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CASE REPORT / ПРИКАЗ БОЛЕСНИКА

Intrathecal baclofen therapy and COVID-19 infection – report of three cases

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SUMMARY

Introduction Patients with severe spasticity are effectively treated with intrathecal baclofen therapy (ITB), but because of their invalidity, in case of infection, prognosis is poor.

Case outline We present three cases (two men and one woman) of patients treated with baclofen intrathecal therapy due to spasticity of all four extremities who underwent SARS-CoV2 virus infection. Two of them have multiple sclerosis, and one has trauma of the cervical segment of the spinal cord. In all three patients, the clinical presentation of COVID-19 infection occurred within six months of implantation of the pump for ITB. They were successfully treated in hospital with same dose of the drug and without exacerbation of neurological status. Barthel index (BI) and modified Rankin score were same before and after COVID-19 infection. In two cases BI was 20, and in one 69; and modified Rankin score (mRS) was 3 in one case, and 5 in two cases.

Conclusion Patients with severe spasticity who require intrathecal baclofen therapy can be safely treated regardless of the pandemic.

Keywords: intrathecal therapy; baclofen; spasticity; COVID-19

INTRODUCTION

Spasticity is a consequential symptom of several neurologic conditions that result in central paresis. It has been described in stroke, multiple sclerosis (MS), brain trauma, and in children with cerebral palsy and can heavily affect quality of patients' life [1]. Treatment of spasticity is based on medication and rehabilitation in order to improve their daily activities. They are usually treated with oral administration of baclofen (GABA-B agonist), tizanidine (alpha-2 adrenergic agonist) or tolperisone (sodium and calcium channel blocker at the level of brain stem) [2, 3]. When oral therapy is insufficient or the patient does not tolerate the drug side effects, intrathecal therapy may be considered. If testing for intrathecal baclofen therapy (ITB) is successful, these patients can be effectively treated [4].

Recent Corona virus pandemic caused major turbulence in the majority of services, including health care. Patients with ITB are prone to poor prognosis in case of infection [5].

We present three cases of patients treated with ITB due to spasticity of all four extremities who have been infected with COVID-19. Degree of neurological disability was measured with several scales: spasticity by the Ashworth scale, performance in activities of daily living by the Modified Barthel Index (BI), level of pain by the visual analogue scale (VAS) and level of function by the Modified Rankin scale (mRS) [6, 7, 8].

CASE REPORT

Case 1

A 60-year-old male patient, previously diagnosed with C7-Th1 discus hernia, was admitted to our hospital due to the spinal cord trauma at the C7-Th1 level in November 2019. Lower extremity plegia and high-grade palsy of the upper extremities on both sides were stated during examination. Four days after the trauma a massive pulmonary embolism occurred, limiting possible therapy for next two months. Also, spastic type of paralysis (Ashworth grade III) has developed. Patient's therapy was continued on the physical medicine ward (BI 2, mRS 5). Since maximum dosage of tizanidine therapy gave no results considering spasmolysis (Ashworth grade III, pain level 9 on VAS scale), it was decided that the patient should be tested for intrathecal Baclofen application (positive test on 100 μg bolus for four hours) and Synchromed II pump (Medtronic Inc., Dublin, Ireland) was implanted in September 2020. After the operation, tizanidine therapy was canceled, and daily dosage of Baclofen was gradually risen during physical therapy to 800 μg in 24-hour intrathecal continuous infusion. Significant reduction of pain (VAS 3) and extremities spasticity (more notably on upper extremities) were achieved, BI was 12 and mRS 5.

