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Single and 28-Day Repeated Intramuscular dose Toxicity Studies of Botulinum Toxin Type a in Rats

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Botulinum toxin type A was intramuscularly administered to Sprague-Dawley rats in both single and 28-day repeated dose toxicity studies. In the single dose toxicity study performed at 25, 50, 100, and 200 ng/kg, LD50 was estimated to be 70.71 ng/kg for males and 97.63 ng/kg for females. The major clinical signs observed were paralytic gait, decrease of locomotor activity, ananastasia, and death. The 28-day repeated dose toxicity study performed at dose levels of 1, 3, and 9 ng/kg/day showed an attenuation of body weight gain in a dose-dependent manner. This attenuation of body weight gain was considered due to the decrease of food and water consumption observed in the animals treated at 9 ng/kg/day and continued throughout a 4-week withdrawal period on completion of dosing. Paralytic gait was a common clinical sign observed in the animals treated at 3 ng/kg/day and muscle atrophy as well as paralytic gait were monitored at 9 ng/kg/day. Serum creatinine level in both males and females treated at 9 ng/kg/day was significantly lower than that of the vehicle-control animals. No changes attributable to the administration of the botulinum toxin were observed in organ weight, ophthalmologic and hematological examinations. Histopathological examination of femoral muscle, which was the test substance-application site, revealed an atrophy of skeletal muscle. It showed a decrease in myofibre diameter and an increase of myofibre nuclei and intermyofibre connective tissue. The NOAEL of botulinum toxin type A is 1 ng/kg for 28-day repeated intramuscular dose toxicity in rats.

Keyword : Botulinum Toxin, Acute toxicity, Repeated dose toxicity