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Clinical symptomatology and management of a severe intrathecal baclofen intoxication

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Intrathecal baclofen application by means of implanted drug delivery systems has proved to be an effective treatment for severe spasticity[1,2]. Overdosage caused by rostral spread in the cerebrospinal fluid is an inherent risk of this approach[3,4]. Prevention of accidental intoxication, and its adequate management if it occurs, is essential to further establish this promising technique.

We report a case of severe accidental intrathecal baclofen overdose with special regard to the clinical evolution and to therapeutical aspects. A 16-year-old male patient suffered from severe spasticity due to traumatic brain injury, with a right hemispheric subdural hematoma causing tentorial herniation and a transient compression of the brainstem. He developed an apallic syndrome with persistent decortication pattern. Oral antispastic treatment failed, but with intrathecal baclofen – supplied through a mechanical drug delivery system (Secor, Cordis Corp.) – spasticity assessed bilaterally in the elbow, wrist, hip, knee and ankle joints could be reduced from a mean Ashworth score of 4.3 to one of 2.8.

Ten weeks after implantation, the first refilling of the reservoir was performed by the surgeon who had implanted the device and who was familiar with the technique. After draining the pump reservoir, 10 mg of baclofen (Ciba-Geigy) in 10 ml of saline were injected transcutaneously into the pump. After 50 min the patient presented with somnolence, nystagmus and non-purposeful defence reactions. A

baclofen overdose was suspected due to a drug device failure. After a further 30 min (80 min after the refilling procedure), the patient was deeply comatose and had to be artificially ventilated due to respiratory arrest. Ten minutes later the catheter connecting the pump with the intrathecal space was surgically explored. A ligature was performed with conventional surgical suture 5 cm distal to the reservoir to prevent further leakage, which was presumed to be the cause for the patient's deterioration.

Intravenous physostigmine was given 2 h after refilling – a 4 mg bolus within 3 min initially followed by 2 mg boli over 2 min every hour up to a total amount of 14 mg – but this did not improve the patient's condition. More physostigmine was not given in order not to increase the side-effects of baclofen – such as bradycardia and hypotension.

Eight hours after the intoxication, the pump was explanted and 30 ml of cerebrospinal fluid were tapped through the *in situ* located catheter in order to reduce the large amount of the drug. A high performance liquid chromatography examination of paired samples of five consecutive cerebrospinal fluid samples of 6 ml each, revealed a baclofen concentration of 17.74, 3.87, 4.16, 4.93 and 4.10 μg/ml, respectively. The high value in the first sample can be explained by the contamination of the catheter volume of 400 μl containing the drug in a concentration of 1000 μg/ml. A minute examination of the pump showed that the needle had perforated the seal of the extrusion chamber instead of the pump's reservoir dome, both being within a distance of only 5 mm (Figure 1).

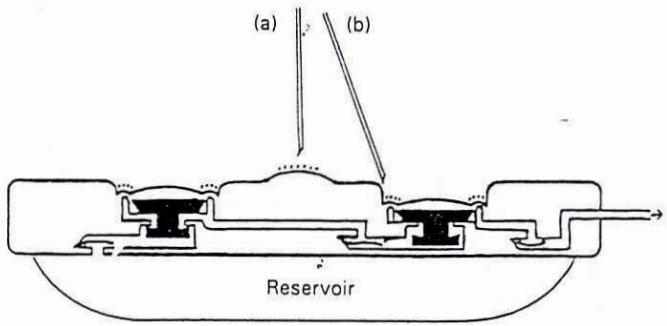

Figure 1 Perforation by the needle of the seal of the extrusion chamber (a) rather than the reservoir dome (b)

