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Short communication

Constitution, storage and delivery of risdiplam is easy to manage by the hospital pharmacist - single case study

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Introduction

Spinal muscular atrophy (SMA) is a rare, progressive, recessive neuromuscular disease that is caused by deletions or loss-of-function mutations in the survival of motor neuron 1 gene (SMN1), which result in insufficient levels of survival of motor neuron (SMN) protein (Lefebvre et al., 1995; Mercuri et al., 2012). SMN protein is found throughout the body and increasing evidence suggests SMA is a multi-system disorder and the loss of SMN protein may affect many tissues and cells, which can stop the body from functioning.

SMA is the most common genetic cause of infant mortality and one of the most common rare diseases, affecting approximately one in 10,000 babies. SMA leads to the progressive loss of nerve cells in the spinal cord that control muscle movement.

SMA is categorized in 5 types (ranging from 0 to 4, with lower numbers indicating greater severity), which are defined according to the maximum motor milestone attained and the age of symptom onset (Mercuri et al., 2012; Yeo and Darras, 2020). SMA Type 0 is very rare and very severe. Symptoms begin prior to birth and are seen as decreased fetal movement in the weeks prior to delivery. SMA Type 1 is the most common (60%) and severe form, usually diagnosed during an infant's first 6 months. Type 2 is usually diagnosed after 6 months of age, but before 2 years of age. SMA Type 3 is usually diagnosed after 18 months of age, but before 3 years of age. SMA Type 4 is very rare, less than 1% of all diagnosed cases. It usually surfaces in adulthood.

The Macedonian Agency for Medicines and Medical Equipment (MALMED) in 2021 has approved two therapies for SMA: nusinersen, and risdiplam. Nusinersen is an intrathecally administered SMN2-targeting antisense oligonucleotide therapy for adults and children (MALMED, 2021). Risdiplam is a systematically distributed small molecule, administered orally in liquid form, that modifies SMN2 pre–messenger RNA splicing. It has been approved for the treatment of 5q SMA in patients 2 months of age and older, with a clinical diagnosis of SMA Type 1, Type 2 or Type 3 or with one to four SMN2 copies (MALMED, 2021). Each of these two medicines has led to improvements in survival and motor function in patients with SMA.

Aim and objective

The objective of our study was to assess and evaluate the burden of workload that causes, the whole process of management of risdiplam prior oral administration, to the hospital pharmacist in our center.

Materials and methods

We have done a retrospective analysis using the data from the patient's history and records from the two SMA centers: PHI University Clinic of pediatric diseases and the PHI University clinic of neurology – Skopje.

Results and discussion

Our analysis shown that there are 21 people living with genetically 5q confirmed diagnosis of SMA. Patients are of different ages and types of SMA. According to the age, 55% of patients (n=11) are children, while the remaining 45% (n=9) of patients are over 18 years of age. Currently, 8 patients are on treatment with nusinersen and 11 patients are on treatment with risdiplam in both centers, and one SMA Type 4 patient is not eligible for treatment.

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Starting from November 24, 2020 until May 2022, a neurologist from the University clinic of neurology prescribed and initiated treatment with risdiplam in 9 SMA patients with Type 2 (n=3) and Type 3 (n=6).

Risdiplam comes in our Clinical Pharmacy in a carton box containing 2 reusable oral syringes from 6 mL and 2 from 12 ml, one ENFit® Press-in bottle adapter and a bottle of 60 mg powder for oral solution (including a cap). Unconstituted powder of risdiplam is stored at room temperature in the original amber glass bottle protected from light. Prior to dispensing to the patient/caregiver, a clinical pharmacist constitutes the oral solution. Preparation of the oral solution involves a straightforward, 6-step process.[5] When constituted; the volume of the oral solution is 80 mL. We are using the following required materials and equipment for preparation: risdiplam powder for oral solution (60 mg), 79 ml of purified water or water for injection, a suitable measuring cylinder and Press-in bottle adapter. The constituted oral solution of risdiplam is kept in the original amber bottle protected from light. It is stored in a refrigerator at a temperature of 2°C to 8°C at all times for maximum 64 days after constitution in an upright position with the cap tightly closed. Based on the latest unpublished stability studies, the risdiplam oral solution can be left at room temperature (up to 40°C) from 24 hours to 5 days. The 5 days are cumulative over the life of the bottle and include any excursions happening after constitution (i.e. during transportation of the constituted solution, excursions at the patient's house etc.). These conditions had no impact on the stability of risdiplam. Prior dispensing to the patient/caregiver, bottles of risdiplam are placed in a validated and certified cooling bag (Initial bag 4L – KITCIS04NP12, Sofrigram®) for transportation to the patient's home by the patient him/herself/caregiver. So far, we constituted more than 200 bottles of risdiplam and had not experienced any issues within the whole process from receiving, preparation, constitution, storing and delivery to the patients/caregivers.

Conclusion

Additionally to the efficacy and safety of risdiplam seen in more than 5.000 SMA patients worldwide, we concluded that the whole process of constitution, storage and delivery is easy to manage and does not create a huge additional burden on the workload of the hospital pharmacist in our center.

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