Pediatric Neurology 52 (2015) 410–413

Contents lists available at ScienceDirect

Pediatric Neurology

journal homepage: www.elsevier.com/locate/pnu

Original Article

Hyperventilation During Routine Electroencephalography: Are Three Minutes Really Necessary?

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ABSTRACT

OBJECTIVE: Hyperventilation induces absence seizures in children with absence epilepsy, and routine electroencephalography studies include three minutes of hyperventilation. We studied the duration of hyperventilation required to provoke a first absence seizure to determine whether three minutes of the procedure are indeed necessary. **METHODS:** Electroencephalography records of children who experienced absence seizures during hyperventilation were reviewed. The time from hyperventilation onset to a first and further seizure(s) was measured, and the occurrence of absences during the posthyperventilation phase was also noted. **RESULTS:** Sixty-two studies were evaluated. Mean time from hyperventilation onset to a first absence was 52 seconds (median 32 seconds). The vast majority (85.5%) had an absence within 90 seconds. Most (68%) children sustained a single event. All eight children with posthyperventilation seizures had experienced at least one event during hyperventilation. **CONCLUSIONS:** Our findings suggest that current guidelines for routine pediatric electroencephalography recording requiring three minutes of hyperventilation may not be clinically necessary. We found that the vast majority of children referred for suspected absence seizures experience a seizure less than 90 seconds after hyperventilation onset, and even more so by 120 seconds. Hence, a larger prospective study is warranted to establish more accurate hyperventilation duration parameters. We also suggest that once an absence seizure has been recorded at any time during hyperventilation, this procedure could be stopped, thus reducing the amount of discomfort for the child.

Keywords: absence seizures, EEG, time-to-event, hyperventilation, child, electroencephalography

Pediatr Neurol 2015; 52: 410-413

Introduction

Absence seizures are a common seizure type in childhood. They most commonly occur as the main seizure type in childhood absence epilepsy and as a major component of juvenile absence epilepsy. The average attack lasts 9-12 seconds (range 3-40 seconds).[1,2] The ictal electroencephalographic correlate of the absence seizure consists of high amplitude, bilateral, synchronous, symmetrical 3-Hz spike-and-wave discharges, with the highest voltage observed in the anterior regions.[1-4]

Hyperventilation (HV) is a well-recognized trigger for absence seizures in children with absence epilepsy,[2-4] provoking the seizures in virtually all children when performed correctly.[2] Long-standing recommendations for minimal technical standards for routine electroencephalograph (EEG) established by the American Clinical Neurophysiology Society include three minutes of HV followed by at least 1 minute of postventilation recording.[5,6] The European Commission of the International League Against Epilepsy also recommends for standard EEG performance to include three minutes of recording during hyperventilation with a continued recording for at least 2 minutes after cessation of HV.[7]

No external funding/grants were used in this study.
Article History:
Received September 27, 2014; Accepted in final form December 22, 2014
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http://dx.doi.org/10.1016/j.pediatrneurol.2014.12.003

HV can be safely performed in the office setting.[8] If HV is well-performed, our clinical experience suggests that most children with a history of absences will experience at least one episode in this situation. In this setting, it appears that most patients sustain the absence event within less than 90 seconds of starting HV. Therefore, we aimed at determining whether this clinical observation is correct and at establishing whether performing HV for a full three minutes was really necessary to elicit an absence seizure in children during routine EEG recording. Because HV is a relatively uncomfortable procedure, usually accompanied by dizziness and headaches, shortening this routine EEG activation procedure may also reduce the amount of discomfort for these patients.

Methods

This study was performed under the authorization of all three medical centers' institutional review boards.

Records of all routine EEGs of children who experienced at least one absence seizure during hyperventilation were reviewed at our three medical centers. All studies were done using the 10-20 system for electrode placement[5,6] and included two standard activation procedures: three minute hyperventilation followed by at least 10 minutes of post-HV recording and photic stimulation.

All records were reviewed by one of the authors (M.H., M.F., T.S.) and the findings compared with the official EEG report from the actual time of the study. Demographic data of all cases were obtained from the EEG report/study request. Clinical information on patients included: indication for study, past EEG records (if any), and current antiepileptic drug regimen (if any). Only records in which the child succeeded in performing the full three minutes of HV were included.

