behavioral observations¹⁴.

We are now probably recognizing only those cases with early clinically evident epilepsy with major structural lesions on brain imaging .It is likely that very subtle seizures due to small but strategically located dysplasias (not visible on standard neuroimaging) might have a devastating effect on cognition and behavior^{15,16}.

Conclusion:

As long as the child is making progress, epileptic hemiplegic's cerebral palsy patients are often associated with low oxygen tension and saturation as a static developmental disorder in these chronic ill patients². Hypoxemia in hemiplegic's cerebral palsy with epileptic seizure activity play a major role as an underlying pathophysiology and should be put in consideration in the evaluation and management of these cases.

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الملخص العربي

نقص الأكسجين عامل مسبب للنوبات الصرعية عند أطفال الشلل الدماغي

الذين يعانون من خذل نصفي هرمي

الهدف من الدراسة: دراسة نقص الأكسجين كعامل هام في نشوء النوبات الصرعية عند أطفال الشلل الدماغي الذين يعانون من خذل نصفي هرمي. حيث انه من الملاحظ تأثر الوظائف المعرفية لهذا المريض متأثراً سلبياً كنتيجة مباشرة لحدوث النوبات الصرعية. وبالتالي يمكن توقع تأثير سلبى مماثل لنقص الأكسجين أو الزرقعة.

العينة والطرق: تم دراسة ستين من مرضى الشلل الدماغي الذين يعانون من خذل نصفي هرمي دراسة طويلة لمدة ستة أشهر، وتراوحت أعمار هؤلاء المرضى ما بين 3-8 سنوات. نصفهم يعانون من الصرع و النصف الآخر لا يعاني. وتم عمل الأبحاث الآتية لهم:

1- قياس المستوى القاعدي للأوكسجين بالدم

2- قياس الغازات بالدم الشرياني

3- قياس غاز ثاني أوكسيد الكربون أثناء حدوث النوبات الصرعية، وأثناء النوم، مع المتابعة لمدة ستة أشهر.

النتائج: تبين النتائج أن 25 من مرضى الصرع يعانون من أعراض نقص شديد في الأكسجين بالدم أثناء النوبات وأيضاً أثناء حالات الراحة (35-40 مم زئبق، 40-50 بالترتيب)، ووجد أن الخمسة الباقين من مرضى الصرع يعانون من أعراض نقص متوسط في الأكسجين بالدم أثناء النوبات ولا يعانون من هذا النقص أثناء حالات الراحة. على النقيض فتبين أن بعض مرضى الشلل الدماغي الذين لا يعانون من الصرع قد يعانون من نقص أكسجين بسيط أثناء النوم فقط.

الخلاصة: قد يعاني مرضى الشلل الدماغي من ضعف في تشبع الدم بالأكسجين أثناء فترات نموهم، مما قد يتسبب في نشوء النوبات الصرعية لدى هؤلاء المرضى.