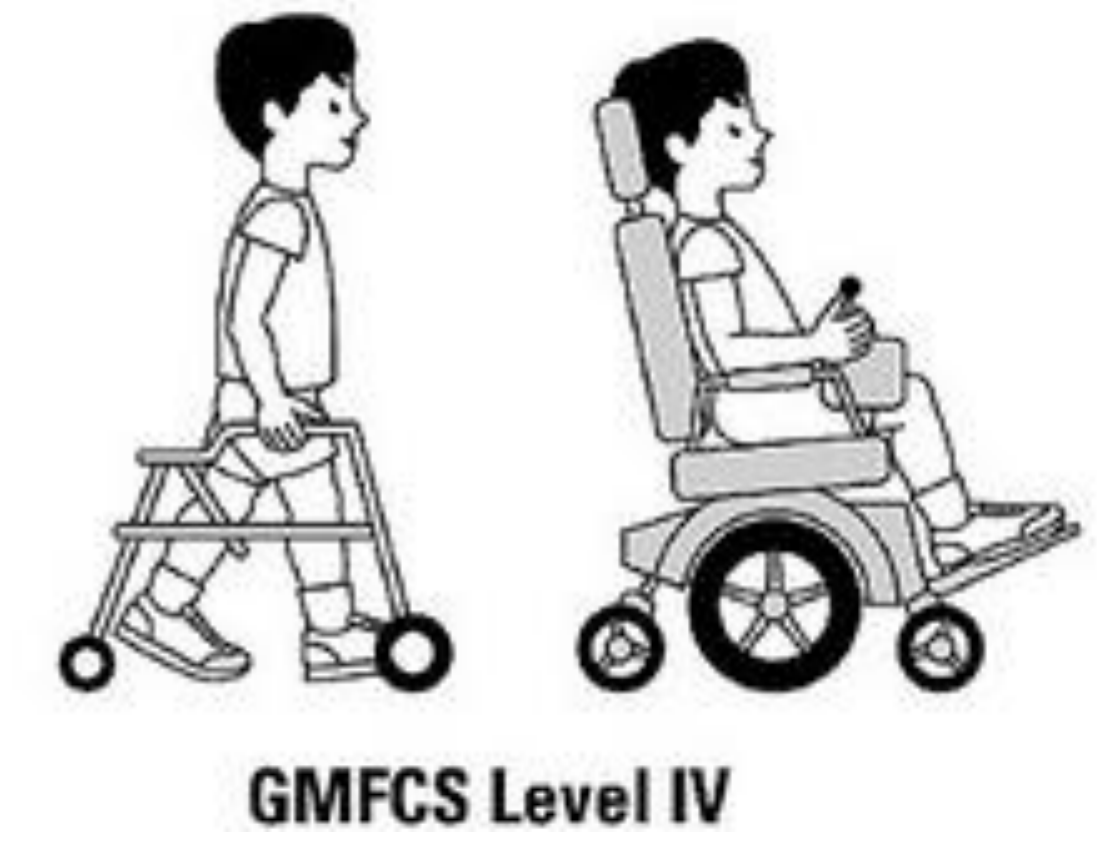


THE MAXIMUM TOTAL DOSAGE OF *ABOBOTULINUMTOXINA* FOR MULTILEVEL INJECTIONS IN PATIENTS WITH CEREBRAL PALSY, GMFCS IV-V

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Introduction: Botulinum toxin type A (BTA) multilevel injections are an effective and safe method for the treatment of local spasticity in cerebral palsy (CP). According to the European Consensus 2009 [1] and the official product information, the recommended total dosage of abobotulinumtoxinA (AboA) is 30 U/kg and not more than 1000 U. However, there is still debate about the upper level of total dosage, especially in severely disabled patients.



The aim of this study was to analyze the safe and effective use of AboA total dosage in our center for the first and repeated multilevel injections in children with severe CP - Gross Motor Function Classification System level IV-V (GMFCS IV-V).

Methods: 677 repeated multilevel injections of AboA for 333 patients with CP were retrospectively analyzed. We included patients with effective injections (at least 1 Ashworth scale point muscle tone decrease in injected muscles).

215 (64.6%) patients with GMFCS IV and 118 (35.4%) with GMFCS V were included. Among them were 210 (63.1%) boys and 123 (36.9%) girls.

The age at first injection (median; minimum-maximum; 25%-75%) was 4.8 years (1.3-17.9; 3.5-7.7) without significant difference between GMFCS levels.

In the GMFCS V group, the children's weight before the first injection was significantly lower (14 kg [7.5-34; 11.5-17.5]) compared with the GMFCS IV group (15.5 kg [8.1-55; 12.7-21.5]); $p=0.001$, Mann-Whitney U test).

Children received from 1 to 12 repeat injections in intervals of not less than 90 days.