The time (in seconds) from the onset of HV until the occurrence of an electrographic generalized spike-and-wave seizure lasting a minimum of 5 seconds was measured. Also, the time to a second and to further absences from HV onset was recorded. Finally, whether electrographic absences appeared during the 2 minute post-HV phase was also noted and the time of occurrence with respect to HV ending was determined. Clinical correlation of the EEG seizure was obtained from the EEG technician's annotations, where available.

Statistical analysis

Because data were not distributed normally (Shapiro-Wilk test), continuous variables are described as mean ± standard deviation, median and minimum-maximum (min-max). Nominal parameters were shown as numbers and percentage. Comparison between two parameters was done—for nominal parameters—by chi-square or Fisher's exact test. For continuous data, Mann-Whitney nonparametric test was done, and among three hospitals, by Kruskal-Wallis nonparametric test and Bonferroni post-hoc comparisons. Difference was considered statistically different when $P < 0.05$. All differences were two-tailed when appropriate. All analyses were performed with SPSS-21 software.

Results

Sixty-two records were reviewed. Most (59.7%) patients were girls. Age range was 4-15 years (average 9.3 years, median 8.5), of whom almost 60% were younger than age 10. The geographical distribution of the records was 58% Israeli and 42% Turkish children (Table 1).

The time elapsed between HV onset and EEG seizure occurrence is depicted in Table 2. The average time to the first episode was 50.16 ± 73.3 seconds (median 32 seconds [min-max 2-130]). Twenty-four children sustained a second event (mean 105.88 ± 51.5 seconds, median 100 seconds [min-max 28-180]), whereas only four experienced a third absence. In the vast majority of the records (85.5%), the first EEG seizure occurred within 90 seconds from HV onset. Among the remaining 14.5%, the first event took place after an average of 110 seconds (median 100 seconds). In three of the 62 cases, the first event occurred between 120 and 130 seconds. When comparing by age groups, we found that the average time for first event was 47 seconds for those younger than 10 years of age, and 55 seconds for those older. Nevertheless, this difference was not statistically significant. Eight children experienced absences during the post-HV period. All had sustained at least one event during HV itself.

Seventeen of the 62 children had EEG performed while receiving antiepileptic medications (10 of the 17 had also had an EEG on no medications). No significant difference was noted in the time to first event between treated and untreated children.

Discussion

Generalized spike-and-wave discharges, the EEG correlate of childhood absences, are believed to represent a pathological phenomenon because of the malfunction of any of several specific voltage- or ligand-gated mechanisms in the thalamocorticothalamic network.[9] This allows burst activation of the cortex, normally seen only in a sleeping state, to occur during wakefulness, resulting in the EEG appearance of rhythmic spike-and-wave discharges and interrupting responsiveness to external stimuli.[10] In particular, the thalamic reticular nucleus and the frontal cortex appear to play a major role, suggesting that absence seizures may not be truly generalized, but may involve selective networks.[1]

Alkalosis resulting from reduction of blood carbon dioxide levels has been suggested as the mechanism behind the occurrence of absence seizures during hyperventilation. Thus, forced hyperventilation, by virtue of provoking alkalosis, induces absences.[11] This conclusion is supported by the fact that children with absence epilepsy do not sustain absences during physical exercise, when hyperventilation occurs as a compensatory mechanism to eliminate carbon dioxide and to raise blood pH.[12] Nevertheless, one study showed that low carbon dioxide levels may not entirely explain the induction of absences because some children did not sustain the seizures despite critically low end-expiratory carbon dioxide values.[13] Blood alkalinization from hyperthermia-induced hyperventilation causes

TABLE 1.
Characteristics of Israeli and Turkish Patients

Gender (%)	Age (years)	No. of Patients by Age (%)	Country (%)
Female: 37 (59.7)	Range 4-15	4-10 years: 37 (59.7)	Israel: 36 (58)
Male: 25 (40.3)	Mean 9.3	11-15 years: 25 (40.3)	Turkey: 26 (42)