



ANALYSIS OF TOTAL DOSAGES AND INTERVALS BETWEEN THE REPEATED ABOBOTULINUMTOXIN A INJECTIONS IN CHILDREN WITH SPASTIC CEREBRAL PALSY: MULTICENTRAL RUSSIAN STUDY

Olga A. Klochkova^{a*}, Alexey L. Kurenkov^a, Leyla S. Namazova-Baranova^a, Ayaz M. Mamedyarov^a, Lyudmila M. Kuzenkova^a, Il'ya V. Fal'kovskiy^b, Vera A. Zmanovskaya^c, Dmitriy A. Popkov^d, Lyudmila N. Vladykina^e, Vladimir M. Kenis^f, Diana A. Krasavina^g, Anastasia S. Nosko^h, Lybov V. Rychkovaⁱ

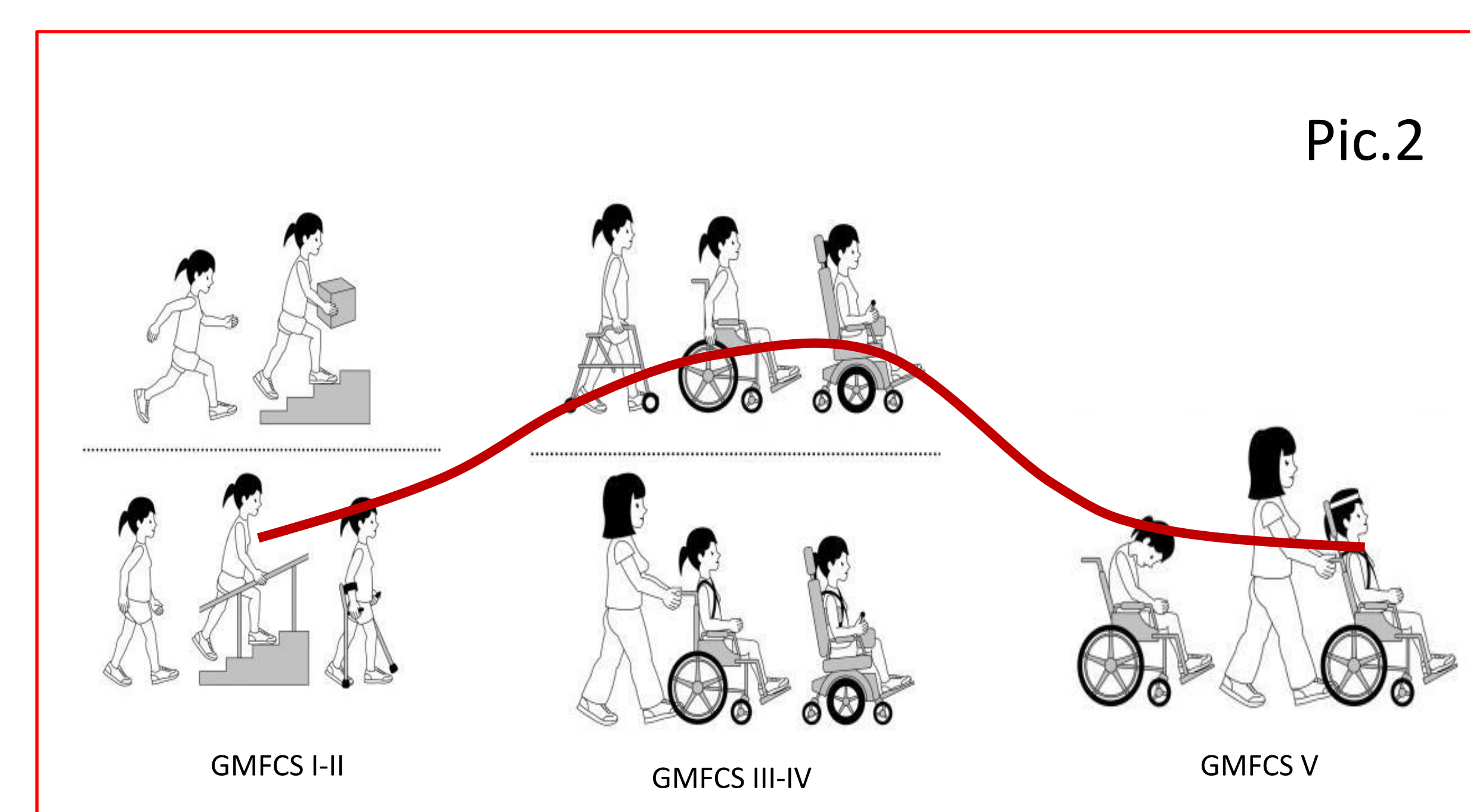
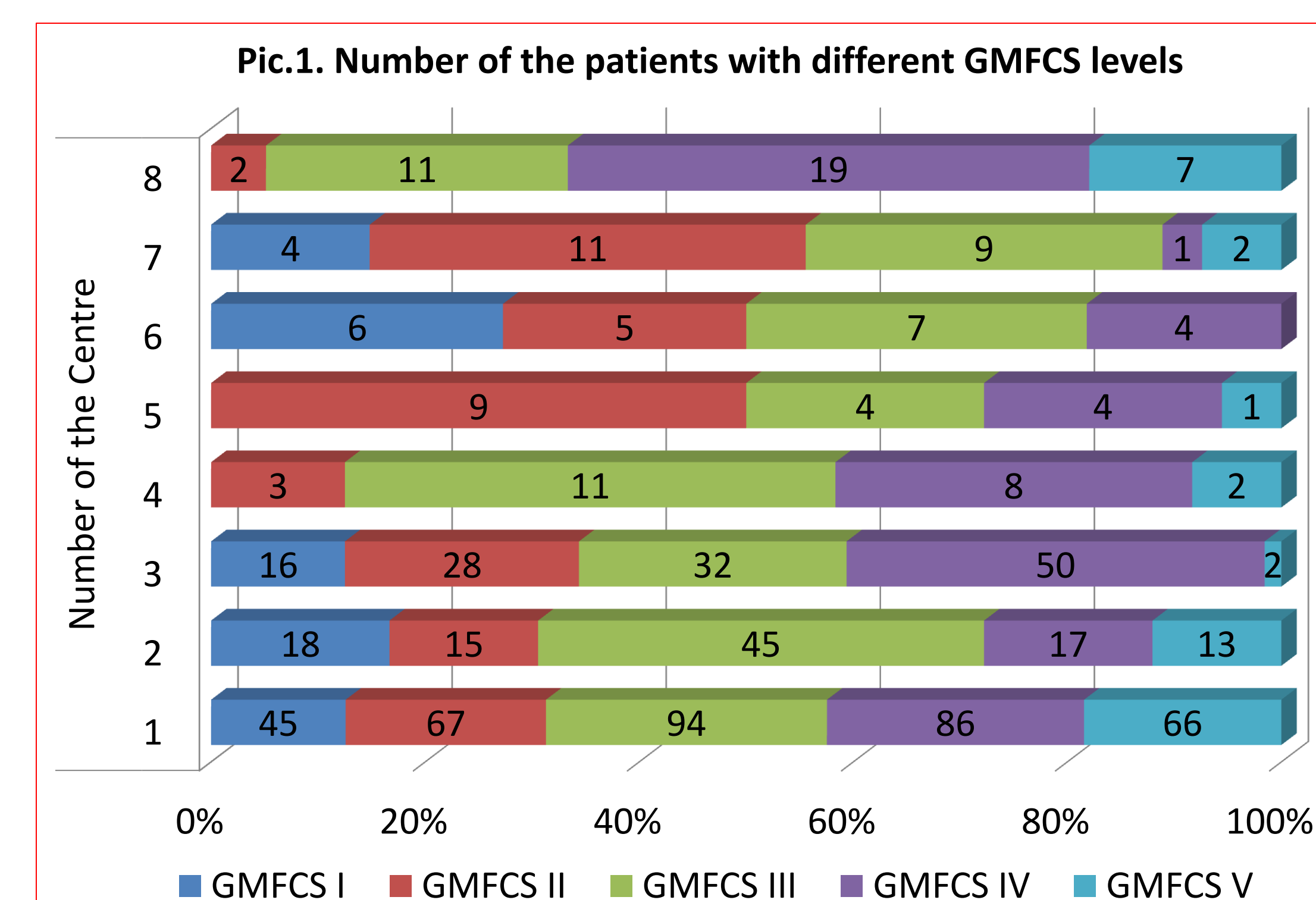
^a Scientific Centre of Children's Health under the Ministry of Health of the Russian Federation, Moscow, Russian Federation; ^b «Neyroklínika» LLC, Khabarovsk, Russian Federation; ^c Centre for Restorative Treatment and Rehabilitation «Nadezhda», Tyumen, Russian Federation; ^d Russian Ilizarov Scientific Centre for Restorative Traumatology and Orthopaedics, Kurgan, Russian Federation; ^e Altai Regional Mental Hospital for Children, Barnaul, Russian Federation; ^f The Turner Scientific Research Institute for Children's Orthopedics, Saint-Petersburg, Russian Federation; ^g Saint-Petersburg State Pediatric Medical University, Saint-Petersburg, Russian Federation; ^h Russian Medical Academy of Postgraduate Education, Moscow, Russian Federation; ⁱ Scientific Centre for Family Health and Human Reproduction Problems, Irkutsk, Russian Federation

