Age and Outcome


Abstract

Object. The object of this study was to investigate whether a failure of cerebrovascular autoregulation contributes to the relationship between age and outcome in patients following head injury.

Methods. Data obtained from continuous bedside monitoring of intracranial pressure (ICP), arterial blood pressure (ABP), and cerebral perfusion pressure (CPP = ABP – ICP) in 358 patients with head injuries and intermittent monitoring of transcranial Doppler blood flow velocity (FV) in the middle cerebral artery in 237 patients were analyzed retrospectively. Indices used to describe cerebrovascular autoregulation and pressure reactivity were calculated as correlation coefficients between slow waves of systolic FV and CPP (autoregulation index [ARI]) and between ABP and ICP (pressure reactivity index [PRI]).

Older patients had worse outcomes after brain trauma than younger patients (p = 0.00001), despite the fact that the older patients had higher initial Glasgow Coma Scale scores (p = 0.006). When age was considered as an independent variable, it appeared that ICP decreased with age (p = 0.005), resulting in an increasing mean CPP (p = 0.0005). Blood FV was not dependent on age (p = 0.58). Indices of autoregulation and pressure reactivity demonstrated a deterioration in cerebrovascular control with advancing age (PRI: p = 0.003; ARI: p = 0.007).

Conclusions. An age-related decline in cerebrovascular autoregulation was associated with a relative deterioration in outcome in elderly patients following head trauma.

Regression analyses were used to describe the dependence of age on parameters derived from pressure and blood flow velocity measurements in patients. The relationship of the Glasgow Outcome Scale (GOS) to age was also computed. In a statistical sense significance was widely found in parameters except for blood flow velocity and mean arterial pressure. The authors also mentioned that their study is strictly correlative rather than hypothesis testing, which raises the possibility of patient screening.

In this context an intriguing question came up: is an association among the parameters to be expected at all? Normally, patients in the intensive care unit are treated with the aid of therapy algorithms that maintain vital parameters in a reasonable range and compensate for fluctuations. Ideally the patient and the medical personnel became parts of a control loop allowing only reasonable deviations in the parameters. Thus, any suspected influence (age, for example) is masked by keeping a parameter within limits. This mechanism is likely to hold for all parameters that are externally controlled and therefore one might fail in searching for effects that would normally prevail. Another factor that hints at this circumstance is the low correlation coefficient computed in all analyses.

What can we learn from the contribution of Czosnyka and colleagues? Formally, age and parameter magnitudes appeared associated, and thanks to an enviable sample size of 358 patients, even reach statistical significance when testing it against r = 0. Czosnyka and associates focused on pressure reactivity (in 158 patients) and autoregulation (in 237 patients) indices, obviously because the best correlation coefficients were achieved. Considering that these data came from severely head injured patients, interpretation of results should be made on this basis, that is, the results of all parameters were featured by this fact. Regrettably, the confidence intervals for individual estimations have not been outlined, and thus no impression of the individual variability is given. The GOS scores clearly indicated a trend toward a poor outcome in elderly patients. Would results be the same if they were analyzed with, in our opinion, more appropriate logistic regression models?

We are aware of the profound problems (heteroscedasticity, among others) related to the analysis of clinical data especially when age is involved; however, as patients are part of such a control loop, we propose an acceptance of a grand mean instead of a formally significant but weak relationship to age.

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Response: We thank Drs. König, Heissler, and Rickels for their letter. It is very true that weak relationships in a large population of patients should be treated with appropriate statistical esteem. But this time we intentionally put elaborate statistical methods aside and decided to show our material in the simplest possible way. Apart from its intended simplicity, there was another reason for such an approach. Data were collected over a long period of time (1992–2002). During this period, different organizational arrangements (our Neuroscience Rehabilitation Annex was converted into a specialized 21-bed neurocritical care unit), various protocols, and undoubtedly different drugs were used. These effects and their possible impact on brain monitoring after head injury have been partially illustrated in our later work.2 Therefore, our group was inevitably inhomogeneous and building any prospective model for outcome prediction, however formally possible, appeared unjustified. Therefore, we limited our correlation analysis to only a few modalities. As we found that cerebral perfusion pressure (CPP) had a tendency to increase with age, we wanted to study which cerebral modality might outweigh the possibly beneficial role of improving CPP. Here the detrimental role of worsening pressure autoregulation or cerebrovascular reactivity were obvious—this was the only message of the paper. In patients with head injury, as in other diseases, gradual worsening of vascular function may contribute to a worse outcome. In any concrete building all
pipes require replacement every 20 years, but we do not have such a chance with our vessels. A recent report on the use of statins to increase autoregulatory reserve even in acute cases, such as after subarachnoid hemorrhage, seems to suggest an interesting strategy.

