The effect of oral baclofen and botulinum toxin treatments in hemiplegic spasticity on the nociceptive flexor reflex: A randomized clinical trial

(NCT03860662)

Study Protocol and Statistical Analysis Plan

A total of 29 patients who developed spastic hemiplegia as a result of embolism or hemorrhage with Modified Ashworth Scale (MAS) phases of 2-4 and applied to Hatay Mustafa Kemal University, Faculty of Medicine, Physical Medicine and Rehabilitation polyclinic between the dates May 2018 – March 2019 were included in the study. Randomization was performed by generating random numbers as the Group 1 and Group 2. 15 patients were included in Group 1 to receive Botulinum toxin treatment, whereas 14 patients were included in Group 2 to receive Baclofen treatment.

Individuals who had received botulinum toxin injection treatment in the past 6 months, patients receiving oral antispastic treatment, individuals who have an allergy and hypersensitivity story related to the medication to be used, individuals who had diseases that might cause neuropathy and/or used medication and substances which might cause neuropathy in their medical history, individuals with hematoma, infections or skin lesions in the planned injection area, hemorrhage disorders, joint contracture and patients who were MAS grade were excluded from the study. Our study was regarded as positive and approved by decision 2018/159 of Hatay Mustafa Kemal University, Tayfur Ata Sökmen Faculty of Medicine, Clinical Researches Ethics Committee. Informed consent form was taken from all the participants of the study. The study was carried out in accordance with the Helsinki Declaration. The Clinical Trial number is NCT03860662.

The patients' gender, age, weight, height, cerebrovascular case etiology, symptom durations and hemiplegic sides were recorded. MAS was used to evaluate spasticity intensity. MAS grading is done as 1,1+,2,3,4 and it was graded successively as 1,2,3,4,5 t be able to do statistical analysis. The motor evaluation of the patients was performed using Brunnstrom motor staging (upper extremity, hand, lower extremity). A 10 cm. long Visual Analogue Scale (VAS) was used to evaluate the hemiplegic side pain of the patients. The daily life activities of the patients were evaluated with the Barthel index. The Barthel index consists of 10 questions and the highest total score that can be received is 100 (0-20 points: total dependency;

21-61 points: severe dependency; 62-90 points: moderate dependency; 91-99 points: slight dependency; 100 points: total independence). The nociceptive flexor reflex (NFR) threshold value measurement was performed with electromyography on the unaffected lower extremities of the patients. The electrical stimulations were given with a bipolar stimulator from the sural nerve, near side of the lateral malleolus. In order to achieve a threshold value, the electrical stimulation was started from 0mA and increased in intervals (4mA intervals) until a NFR response was achieved. After the initial NFR response was achieved, the stimulation intensity was decreased in 2mA intervals until the response disappeared. Then, the stimulation intensity was arranged with high and low stimulations of 1mA until a stabile NFR response was achieved. The stabile NFR threshold value achieved in this manner was recorded. The electrical stimulation intensity which made it possible for the NFR threshold response to be achieved was recorded as mA unit. Prior to the treatment and on the 6th week which was the end of treatment, MAS, Brunnstrom stages, VAS values, Barthel daily life activities index and electromyographic NFR thresholds of all patients were recorded.

The 15 patients in the first group were injected onabotulinumtoxin A under ultrasonography guidance in their upper and lower extremity muscles which were 2 and over according to MAS, in suitable dosages according to the pre-determined dosage diagram (total dosage 100-300 İU). The 14 patients in the second group were given 5 mg of oral baclofen twice daily as the initial dosage starting from the first day. This was increased 5mg every 5 to 7 days up to 80mg until the effective antispasticity dosage was achieved (total dosage 30-80 mg). The dosage was not increased anymore since the patients were not able to tolerate higher dosages. Both patient groups were applied a physical therapy and rehabilitation program together with antispastic treatment. In the rehabilitation procedure, positioning, joint range of motion and stretching exercises, strengthening exercises, balance and coordination, ambulation exercises, hot or cold compress, functional electrical stimulation treatments were applied to each patient for 60 minutes. The treatment program was applied by the same physiotherapist for 6 weeks, 5 times a week and once each day.

All obtained data were recorded with the Statistical Package Social Sciences (SPSS) version 21.0 statistical software. The control and analyses of the data were performed with the same software. In the statistical analyses, frequency (%) (median – minimum and maximum) was used for descriptive statistics. The mean and standard deviation values were expressed as (m±SD). The data obtained through the measurements were evaluated separately each group with ShapiroWilk test in terms of normal distribution. In the comparison of values

which did not display normal distribution, nonparametric tests were used. While Mann-Whitney U test was used in the comparison of the two groups, Wilcoxon Signed Ranks test was used within the same group prior to and after comparisons. In the statistical analyses, p values lower than 0,05 were accepted as significant.