ELECTROENCEPHALOGRAM INVESTIGATIONS OF THE DISEQUILIBRIUM SYNDROME DURING BICARBONATE AND ACETATE DIALYSIS

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Summary

Continuous long-time electroencephalographic (EEG) monitoring was performed during acetate and bicarbonate dialysis in 20 patients. Persisting normal basic activity of the EEG without neurological symptoms was found only during the course of bicarbonate dialysis. However, in acetate dialysis, during the decrease of arterial CO₂ tension (PaCO₂), we registered EEG disturbances with moderate to severe slowing, dysrhythmic activity and high voltage discharges. The decrease in PaCO₂ and the deterioration in EEG activity in the patients during acetate dialysis was concomitant with severe neurological alterations, e.g. the typical symptoms of so-called 'disequilibrium' causing a cessation of dialysis in three patients.

Introduction

Neurological symptoms during haemodialysis combined with EEG alterations are summarised under the term 'disequilibrium' syndrome. Its clinical features are characterised by headache, restlessness, nausea, vomiting, tiredness, alteration of consciousness and convulsions in severe cases [1].

Kennedy [1] offered the hypothesis that the delayed clearance of urea from the cerebrospinal fluid (CSF) during haemodialysis results in an osmotic gradient between plasma and brain. This might be sufficient to draw water into the CSF, thus raising its pressure and causing the neurological symptoms.

A similar delay in the correction of acid-base relationships in the CSF relative to plasma is probably due to a slow transport of bicarbonate across the blood-brain barrier [2].

Klinkmann [3] has demonstrated that it is the pCO₂ which the uraemic organism uses as a regulatory system for maintaining the stability of acid-base metabolism in the central nervous system. Despite a severe metabolic acidosis in uraemia, the central nervous system is able to maintain a relative alkalosis.
The multifactorial pathogenesis of disturbances of the central nervous system was described by Wakim [4]; hyponatraemia, rather than change in the urea concentration, is involved in the EEG abnormality. In addition, overhydration, hypo-osmolality, acid-base disturbances and circulatory insufficiency are also involved. Experimental studies by Arieff [5] did not confirm all these findings.

In our clinical practice patients have shown, surprisingly, a very good tolerance of bicarbonate dialysis without neurological disorders. This stimulated us to investigate whether the disequilibrium syndrome could be explained by disturbances of arterial acid-base status.

Patients and methods

Twenty patients who had frequent episodes of disequilibrium during acetate haemodialysis (HDA) received bicarbonate haemodialysis (HDB) and were investigated for arterial acid-base status every 30 minutes during both HDA and HDB. In addition, continuous long-time electroencephalographic (EEG) monitoring was performed during HDA and HDB.

Patients suffered from chronic glomerulonephritis (n=9), pyelonephritis (n=4), cystic disease of the kidney (n=4), nephronphthisis (n=2), diabetic nephropathy (n=1). The average age was 38.2 years. Eleven were female and nine male. All were more than six months on haemodialysis. Informed consent was obtained.

Dialysate composition for HDA was (mEq/L): sodium 140.0, potassium 2.0, calcium 3.5, magnesium 2.0, chloride 104.5, and acetate 38.0.

Dialysate composition for HDB was (mEq/L): sodium 105.5, potassium 2.0, calcium 3.5, magnesium 1.0, chloride 111.5, and acetate 2.1. Additionally, in the latter dialysate a final sodium concentration of 140.0mEq/L was reached by means of the continuous addition of 38.0mEq/L sodium bicarbonate (Salvia Company, Germany).

Patients were dialysed thrice weekly for four hours, using a hollow fibre dialyser of 1.4m² surface area (CDAK 4,000, Cordis Dow Corporation, Miami, FL, USA). The patients were always dialysed with the same blood-flow. (Blood- and dialysate-flow were respectively 200ml/min and 500ml/min during HDA and HDB).

Heparinised arterial blood samples were measured immediately for pH, PCO₂ and PO₂ with a Radiometer (ABL, Copenhagen, Denmark).