Answering in a straightforward way to the questions König et al. pose, we can state: a significant correlation simply means that we ought to reject the null hypothesis of \( r = 0 \), and then conclude that the two parameters are correlated. However the correlation coefficient does not necessarily strengthen the link between two parameters but only allows us to reject or not reject the null hypothesis. A relationship should not be considered as weak or strong, but significant or not.

Regrettably we cannot give any confidence intervals as we do not believe in any justification for a prospective model built on our data.

Finally, using logistic regression to assess outcome does not change anything: older age, greater intracranial pressure, and worse pressure reactivity, but not CPP—most of the material was acquired in the time when a quasi-aggressive CPP-oriented protocol was used, and not one oriented toward Glasgow Coma Scale scores—are the only significant independent associates with fatal outcome.

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References

Intraoperative Facial Motor Evoked Potentials?

To the Editor: We read the article by Wilkinson and Kaufmann with interest (Wilkinson MF, Kaufmann AM: Monitoring of facial muscle evoked potentials during microvascular decompression for hemifacial spasm: evidence of changes in motor neuron excitability. J Neurosurg 103: 64–69, July, 2005).

Abstract

Object. Hemifacial spasm (HFS) is thought to be due to a hyperactive facial motor nucleus consequent to chronic neurovascular contact. The lateral spread (LS) response is presumed to reflect changes in facial motor neuron excitability. Facial muscle motor evoked potentials (MEPs) use the same efferent pathway as LS, therefore the authors speculated that these potentials should reflect differences consistent with changes at the facial motor nucleus level.

Methods. Monitoring of LS and bilateral facial MEP was performed in 10 consecutive patients undergoing MVD for HFS. Ipsilateral facial MEPs were monitored in 17 patients undergoing MVD for trigeminal neuralgia (TN). Latency, amplitude, and duration of the MEPs were compared before and after MVD.

Following MVD the duration of ipsilateral MEPs decreased from 17.6 ± 1.2 to 7.6 ± 0.7 msec and their amplitude decreased from 269.9 ± 66.3 to 76.5 ± 26.2 µV (p < 0.01). These changes were consequent to the abolition of LS in eight of 10 patients and an approximately 50% reduction in two patients. The relationship between the reduction in MEPs and changes in LS was significant (p < 0.01). Control facial muscle MEPs (nonspastic side in patients with HFS and in those with TN) did not change significantly during the MVD procedure. Spasms were alleviated in nine of 10 patients, and there was no indication of facial nerve damage intraoperatively or postoperatively.

Conclusions. Facial muscle MEPs represent a novel tool for studying the neurophysiological mechanisms of HFS in particular and monitoring the facial nerve in general. Data in this study support the hypothesis that the development of HFS and its alleviation with MVD are related to changes in facial motor nucleus activity.

The authors of the above article claim that intraoperative facial motor evoked potentials (MEPs) are previously undescribed, show long duration and high amplitude corrected by microvascular decompression in hemifacial spasm and that this supports the hypothesis that hemifacial spasm is related to changes in facial motor nucleus activity. Unfortunately, serious flaws invalidate each conclusion and could mislead practitioners.

First, the true original description of intraoperative facial MEP monitoring was published by Dong et al. in Clinical Neurophysiology and was available online in October 2004 and in print in March 2005. Moreover, the technique the authors used does not produce facial MEPs. The stimulus montage was C3–C4 (anode to cathode) for the right facial muscle response and C4–C3 for the left. This promotes direct facial nerve excitation by current spread because of cathode proximity to the nerve on the targeted side. The correct stimulus montage is C3–Cz for the right facial MEP and C4–Cz for the left because the vertex cathode is farther from the facial nerve on the targeted side. Single electrical pulses were used and evoked facial muscle responses of 5 to 8 msec onset latency. Clearly, these responses represent direct responses to facial nerve excitation rather than MEPs of corticobulbar pathway origin. Muscle MEPs require temporal summation from pulse train stimuli for lower motor neurons to reach firing threshold under anesthesia. In contrast, facial nerve axons readily fire in response to single electric pulses of low intensity. In fact, Dong and colleagues showed that single-pulse responses represent technical failure when attempting to evoke a facial MEP. Furthermore, the reported short onset latency indicates direct facial nerve electrical stimulation. True intraoperative facial MEPs have a longer average onset latency of 13 msec because of the extra time required for corticobulbar tract conduction and temporally summated synaptic transfer at the facial motor nucleus.

The long duration and high amplitude of the observed facial muscle responses must have been due to lateral spread adding to the direct response. Naturally, when lateral spread was alleviated by microvascular decompression, the duration and amplitude of the responses decreased because only the direct response remained. All of the results are explained by facial nerve excitation from single C3/C4 pulses. The facial nucleus was not evaluated and therefore there