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Acute overdose of intrathecal baclofen

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Sirs: There have been few reports of accidental overdose of intrathecal baclofen used for the treatment of spinal spasticity [1–3]. We report the unplanned infusion of 18 ml baclofen (500 μg/ml) by a programmable pump without a programming error being made.

A 44-year-old women with a 7-year history of multiple sclerosis had developed spasticity in her legs. Although she took 24 mg tizanidine, the muscle tone increased to grade 4 on the Ashworth scale [4] in her left leg and grade 2 in her right leg. She could still walk with crutches. A trial with an intrathecal baclofen bolus of 50 μg improved her ambulatory capabilities. For therapy with intrathecal baclofen a programmable pump (Medtronic Synchromed 8611H) was implanted. The pump, which had been programmed in the stop mode, was filled during surgery. Prior to implantation the pump was warmed up in a warmer, the reservoir was drained and then filled with 18 ml baclofen (500 μg/ml) without using a three-way stopcock. During usual implantations a stopcock was used or the syringe changed twice first during the draining and then during the filling procedure; and only a volume of 12 ml was used. On this occasion, a new surgery nurse was carrying out the procedure and the surgeon did not notice the mistake. One day after surgery the pump was started by programming a bolus of 0.2 ml to fill the catheter. Twenty minutes later the patient developed severe extensor spasms with elevated muscle tone of grade 5 (Ashworth scale) in both legs and grade 4 in the arms for a period of approximately 20 min. Sixty minutes after the bolus the patient became disoriented in time but not in place, was somnolent, but could still be woken. She could not move her legs but could squeeze the investigator's hand with markedly reduced strength. The muscle tone had become flaccid (grade 1) in the legs and arms. Breathing was slow and weak but complete depression of the respiratory drive did not occur. The pupillary reflex was sluggish, there was a bradycardia of 48 beats/min and the Glasgow Coma Scale score was 13. The patient was transferred to an intensive care unit for observation and received oxygen-enriched air for breathing. No other supportive measures had to be carried out. Seven hours after the bolus the patient was awake again, oriented and progressively regained strength in her extremities. When the patient was back from the intensive care unit 24 h after programming the bolus of 0.2 ml the pump was emptied, revealing a rest volume of 0.5 ml. Thus a volume of 17.5 ml containing 8700 μg baclofen must have been infused in a short time period. The reservoir was drained only 24 h later because the pump was programmed in the stop mode and the physician was not aware of the possibility of this type of malfunction. After this complication the pump was tested for several days with 0.9% NaCl-saline solution and functioned normally. Therapy with intrathecal baclofen infusion was started and was effective at a dose of 50 μg/day.

There have been few case reports of such high overdoses of intrathecal baclofen as in our case [2]. We use a programmable pump without a side port to prevent unplanned injection into the side port. Thus we were astonished by the possibility that 18 ml baclofen could accidentally be infused directly into the cerebrospinal fluid at once. The most likely cause of this sudden emptying of the pump is an influx of air during the filling procedure, which resulted in increased pressure in the reservoir after 18 ml baclofen solution had been injected into the pump's reservoir. As soon as the stop mode of the pump was changed, the increased pressure inside the pump's reservoir forced the reservoir's content past the roller mechanism of the pump into the intrathecal space. The exact time during which almost the whole reservoir's content was infused cannot be given, but because the half-life of baclofen in the spinal fluid is 2–5 h [5] and because symptoms of the overdose such as somnolence subsided 7 h after programming the bolus, the time during which most of the baclofen was infused was likely to have been within the first 2–5 h or less.

A reason for the initial increase of muscle tone with extensor spasms before the tone became flaccid could be that the fast infusion at high pressure led to overpressure within the cerebrospinal fluid system, causing compression symptoms. Another possibility is that baclofen depresses inhibitory systems prior to excitatory systems either at the spinal or supraspinal level. The brain stem seems more likely to be the site at which baclofen blocked inhibitory neural systems, because the clinical picture with extensor spasms resembled the state of decerebrate rigidity. An effect of baclofen on supraspinal centres is possible, because of the high dose and high volume of baclofen being suddenly infused. The reason why similar events with intrathecal baclofen bolus overdose did not show an initial increase of the muscle tone in extensors may be that the other patients had brain-stem le-

sions [2] or more severe spinal cord lesions, which also interrupted connections between the brain stem and the spinal cord neurons. In our patient there must have been some influence of supraspinal centres upon spinal cord neurons, because the patient could still walk.