Introduction: multilevel injections of Botulinum toxin A (BTA) are widely used in spastic cerebral palsy (SCP) complex treatment. However, there is no single international opinion on the effective and safe upper dosages and optimal intervals between the injections. In Russia BTA injections are included into CP rehabilitations but we still don't have the consolidated recommendations for the "off-label" injections that could be used as a basic document for the specialists and the official authorities.

Aim: to analyze the Russian multicenter independent experience in the use of single and repeated multilevel injections of Abobotulinum toxin A in spastic forms of CP

Patients and methods:

- 8 independent expert CP-centers (10 hospitals) in different regions of Russia with >10 years BTA experience;
- 724 patients with spastic CP (8 months – 17 years 4 months old at the beginning of the treatment, median - 3y. 10m.), classified according to GMFCS (Pic.1);
- 1872 protocols of effective BTA (AbobotulinumtoxinA) injections (1-14 repeated injections during 2001-2016 years).



Results: 421 children (58,1%) were injected at least twice. 6 injections and more were done for 62 (8,6%) of the patients.

Multilevel BTA injections were done for 634 (87,6%) of the patients.

The medians of the dosages for the first injection were between 30–31 U/kg (500 U) (min-max: 1,0-48,7 U/kg, 40-1200 U) (Tab.1).

Dosages >30 U/kg for the first BTA injections were used for 279 (38,5%) of children. More than **half of the centers used 40-45 U/kg (up to 1000 U)** for the first injections and even more for the repeated injections (max: 53,3U/kg, 1300 U). The highest total dosages were used for the GMFCS III-IV patients (Pic. 2).

The median intervals between the injections were 180–200 days in 484 (66,9%) patients and 140–180 days in 157 (24,7%) patients.

Tab. 1. Total Abobotulinumtoxin A dosages for the first and repeated injections in different centres

No of the centre	The dosage for the first BTA injection		Dosage range for the repeated injections (medians)		Maximal dosage	
	Total, U	Per kg (U/kg)	Total, U	Per kg (U/kg)	Total, U	Per kg (U/kg)
1	400 (40; 1130)	25,1 (1,0; 45,5)	400-670	23,2-39,9	1280	45,5
2	500 (240; 900)	31,6 (13,9; 46,9)	500	27,8-31,6	900	46,9
3	450 (180; 1000)	31 (10,3; 48,7)	450-1000	26,9-32,9	1000	48,7
4	410 (200; 800)	36,4 (14,5; 44,4)	410-600	34,2-37,4	1000	45,5
5	510 (300; 1200)	28,9 (20,0; 36,0)	510-900	24,0-30,0	1300	53,3
6	500 (500; 1000)	27,8 (12,5; 45,5)	500	26,4-31,3	1000	45,5
7	420 (190; 1040)	23,8 (12,7; 33,3)	420-500	22,7-28	1040	33,3
8	300 (120; 720)	21,1 (3,3; 32,1)	300-480	21,1-32,9	800	35,7

Conclusion: in our study most Russian centers started with the initial dose of Abobotulinumtoxin A 30–31 U/kg. The repeated injections dose could increase up to 40-45 U/kg with intervals 140–200 days. The real necessity and effectiveness of these high dosages should be discussed.