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BRIEF COMMUNICATION

Early intraventricular baclofen therapy (IVB) for children with dystonic and dysautonomic storm

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Abstract

Introduction Intrathecal baclofen (ITB) is an effective treatment for managing primary and secondary dystonia. Intraventricular baclofen (IVB) was first developed to allow treating patients in which the use of ITB was difficult due to anatomic anomalies. After that, several studies indicate that intraventricular administration of baclofen, is more effective than ITB in refractory dystonia.

Clinical material We report three cases of children with acute dystonic and dysautonomic storm, treated with IVB. The clinical outcome was satisfactory. The response to the treatment continued after the pump disconnection, suggesting that in this kind of cerebral dysregulations, short-term IVB is an effective treatment.

Conclusion Early treatment with IVB may be an effective option in patients with post-anoxic dysautonomic and dystonic storm.

Keywords Intraventricular baclofen therapy · Dystonia · Baclofen

Introduction

Intrathecal baclofen (ITB) (administration of baclofen in the spinal subarachnoid space), is the standard treatment of various forms of spasticity, and is also used in case of dystonia. However, according to several studies, intraventricular administration of baclofen (IVB), is more effective than ITB in refractory dystonia [1, 2, 5, 6, 11]. We report our experience, using early IVB in three children with severe anoxic brain injury, presenting in a dystonic and dysautonomic storm setting.

Case reports

Case 1

The first patient was a 14-year-old girl, affected by a post-anoxic perinatal encephalopathy causing dystonia and kidney failure, treated with peritoneal dialysis. She presented in emergency department, with acute worsening of her dystonic status and with sympathetic storm. Her dystonic movements were graded as 32, according to the Barry–Albright Dystonia (BAD) scale. This scale assesses dystonia in eight body regions, and severity is scored from 0 to 4: 0 indicates no dystonia and 4 represents dystonia severe enough to interfere with function more than 50% of the time [4].

She was first treated, in intensive care, with pharmacological therapy using tetrabenazine, trazodone, clonazepam, and oral baclofen, but no results were observed. A screening test with ITB was done (100 mcg, through lumbar puncture), but there was not clinical improvement. IVB was then scheduled. Under general anesthesia, through a coronal, right paramedian burr hole, a ventricular catheter was positioned in the third ventricle. Neuronavigation and endoscopic guidance were used. The catheter was then tunneled to the abdomen and connected to a pump for drug delivery (Synchromed II, Medtronic Inc., Minneapolis, MN-55440, USA), implanted in a subcutaneous pocket (Fig. 1). The pump was filled with baclofen (Lioresal Intratec, 10 mg/5 ml, Novartis-Farma-Spa, Va- Italy). Initially dose was 200 mcg daily. The dose was increased by 20% every other day. Autonomic instabilities and dystonic crisis disappeared with the IVB dosage of 500 mcg daily. No problems occurred in the first year. One year later, dystonic crisis recurred and a CT-scan showed

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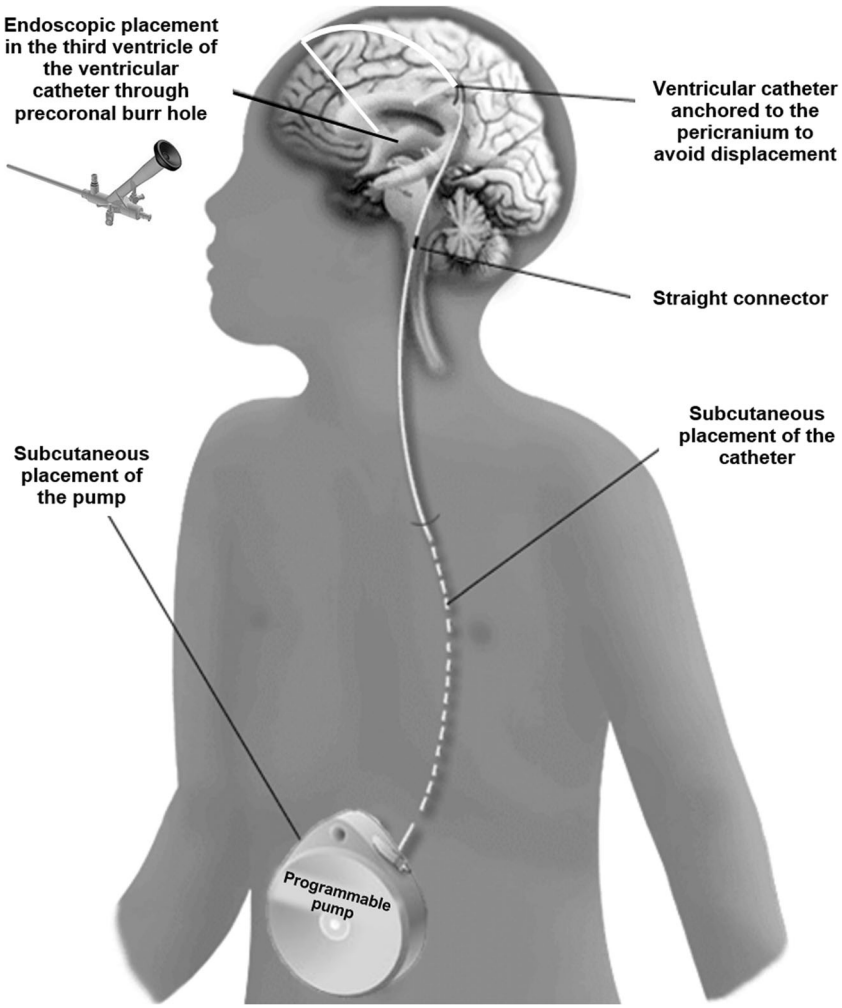

