Hyperventilation, More Than Just Hot Air

Hyperventilation Revisited: Physiological Effects and Efficacy on Focal Seizure Activation in the Era of Video-EEG Monitoring

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PURPOSE: Hyperventilation is an activation method that provokes physiological slowing of brain rhythms, interictal discharges, and seizures, especially in generalized idiopathic epilepsies. In this study, we assessed its effectiveness in inducing focal seizures during video-EEG monitoring.

METHODS: We analyzed the effects of hyperventilation (HV) during video-EEG monitoring of patients with medically intractable focal epilepsies. We excluded children younger than 10 years, mentally retarded patients, and individuals with frequent seizures.

RESULTS: We analyzed 97 patients; 24 had positive seizure activation (PSA), and 73 had negative seizure activation (NSA). No differences were found between groups regarding sex, age, age at epilepsy onset, duration of epilepsy, frequency of seizures, and etiology. Temporal lobe epilepsies were significantly more activated than frontal lobe epilepsies. Spontaneous and activated seizures did not differ in terms of their clinical characteristics, and the activation did not affect the performance of ictal single-photon emission computed tomography (SPECT).

CONCLUSIONS: HV is a safe and effective method of seizure activation during monitoring. It does not modify any of the characteristics of the seizures and allows the obtaining of valuable ictal SPECTs. This observation is clinically relevant and suggests the effectiveness and the potential of HV in shortening the presurgical evaluation, especially of temporal lobe epilepsy patients, consequently reducing its costs and increasing the number of candidates for epilepsy surgery.

COMMENTARY

Hyperventilation (HV) has been routinely used to evoke seizures for standard EEG since its seizure-precipitating effect on EEG was discovered by Berger in 1934 and further studied by Gibbs and colleagues in 1935; however, remarkably few quantitative studies have appeared concerning its ability to elicit focal seizures. Miley and Forster found HV-activated focal spikes or spikes and seizures in 11% of 255 patients, including seizures in 4% (1). Holmes, et al. found that HV rarely evokes seizures (0.52%) or spikes (3.4%) during standard EEGs among 384 patients with focal epilepsy (2). Although HV procedures were similar, antiepileptic medication was apparently maintained in the Holmes et al. report, while it was tapered to omission for inpatient video-EEG telemetry in the Guaranha et al. study (3).

The Guaranha et al. study explored the effectiveness of HV in eliciting clinical and electrographic focal seizures. The authors defined a HV-activated seizure as one occurring during a 10-minute HV epoch, comprised of a 5-minute HV period and a 5-minute post-HV period. Although the data appear to be competently gathered, evaluating how effective HV is as an activation agent could have been better assessed using an age-matched control group. Lacking these data, an alternate method to assess the efficacy could be to compare the number of seizures during HV with those spontaneously occurring during resting, wakefulness, and sleep, using 10-minute epochs as denominators.

According to the Guaranha et al. study, 97 patients averaged 3.3 days in monitoring. Using these figures but basing an analysis on 10-minute HV and 10-minute non-HV epochs over the 3.3 days, it can be extrapolated that a combination of 46,094 HV and non-HV 10-minute epochs occurred. As HV was performed six times daily, there were 1,920 HV epochs of 10-minute duration, leaving 44,174 non-HV epochs, including resting, wakefulness, and sleep. Assuming that HV elicited 32 seizures (somewhat conflicting data appear in the *Results* section) and that a total of 708 seizures occurred (mean = 7.3 per patient), 676 seizures arose spontaneously. Calculation of these data demonstrate that the seizure to epoch ratio for HV (32:1,920) and non-HV (676:44,174) epochs do not differ significantly ($p = 0.7033$).

However, HV more readily elicited temporal lobe seizures. The 61 temporal lobe patients had 28,987 10-minute epochs,

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of which 1,208 were HV and 27,779 were non-HV, presuming their average length of stay approximated that of the entire group (i.e., 3.3 days). Assuming that the mean number of seizures of the 97 patients can be accurately applied to the 61 temporal lobe cases, 445 such seizures occurred. Assuming further that the proportions of activated and spontaneous temporal lobe seizures were reflected in the proportions of temporal patients activated by HV (18/61) and not activated by HV (43/61), then seizure to nonseizure ratios for HV and non-HV epochs were 131:1,208 and 314:27,779, or 0.1084 and 0.0113, which is a significant finding ($p < 0.0001$). Thus, among temporal lobe patients, seizures were about 10 times more likely to occur during HV than during resting, wakefulness, and sleep. The flaw in this argument is the possibility that some of the 18 patients in the HV-activated group also could have had spontaneous seizures that would augment the spontaneous seizure ratio. However, this factor doubtfully alters the principle of a significant temporal lobe seizure activating effect that occurs with HV. Similarly, Guaranha et al. found temporal lobe epilepsy patients more likely activate (30%) by HV than patients with other foci (17%). The investigators' results and the analysis of their data presented here suggest that seizures are almost 10 times more likely to occur during the 10-minute HV and post-HV period than at other times in the medication-free temporal lobe patient. Thus, HV is a useful adjunct in this situation, particularly for health care systems with significant time constraints.

How HV can precipitate seizures and augment or evoke theta and delta activity remains unresolved; but it is probably because of alkalosis and decreases that occur in cerebral blood flow, pO2, and pCO2 (4,5). The relative contributions of these factors to seizure precipitation and theta/delta activity may differ. Alkalosis induces epileptiform activity in low magnesium rat neocortical slices, an effect blocked by *N*-methyl-D-aspartate (NMDA) antagonists (6). Increasing gap junctional conductance by intracellular alkalinization augmented epileptiform activity in calcium-free hippocampal slices (7). These data suggest that alkalinization is at least one mechanism by which HV evokes temporal lobe seizures.

In conclusion, HV appears to effectively activate clinical and electrographic seizures in video-EEG telemetered temporal lobe patients for whom antiepileptic drugs have been reduced or omitted. Its value for patients with other focally originating seizures remains less certain.

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