Written informed consent for the injections was taken from all patients' official representatives.

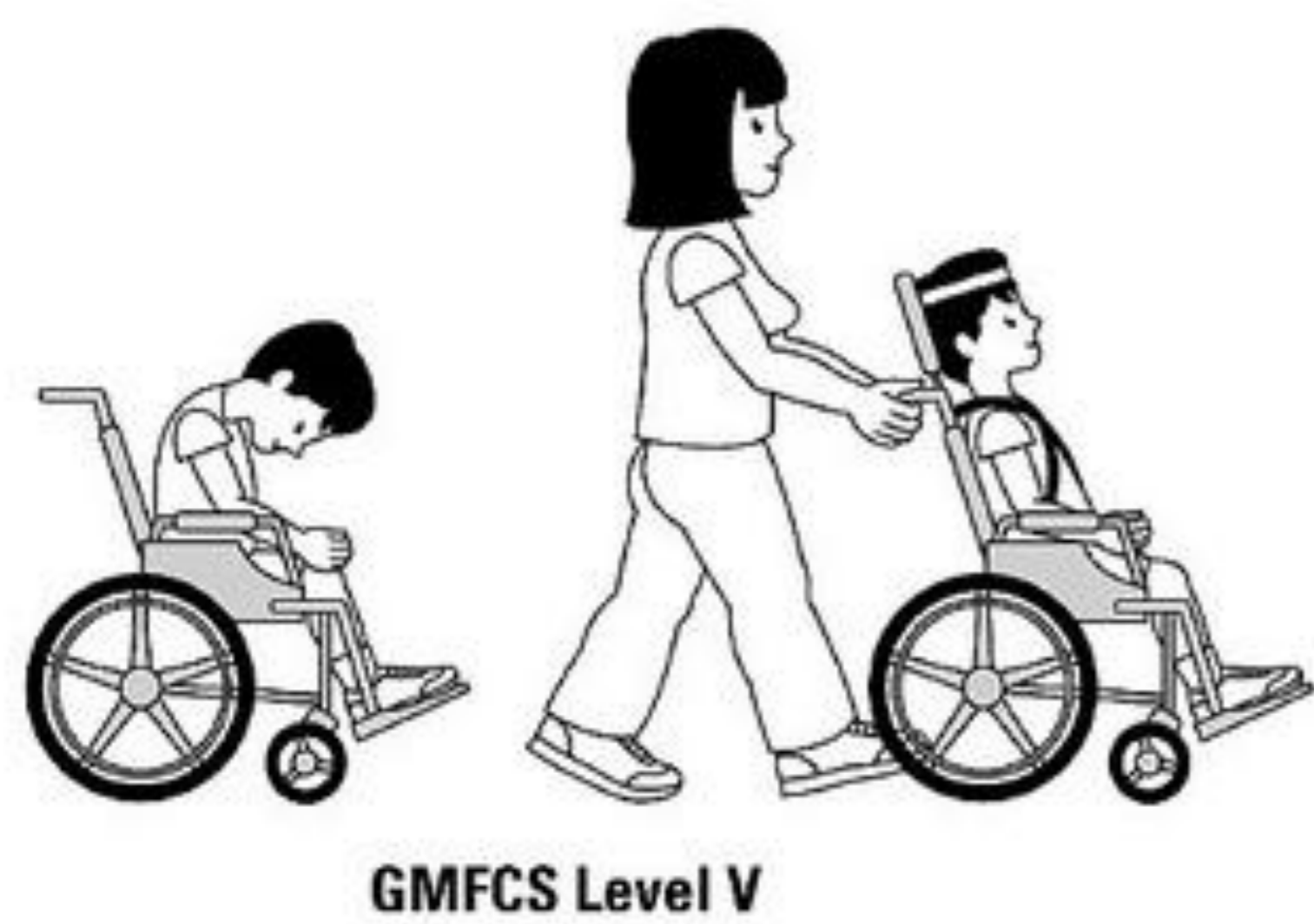
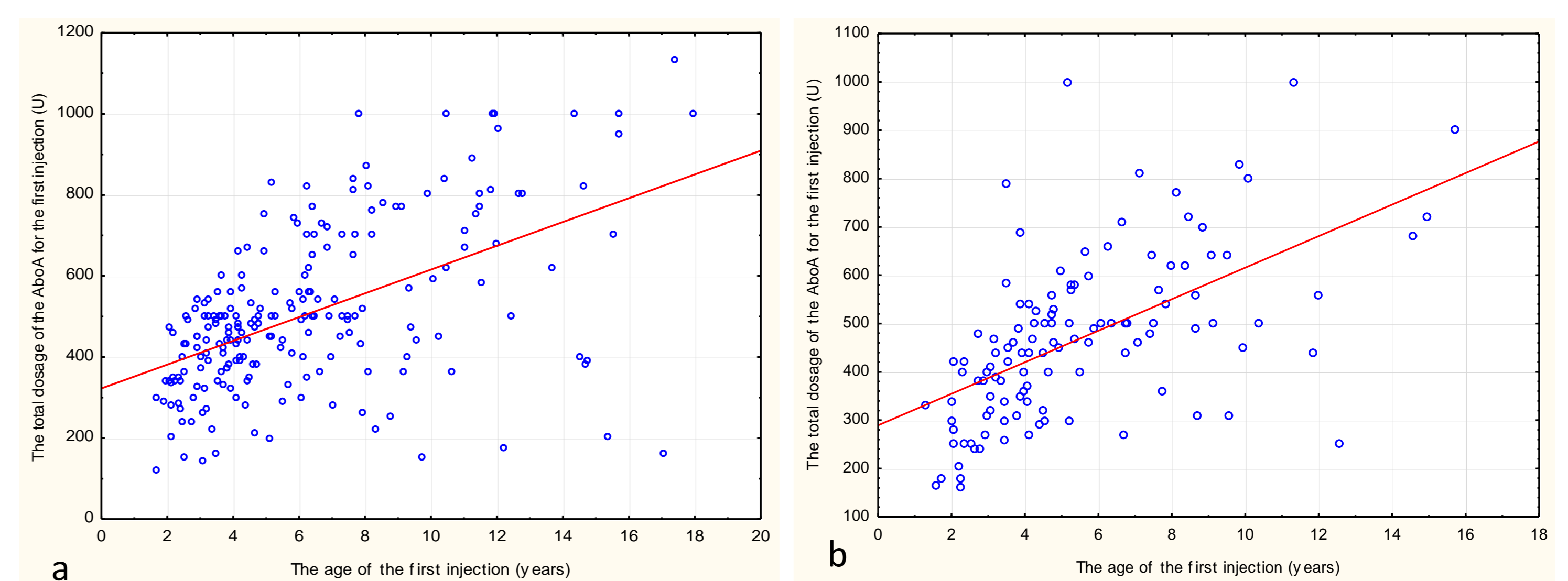