Fig. 1 Scheme of the hardware for intraventricular baclofen therapy

migration of the catheter. The catheter was revised and repositioned. One year later, the catheter slipped again out from the ventricle, but dystonia did not recur. The implant was entirely removed.

Case 2

The second patient was a 7-year-old girl who presented in our emergency department after drowning. Her clinical conditions were critical, and the sustained anoxia caused the development of severe generalized dystonic and spastic movements and dysautonomia. Preoperative BAD Scale score was 32. She was initially treated with pharmacological therapy (tetrabenazine, trazodone, clonazepam, oral Baclofen), then with ITB, for 2 months, reaching a daily dose of 2000 mcg, without significant improvement. With the substitution of ITB with IVB, both dystonia and autonomic instabilities significantly decreased at the daily dosage of 1000 mcg. No catheter infection or malfunction occurred. No baclofen adverse side effect was detected. Two years later, the baclofen dosage was gradually reduced, with no increasing of dystonia and spasticity; the system was finally removed.

Case 3

The third patient was a 7-year-old boy affected by psychomotor impairment and myopathy. He was admitted in our emergency department in a shock status with dysautonomic disorders, severe, generalized dystonic movements, acute left leg ischemia, and a big thrombotic formation in the left cardiac ventricle. The MRI showed the presence of an anoxic brain damage (Fig. 2a), related to the embolic phenomena, which explained the worsening of the neurological status and appearance of dystonic and sympathetic storm. Preoperative BAD Scale score was 32 (Fig. 2b). The dystonic storm was initially treated with pharmacological therapy, without improvements. IVB was performed (Fig. 2c–d). Autonomic instabilities completely disappeared at day 16 (at daily dose of 520 mcg). The dystonic movements disappeared with the IVB daily dosage of 1800 mcg. No complications occurred.