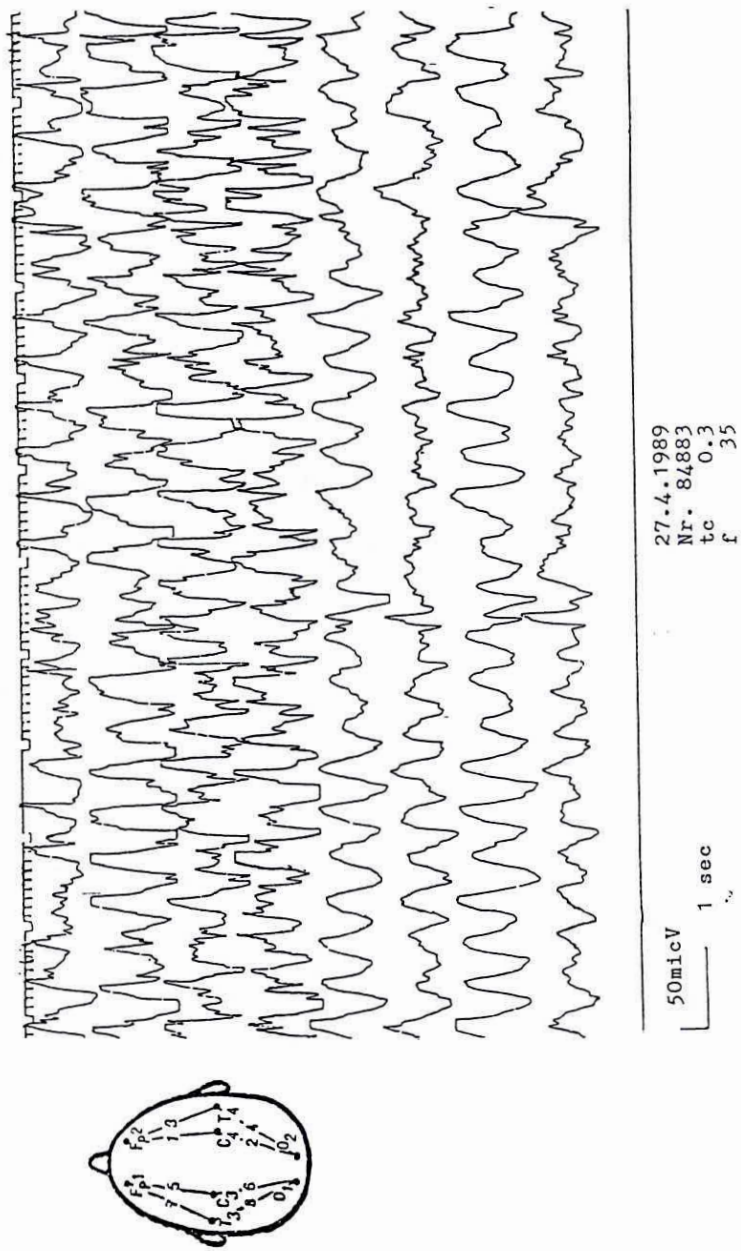

Figure 2 Electroencephalogram 3 h after the intoxication showing a diffuse slowing with constant right hemispheric spike and wave pattern

After 5 days the patient's neurological condition had improved gradually to the status before the intoxication.

An electroencephalogram (EEG) examination 3 h after the intoxication showed diffuse slowing with constant right hemispheric spike and wave pattern (Figure 2). Focal seizures with secondary generalization occurred 6 h after the refilling procedure, and were successfully treated with diazepam, phenytoin and clonazepam[5,6]. However, 24 h after the poisoning, EEG recordings still revealed diffuse slowing and right hemispheric epileptic activity. After 5 days the patient's EEG had largely returned to that recorded prior to the intoxication, showing a moderately abnormal pattern with reactivity to external stimuli, and without epileptic activities.

Electrophysiological findings showed no additional changes of acoustic and median nerve somatosensory-evoked potentials after recovery. Motor-evoked potentials showed a complete loss of compound muscle action potentials after transcranial electrical stimulation initially, and a gradual reappearance of amplitudes and improvement of prolonged latencies simultaneously, in accordance with the clinical progress. In contrast, cervical stimulation remained largely unaffected.

Summarizing our results, physostigmine proved to be inefficient in reversing the symptoms of severe intrathecal baclofen overdose caused by a bolus of 10 mg, and might jeopardize intensive care efforts due to its side-effects such as vomiting, bradycardia or hypotension. We believe that, in cases of intoxication, replacement of cerebrospinal fluid by Ringer's solution should be performed as soon as possible to reduce further baclofen diffusion into the tissue. Anticonvulsant prophylaxis should be considered in susceptible patients. However, if intensive care support is provided, it seems that even the highest overdoses of intrathecal baclofen can be survived without remaining neurological deficit, as has been the case with our patient.

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