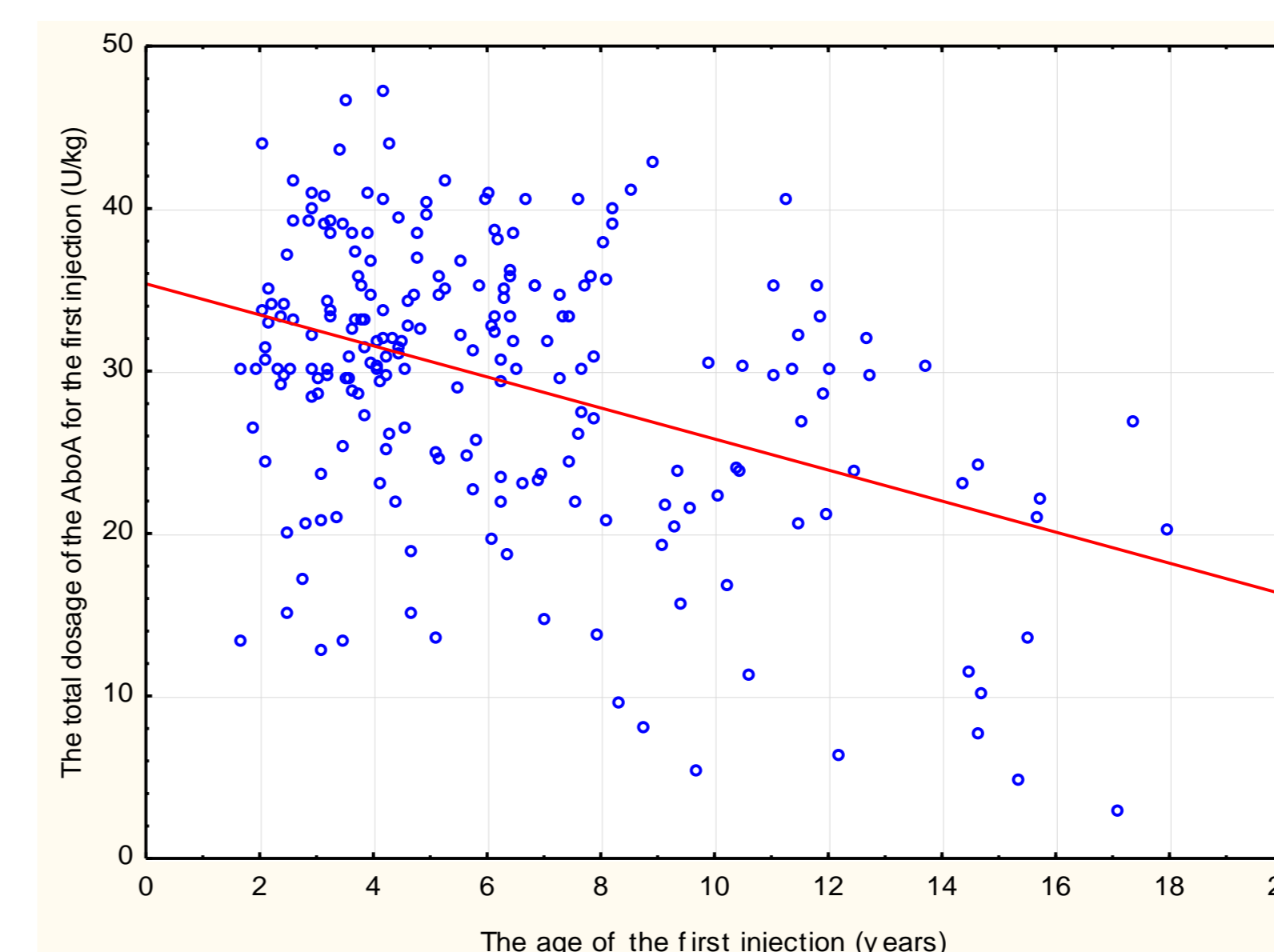
Table 1. Total dosages of the Abobotulinumtoxin A for the first and repeated injections in GMFCS IV and GMFCS V groups (Me; min-max; 25-75%)

