NEWBORN SCREENING AND EARLY NUSINERSEN TREATMENT IN SPINAL MUSCULAR ATROPHY: A COMPARATIVE STUDY

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INTRODUCTION

Spinal Muscular Atrophy (SMA) is a progressive neuromuscular disease characterized by irreversible loss of motor neurons in the cranial nerve motor nuclei and anterior horn of the spinal cord, leading to muscle weakness and atrophy. SMA is one of the most common genetic causes of infant mortality worldwide. Globally, it is estimated to occur in approximately **1-3 out of every 10,000 live births.** It is estimated that there are between 130-180 new cases annually. According to data from the Ministry of Health, approximately 3000 SMA patients are being followed in our country . Newborn screening (NBS) is started on 9 May 2022 and is continuing successfully in Türkiye.

In Type 1 SMA, the expected lifespan in the natural course of the disease is only a few years, but new therapeutic approaches in treatment have changed the prognosis of this usually fatal disease. Data from many studies indicate that initiating treatment in Type 1 SMA patients before or shortly after symptom onset is most effective. Molecules such as nusinersen, risdiplam, and onasemnogene abeparvovec-xioi have been shown to increase survival, motor strength, endurance, and growth development in patients, potentially allowing many patients to lead a nearly normal life with appropriate treatment. Beside survival and observational outcome there are some clinical and laboratory parameters disease course and follow up.

-**Motor functions:** The evaluation of motor functions are assessed using The Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND) scoring system. The test consists of 16 sections, each parameter is scored between 0 and 4, with 0 indicating no response/movement ability and 4 indicating a 'complete response' , the highest score that can be obtained is 64.

-Electrophysiology: Electrophysiological studies in SMA have reported decreased motor conduction velocities (MCVs) and lower compound muscle action potential (CMAP) amplitudes, which are attributed to significant loss of large myelinated fibers in some Type 1 SMA patients.

OBJECTIVES

Assessing the demographic characteristics, clinical, and laboratory data of SMA 1 patients diagnosed and initiated on the first dose of Nusinersen treatment within the first 90 days

Comparing the clinical and laboratory data of patients diagnosed and initiated on treatment through **the newborn screening (NBS) program** with those who started **treatment within the first 90 days before screening era.**

MATERIALS AND METHODS

Two groups of SMA Type 1 Patients who completed at least 4 doses of nusinersen treatment included to this single center study. The data from medical records of patients were analyzed retrospectively.

Group 1 : NBS-diagnosed SMA patients

SMA patients that diagnosed via newborn screening program

Group 2 Early-treated SMA patients

Before NBS program, Nusinersen initiated before 90 days of age.

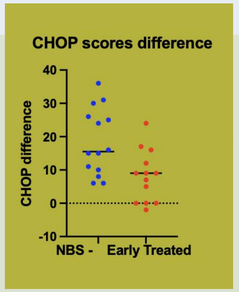
The study includes; calculation and comparison of Compound Muscle Action Potential (CMAP) values from pre-treatment and post-treatment electrodiagnostic data in the NBS group, comparison of CHOP scores between the two groups; and its statistical analysis using the SPSS program

RESULTS

The total of 33 patients (Nineteen NBS patients and fourteen early-treated SMA-1 patients) were included in this study.

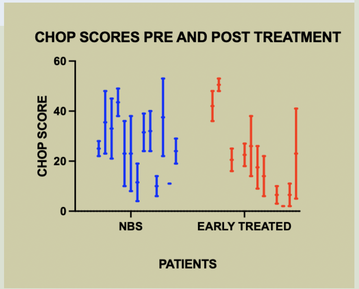
In the early treated group, all patients had an SMN-2 gene copy number of 2, while in the NBS group, one patient had 3 and one had 4 copies, with the remaining 17 patients (89.4%) having 2 copies.

In the NBS group, diagnosis and referral times means are **12.3 ± 9.9** and **20.2 ± 26.5** days, respectively. NBS patients started treatment at **28.9 ± 1.8** days, while early-treated patients started at **79.9 ± 4** days. . Five patients were excluded from NBS group exlclued for clinical and electophysiologic measurements because of treatment delays. (First treatment day mean of excluded group: **77.6 ± 19.1** days)



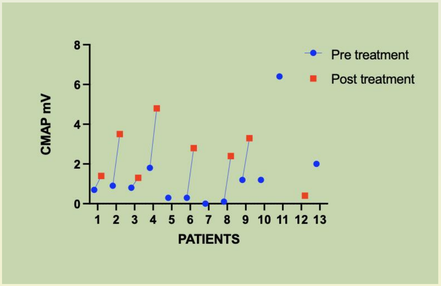
GRAPH 1 : CHOP score difference of patients

CHOP scores were compared for fourteen early-treated and NBS patients who received at least four doses. Both groups improved in CHOP scores at baseline and day 180, with no statistically significant between-group score differences (median increases of 15.5 and 9 points, respectively, p=0.09).



GRAPH 2 : Pre-treatment and Post-treatmentCHOP scores of groups

Pre treatment CMAP amplitudes significantly increased in NBS group from 0.83 ± 0.33 mV to 2.4 ± 1.5 mV after four doses of Nusinersen treatment. (n=7, p=0.0027)



GRAPH 3 : Pre-treatment and Post-treatment CMAP amplitudes of NBS patients

CONCLUSIONS

In conclusion, NBS provides earlier Nusinersen treatment and better outcome. Receiving nusinersen treatment, it has been reported that CMAP amplitudes in nerve conduction studies (NCS) increase over time compared to untreated patients, Our study's data also demonstrates strong consistency and alignment with the literature. Although differences in CHOP scores were not statistically significant but showed noticeable improvement between groups. In addition to clinical improvement, these data shows; the importance of **VERY** early diagnosis and treatment of SMA.

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