The use of a three-way stopcock during emptying and refilling is mandatory in the type of pump described. For safety reasons this pump type should be filled by the surgeon himself or under his supervision during surgery or by the attending physician after surgery. Further, we would advise an observation period of at least 1 h after a baclofen bolus or filling of a pump to reduce the risk of missing an acute overdose.

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Cheiro-oral syndrome due to severe stenosis of the middle cerebral artery

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Sirs: The cheiro-oral syndrome (COS), a pure sensory disorder restricted to the corner of the mouth and the hand on the same side, has been attributed exclusively to lesions of the central somatosensory pathways [4, 9, 10, 15] visualized on imaging studies [7] or at autopsy [14]. We describe a patient with relapsing-remitting COS due to high-grade stenosis of the contralateral middle cerebral artery (MCA) and without any other abnormality of the arterial system.

A 57-year-old woman was admitted to hospital with an 1-year history of repeated paraesthesias at the right corner of the mouth and the ulnar site of the ipsilateral hand. During the 2 months before admission, the frequency of attacks increased from once monthly to once weekly. She had moderate arterial hypertension, which was well controlled with an angiotensin-converting enzyme inhibitor. There was no history of smoking, hyperlipidaemia, diabetes mellitus or any other cardiovascular disease.

Neurological examination disclosed only a mild hypaesthetic area at the right corner of the mouth and in the right hand, while general examination was normal. After exclusion of intracranial bleeding by computed tomography of the brain, intravenous heparin was administered with a target partial thromboplastin time of 60–80 s. Four hours after initiation of anticoagulation, the sensory symptoms disappeared. Examination of the basal intracranial arteries by means of transcranial Doppler sonography (TCD) revealed an extreme increase in blood flow velocity in the left MCA (mean flow about 245 cm/s) together with low-frequency components due to vessel wall covibrations. The diagnosis of a severe left-sided MCA stenosis was made and later confirmed by magnetic resonance angiography and intra-arterial digital subtraction angiography (Fig. 1). High-resolution magnetic resonance imaging of the brain 6 days after admission, including contrast-enhanced scans, did not disclose any pathological findings. Electrocardiogram, transthoracic echocardiography and coagulation tests were normal. Oral anticoagulation with phenprocoumon (Marcumar) was initiated 8 days after admission, and heparin was discontinued when the international normalized ratio reached target values (2.5–4.0).

Recent studies have suggested that TCD monitoring for microembolic signals (MES) provides information on the anticoagulation efficacy [5, 13] and is potentially of prognostic significance in patients with extracranial occlusive disease [12]. In our case, TCD monitoring for MES was performed on admis-

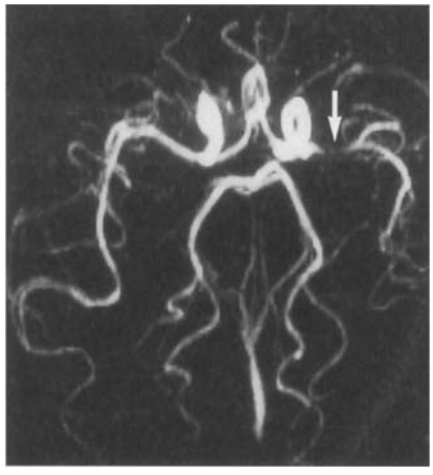

Fig. 1 Magnetic resonance angiography of the basal brain-supplying arteries showed > 70% narrowing (→) of the proximal left middle cerebral artery (MCA). Note that all basal arteries appear symmetrical, thus excluding an artificial loss of MCA flow signal due to erroneous plane section