№ of the injection	N of children	GMFCS IV			GMFCS V		
		N of children	The total dosage (U)	The dosage U/kg	N of children	The total dosage (U)	The dosage U/kg
1	333	215	475 (120-1130) (370; 610)	30,4 (2,9-47,1) (23,9; 35,2)	118	460 (160-1000) (340; 560)	31,8 (7,6-43) (28,6; 36,7)
2	142	90	500 (140-1210) (410; 630)	33,2 (8,0-47,9) (26,5; 37,8)	52	475 (230-870) (405; 560)	32,1 (19,2-43,5) (28,2; 38,6)
3	80	46	530 (150-1000) (440; 680)	32,7 (8,6-46,5) (24,1; 37,7)	34	500 (270-1000) (420; 600)	34,4 (18,1-45,5) (31,2; 39,9)
4	43	22	525 (310-900) (390; 740)	32,1 (6,9-45,0) (24,6; 37,6)	21	500 (290-1000) (410; 610)	35,9 (22,9-45,3) (30,1; 37,6)
5	29	15	520 (340-890) (460; 640)	36,2 (7,7-45,7) (30,1; 41,6)	14	505 (340-940) (450; 580)	35,7 (29,3-40,7) (33,3; 37,8)
6	16	7	500 (345-1000) (350; 840)	32,3 (25,0-41,7) (28,0-37,0)	9	590 (390-920) (460; 650)	40,6 (29,3-43,3) (37,9; 42,1)
7	11	4	485 (440-940) (455; 720)	31,4 (29,4-32,6) (29,8; 32,5)	7	500 (480-910) (480; 740)	41,1 (32,0-43,6) (32,5; 41,7)
8	10	3	670 (450-940) (450; 940)	30,3 (23,7-39,9) (23,7; 39,9)	7	630 (470-950) (480; 680)	39,4 (33,6-43,6) (33,9; 40,0)
9	6	2	680, 990	30,0, 41,2	4	610 (500-900) (545; 765)	34,7 (27,8-39,4) (28,9; 39,4)
10	3	1	720	38,9	2	500, 940	26,3, 30,3
11	2	1	870	37,8	1	530	27,9
12	2	1	950	40,6	1	530	26,5

Results: Total dosages of AboA are presented in the Table 1. We observed a significant correlation ($P<0.05$, Spearman rank) between the age at first injection and the total dosages of AboA in units ($r=0.5$ for GMFCS IV, $r=0.6$ for GMFCS V) and in U/kg ($r=-0.3$ for GMFCS IV) (Pic. 1-2). No severe side effects were noticed.



Pic. 1. Relationship between the age and total AboA dosages in GMFCS IV group ($r=0,5$, $p<0,05$) (a) and in GMFCS V group ($r=0,6$, $p<0,05$) (b)



Pic. 2. Relationship between the age and total AboA dosages in U/kg in GMFCS IV group ($r=-0,3$, $p<0,05$)

Conclusions: Children with severe CP (GMFCS IV-V) may need more than 30 U/kg of AboA for effective multilevel injections and spasticity reduction. Usually, higher dosages were used for younger children and in repeat injections.

Reference:

1. Heinen F, Desloovere K, Schroeder AS, et al. The updated European Consensus 2009 on the use of botulinum toxin for children with cerebral palsy. *Eur J Paediatr Neurol.* 2010;14(1):45-66.