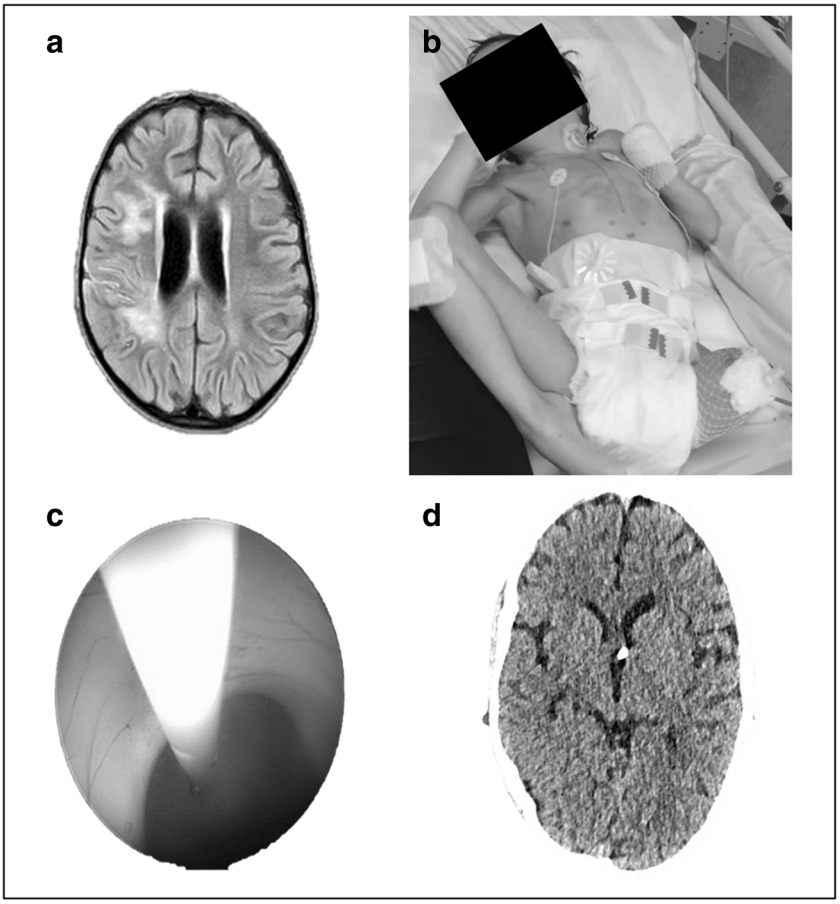

Fig. 2 Case report no. 3. **a** Preoperative MRI flair sequences showing periventricular post-anossic damage. **b** Preoperative status. **c** Endoscopic placement of the tip of the ventricular catheter in the third ventricle. **d** Postoperative CT scan showing the correct placement of the catheter

Discussion

The rationale in using IVB, instead of ITB in dystonia is justified by a different site of baclofen activity in dystonia and spasticity. In spasticity, the site of baclofen activity is located at the spinal cord level; in dystonia, it is supraspinal [2]: baclofen might act through inhibition of excessively stimulated supplementary motor cortex and premotor over the cerebral convexities [3, 7]. Administering baclofen directly in the ventricular system promotes appropriate drug concentration in the target site. Placing the catheter in the third ventricle increases the likelihood that baclofen flows, together with cerebrospinal fluid (CSF), via the aqueduct and fourth ventricle over the cerebral convexities, decreasing the possibility that it might stagnate in a lateral ventricle. In fact, the majority of CSF (and therefore of baclofen) exiting the fourth ventricle migrates upward over the cerebral convexities and the minority downward in the spinal subarachnoid space [2].

Autonomic dysfunctions, such as hypertension, tachycardia, bronchial hypersecretion, hyperthermia, hyperhidrosis, and hypersalivation, often occur after brain or spinal cord injury; these complications are conventionally treated with antiadrenergics, analgesics, and sedatives, that lead to a prolongation of respiratory support and delay in transfer to rehabilitation center [5]. Several authors reported satisfactory results with ITB in patients with spasticity and dysautonomic disorders, that developed after acquired brain injury. These disorders may be considered as a consequence of cerebral hyperactivation due to the loss of control mechanisms. Baclofen, a GABA-B receptor agonist, may act reducing and modulating this cerebral hyperactivity [9, 10].

We used IVB for early treatment of dystonic and dysautonomic storm, both related to post-anoxic brain damages. Patients 2 and 3 were not affected by dystonia before the injury, and the dystonic movements developed together with the dysautonomic disorders. Patient 1 was already affected by severe dystonia; but it sharply worsened. Our results agree that IVB is a valid treatment in patients with dystonic storm, and that IVB is efficient also in case of lack of response to ITB. The three patients had a long-term response to the treatment. No baclofen adverse side effects occurred, confirming that IVB is a safe treatment, despite the high doses required.

In patient 1, there was a catheter migration; in this patient, the thin spinal catheter (4.2 Fr) provided together with the ITB-kit (Indura-catheter, Medtronic Inc), was used. Because of the catheter migration, in the following patients, a thicker (7.5 Fr) “Standard Ventricular Catheter” (Medtronic Inc), about 15 cm of length, was used and connected to the distal

catheter of the pump, in the retroauricular region with a straight connector (Fig. 1). No migration occurred.

Deep brain stimulation (DBS) may be an alternative to IVB for status dystonicus. Response to DBS can be variable and difficult to predict [8]. Children with inherited dystonia without nervous system pathology seem to respond better to DBS than those with other forms of dystonia, such as post-anossic cases. Only 18 patients with status dystonicus treated with DBS were reported in literature [8]: DBS was effective in most patients but with higher incidence of complications [11, 12].

In conclusion, early use of IVB is an effective treatment to control both dystonic disorders and dysautonomia. In the first and in the second patient, the effect obtained continued even after the pump was disconnected.

Compliance with ethical standards

Conflict of interest The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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