Continuous long-time EEG monitoring was performed with the Oxford-Medilog electroencephalogram system (Oxford Medical System Ltd, Abingdon, Oxfordshire, England). Visual evaluation followed by page mode display. EEG sections of interest were printed out on a standard EEG writer. The four bipolar leads were placed: pre-central to temporal (PC – T) and central to parieto – occipital (C – O), or occipital – occipital (O – O), (time constant 0.3 sec upper frequency limit 70/sec, amplitudes 50µV (=5mm). We have applied the term ‘rhythmic’ when a sequence of waves have similar frequencies and no frequency is superimposed; the term ‘dysrhythmic’ is used when a sequence of waves have varying frequencies, and when other frequencies are superimposed. EEG activity
with amplitudes more than 75–100μV was called ‘high voltage’; simultaneous elements with a sharp wave character were defined as ‘high voltage discharges’. Retardation of the basic activity below the aged-normal alpha range into the delta/theta frequency band were termed as ‘slowing down’.

Statistical analysis was by Student’s paired t-test for patient comparisons (acid-base values) in acetate versus bicarbonate dialysis. The data are presented as the mean ± standard deviation.

Results

A correction of metabolic acidosis is reached uniformly in all patients during HDB. The arterial values for PaCO₂ and standard bicarbonate (aHCO₃) were significantly higher during HDB than with HDA. Metabolic acidosis was not as effectively treated with HDA:

<table>
<thead>
<tr>
<th></th>
<th>HDB</th>
<th>HDA</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.45 ± 0.03</td>
<td>7.46 ± 0.06</td>
<td>NS</td>
</tr>
<tr>
<td>aHCO₃</td>
<td>23.45 ± 1.4</td>
<td>21.4 ± 2.5</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>PaCO₂</td>
<td>34.10 ± 2.6</td>
<td>27.4 ± 5.0</td>
<td>p&lt;0.01</td>
</tr>
</tbody>
</table>

During HDB values for PaCO₂ returned to normal in 17 of the 20 patients, only three were less than 30mmHg. However, in HDA only seven patients were in the lower normal range (PaCO₂ ≥ 30mmHg) and 13 patients were below 30 mmHg). In six of these 13 patients marked decreases to 21.2 ± 2.6mmHg, which was apparent after 180 minutes dialysis. At this time these patients suffered from severe neurological symptoms.

Alterations in the EEG basic activity were analysed (Figure 1): A persisting normal alpha pattern (8–12 waves/sec) was found only during the course of HDB. In the 20 patients, the basic activity was normal in 14 cases, and in five of

![Diagram]

Figure 1. Comparison of electroencephalographic (EEG) abnormalities in 20 patients during dialysis with bicarbonate (HDB) and acetate (HDA)
them we found slight to moderate alterations in the form of dysrhythmic waves and high voltage discharges. Only in one young patient, aged 16 years, was a severe slowing registered caused by exceeding the usual volume removal by more than one litre.

In contrast to HDB, during HDA only three of the 20 patients demonstrated normal basic EEG activity. Dysrhythmic and high voltage discharges were monitored in 13 patients. Moderate to severe slowing was measured in 12 of the 20 patients. Hypersynchronous activity with spike waves was detected in three patients. Acute alteration of consciousness during this time led to early cessation of treatment in these patients. These frequent and severe EEG changes during the course of HDA were always accompanied by a decrease of PaCO₂. The EEG at first showed a disappearance of the normal rhythmic alpha pattern, instead generating an irregular dysrhythmic basic activity. With the progression of the PaCO₂ decrease high voltage discharges and/or slowing was found. In the 17 patients with EEG abnormalities during HDA there were two different groups: 10 patients showed, concomitant with the decrease of PaCO₂, a more pronounced slowing, the other seven patients more dysrhythmic activity and high voltage discharges. These typical patterns of EEG abnormalities are demonstrated in Figures 2, 3a and 3b.

The decrease in PaCO₂ and the deterioration in EEG activity in the patients was concomitant with severe neurological alterations, e.g. the typical symptoms of so-called 'disequilibrium', as shown in Figure 4. During HDA all signs of the disequilibrium syndrome occurred frequently but were seldom seen during HDB.

In most cases EEG alterations preceded the clinical symptoms.