Two months after the implantation of ITB system, nasopharyngeal swab was taken and

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PCR test on SARS-CoV-2 was performed, due to high fever (39°C), drop of lymphocytes in leukocytic formula, as well as an occurrence of breathing difficulties. The test came back positive. Chest radiography showed transparency reduction ("ground glass") on both sides. COVID-19 therapy protocol gave subjective improvement in the first days, but on the 18th day of COVID infection, worsening of the patient state was observed. His oxygen saturation has decreased, followed by anuria and deterioration in consciousness which progressed to somnolence. In the following period, lymphocytes continued to drop and there was sudden rise of all inflammatory factors, so the patient was admitted to the Intensive Care Unit (ICU), where he was intubated and started on mechanical ventilation. During his stay at the ICU, spasticity worsened to preoperative level.

One week later, after stabilization of patient's state of consciousness and oxygen saturation recovery to 96%, he was transferred back to the neurosurgical ward and his physical therapy was resumed. One month after the SARS-CoV-2 infection he was vaccinated with the first dose of vaccine. Patient was active in a wheelchair (upper extremities palsy 4/5, lower extremities spastic plegia, on all extremities Ashworth grade II, BI 19, mRS 5) and because of sphincter disfunction, permanent urinary catheter was applied. Baclofen therapy was not discontinued and it was resumed in unchanged dosage (800 μg in 24-hour infusion).

Case 2

Our second patient was 49-year-old female, diagnosed with MS. Her first symptoms occurred in 2010 as sense of tingling in her feet which progressed to lower legs and later occurred in her hands. Her walk was unstable with maximal distance estimated 1 km. Her illness was primarily progressive and she began to use a walking device in 2017. By 2018 she was coerced to use the wheelchair and her condition worsened with leg stiffness and hands tremor. During 2020, she had occasional episodes of generalized fatigue, that could last 12 hours during the day and resolve spontaneously.

In neurological status, she had severe spastic quadriparesis, which was more prominent in lower extremities (Ashworth grade III+ on lower and grade III on upper extremities, BI 12, mRS 5). Because of painful spasticity (VAS 5), she was tested for intrathecal baclofen application which reduced spasticity and pain after 100 μg bolus for 3.5-hour period.

The patient was operated on in May 2021, when Synchromed II pump (Medtronic PLT) was implanted and programmed for 200 μg/24-hour administration. Dose was gradually increased to 320 μg/24-hour during her hospitalization at the clinic for neurosurgery, and in the end reached 500 μg/24-hour during her stay at the clinic for physical rehabilitation (BI 20, mRS 5). During this period, she was not vaccinated against SARS-CoV-2.

Four months after ITB implantation, her body temperature rose to 38°C, oxygen saturation was 75% and interstitial pneumonia pattern was observed on radiography. She was hospitalized and treated according to National standards for COVID-19 infection. Two weeks later, she was discharged in good general and unchanged neurological condition (BI 20, mRS 5). Her daily Baclofen dosage remained the same during her hospitalization. There was no discontinued of ITB therapy during infection.

Case 3

The third patient was 42-year-old man with MS. He was treated since 2009 for primarily progressive form of the disease, and by 2020 he started to use wheelchair (BI 51, mRS4). Because of prominent spasticity (Ashworth grade III) and oral spasmolytic therapy intolerance, he was tested for ITB positive in April 2021 after 50 μg of baclofen bolus. Synchromed II pump (Medtronic PLT) was implanted in May 2021 and dosage was set at 100 μg/24 hrs. After the operation spasticity was reduced and initial rehabilitation treatment was prescribed (BI 69, mRS 3). He was vaccinated with two doses of SARS-CoV-2 vaccine.

Four months after, he was hospitalized in COVID hospital due to confirmed infection (body temperature 39°C, positive PCR). During this time oxygen saturation did not drop below 95% and chest radiography did not show any signs of inflammation. After one week he was discharged from the hospital for house care.

After the end of quarantine period, he was admitted to the hospital for regular follow-up. His neurological status remained unchanged (severe spastic palsy of the lower extremities – Ashworth grade II, BI 69, mRS 3), so his daily dosage was same, without any discontinued during infection.

Written consent for publication of this article has been obtained by the patients.

DISCUSSION

Intrathecal drug delivery systems are widely used as an option for treatment of severe spasticity and intractable pain in last four decades [9, 10, 11]. It is the most effective treatment in situation when conservative methods have proved insufficient or intolerable [12, 13]. This treatment is expensive at first, but two years after implantation the costs of the device equate with alternative therapy [14–17].

As with any therapeutic modality, complications are possible. ITB is often placed in patients who are already in medically difficult state and complex to treat and as such, have higher risk of illness at baseline. Therefore, these devices require close supervision and time-sensitive management by a specially trained medical professionals [18]. Puck-Faes et al. [11] has found that patients with a spinal origin of spasticity, lower mRS and higher BI have a higher risk to sustain complications. Complications can be divided in four categories: drug-related, pump-related, catheter-related, and infections [9, 19]. Infections, as complication, have been reported in 5–26% of cases and were more common among traumatic spinal cord injuries [9]. They may appear at any time, after implantation or after revision [11, 20]. Long-term aftercare with baclofen pump refill was proved to be safe, with an infection rate of 0.6 % per puncture for each refill [4]. In our experience with ITB,

we have not observed any infection related to surgery or refill of the pump to date. Also, no drug, pump or catheter related complication were detected.

COVID-19 outbreak led to significant changes in almost all aspects of everyday life, affecting healthcare practice as well. It poses a great risk for patients on ITB due to increased occurrence of infection, as well as the possibility of missing the pump supplementation with the drug. In some cases, this can be life-threatening [21].

Two out of the three presented patients had severe disability with mRS score of 5 and with BI less than 20, while the third patient had moderate disability with mRS score 3 and BI 69, which is in accordance with experience of Puck-Faes et al. [11]. The patient with spinal trauma had the most severe disability among the presented cases. Presented patients did not had ITB system-related infection, but like all those who have suffered a severe disability, there are higher risks.

Based on our first case in November 2020, we have decided that any patient with ITB and COVID-19 infection, should be treated in hospital conditions in order to avoid complications and aggravation of their already difficult state. Since the effect of spasmolytic therapy was satisfactory, the daily dose of baclofen was not changed. Our opinion is that COVID-19 infection does not require a change in ITB therapy protocol, as well as the refill of the ITB system. It could not be remotely managed according to telemedicine services [22].

During COVID-19 pandemic, special attention should be paid to patients in more severe condition, referring to their mobility. The availability of health service is necessary, both in order to supplement the system and, given their altered immunity, to treat them adequately in case of infections. Patients with severe spasticity who require ITB can be safely treated regardless of the pandemic, as it is a safe method that significantly reduces spasticity and alleviates the degree of disability.

Conflict of interest: None declared.

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Интратекална терапија баклофеном и инфекција ковидом 19 – приказ три болесника

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САЖЕТАК

Увод Болесници са тешким спастицитетом ефикасно се лече интратекалном терапијом баклофеном. Због њихове инвалидности, у случају инфекције прогноза је лоша.

Приказ болесника Представљамо три болесника (два мушкарца и једну жену) лечена интратекалном терапијом баклофеном због израженог спастицитета сва четири екстремитета који су прележали инфекцију вирусом *SARS-CoV2*. Два болесника имају мултиплу склерозу, а један трауму цервикалног сегмента кичмене мождине. Сва три болесника развила су клиничку слику инфекције ковидом 19 унутар шест месеци од уградње пумпе за интратекалну терапију баклофеном. Лечени су у болничким условима са непромењеном дозом лека, без погоршања неуролошког статуса. Бартелов индекс и модификовани Ранкин скор били су исти пре и после инфекције ковидом 19. У два случаја Бартелов индекс је био 20, а у једном 69, а модификовани Ранкин скор био је 3 у једном случају и 5 у два случаја.

Закључак Болесници са тешким степеном спастицитета, код којих је неопходна интратекална терапија баклофеном, могу се безбедно лечити без обзира на пандемију ковида 19.

Кључне речи: интратекална терапија; баклофен; спастицитет; ковид 19