Discussion

Many authors [1,4,6–8] have found pronounced EEG abnormalities in the form of 'slowing down', dysrhythmic waves, high voltage discharges and diminished spike wave activity. The onset of these EEG changes was concomitant with deterioration in the clinical neurological state of the patients. We can fully confirm these findings during HDA. Surprisingly, during HDB the patients showed almost no clinical and electroencephalographic impairment.

In our patients the dialysis regimen was comparable apart from the buffer substances. In these conditions the only significant difference between HDA and HDB was in PaCO₂ and aHCO₃.

The significant decrease of PaCO₂ correlated with the development of EEG abnormalities which preceded clinical manifestations. The most marked EEG disturbances were paralleled with the greatest decrease in PaCO₂ of about 20mmHg in the presence of circulatory insufficiency, nausea, vomiting, restlessness, headache and altered consciousness.

The most critical EEG changes were monitored in two younger patients aged less than 16 years with hypersynchronous activity in the form of sharp and spike wave potentials. This led to early cessation of HDA in three cases.

According to our clinical and EEG experience it is changes in PaCO₂ that plays the most important role in the pathogenesis of the disequilibrium syndrome, as stressed by Klinkmann [3] and Swanson [9].
Figure 2. Electroencephalographic activity in patient D while undergoing bicarbonate (HDB) and acetate (HDA) dialysis.
<table>
<thead>
<tr>
<th>Time</th>
<th>Description</th>
<th>pCO₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>120 min</td>
<td>Moderate abnormal theta-alpha activity</td>
<td>25.3</td>
</tr>
<tr>
<td>150 min</td>
<td>Slow bitemporal rhythms</td>
<td>24</td>
</tr>
<tr>
<td>160 min</td>
<td>Persisting delta-theta background activity</td>
<td></td>
</tr>
<tr>
<td>60 min</td>
<td></td>
<td>31.2</td>
</tr>
<tr>
<td>180 min</td>
<td>Spike-wave pattern</td>
<td>27.9</td>
</tr>
</tbody>
</table>

Figure 3a. Electroencephalographic alterations during the decrease of arterial CO₂ tension (pCO₂) in an 11 year old patient L undergoing acetate dialysis.
bicarbonate-dialysis (HDB)  Pat L, * 6.4.70
(14.9.81)

before start

pc - t l.

o - o.

pc - t r.

60 min

basic activity continuously within normal range.

50 µV  |  1 sec

Figure 3b. Part of the electroencephalogram in the presence of normal arterial CO₂ tension in the same patient as shown in Figure 3a. Here: normal basic activity during bicarbonate-dialysis.
There is a strong correlation between changes in PaCO₂ and cerebral bloodflow [10,11]. A decrease in PaCO₂ results in a rapid decrease of cerebral bloodflow and an increase in cerebral vascular resistance [12].

The fact that cerebral circulatory autoregulation depends mainly on metabolic factors supports our hypothesis that the unsatisfactory correction of acid-base status, especially the decrease in PaCO₂, may be responsible for the occurrence of the disequilibrium syndrome during HDA as opposed to HDB.

We agree with Wakim [4] that other factors may also be involved in the multifactorial pathogenesis of the syndrome, but these are factors which secondarily induce decreases in arterial CO₂ tension. During HDB the PaCO₂ and EEG activity consistently remain in a normal range and no symptoms of neurological disturbances occur.

However, a decrease in PaCO₂ can also occur during HDB if a specific rate of volume removal is exceeded, resulting in a decrease of intravascular volume with diminished tissue perfusion (hypoxaemia). The decrease in oxygen tension (PaO₂) can induce compensatory hyperventilation which causes an increase in PaO₂ and sudden decrease in PaCO₂. In this specific situation neurological symptoms and EEG abnormalities can also occur during the course of HDB (demonstrated by our results, Figures 1 and 4). The same compensatory mechanisms can be induced when patients are dialysed with a low dialysate sodium (<140mEq/L) during HDB. This causes early diminution in intravascular volume, decreased venous return and cardiac output [4]. The consequent circulatory insufficiency and the dialysis-induced disequilibrium in this situation was emphasised 20 years ago [4].

Critical cerebral dysfunction is avoided in dialysis using a sodium concentra-
tion of 140.0mEq/L and bicarbonate as the buffer substance. This is of help in patients with frequent episodes of disequilibrium during HDA and in patients with cerebrovascular complications.

References

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