



Brief considerations on the dispensation profile of the botulinum toxin type A by the Brazilian Unified Health System for treatment of dystonias: Datasus data

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ABSTRACT

Botulinum toxin injections are the most effective approach for the treatment of focal dystonia. Despite growing demand and clinical indications over the years, there are few reports or publications of its use and benefit to patients seen at the Sistema Único de Saúde – SUS (Unified Health System). Analyzing the Datasus data (Unified Health System Information Department of Brazilian Ministry of Health), it was noticed that in Brazil the percentage of dystonic patient benefited from this procedure is still low. We therefore suggest some strategies to increase the dispensation of the toxin by the Brazilian Unified Health system for the dystonic patients.

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1. Introduction

Botulinum toxin was first introduced in Brazil in the 90's for the treatment of focal dystonias. Currently, it is employed in different clinical conditions, but despite growing demand and clinical indications over the years, there are few reports or publications of its use and benefit to patients served by Sistema Único de Saúde – SUS (Unified Health System).

To address this subject, a panel was held in May 2015, in the city of São Paulo, with neurologists specialized in the treatment of dystonia

and working in public health facilities from different states of Brazil. At the meeting that lasted a day and a half, it was discussed the relevance of botulinum toxin in the treatment of dystonia and analyzed the distribution of this product dispensed by SUS from 2009 to 2014. All information was extracted from data published by DATASUS, which is the acronym for Unified Health System Information Department of Brazilian Ministry of Health.

Dystonia is an involuntary movement characterized by the presence of sustained muscle contractions, causing abnormal postures and tremors [1]. The injection of botulinum toxin (BT) is the most effective [2] and safe treatment for dystonias in general [3–5].

Type A BT (BTA) has proved effective for various forms of dystonia [6], particularly, blepharospasm [7–9], cervical dystonia [10],

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oromandibular dystonia [11,12], bucolingual dyskinesia [13] and laryngeal dystonia [14,15]. Several studies have confirmed its long-term efficacy [16–18].

The introduction of BT with therapy purposes began in 1980s and revolutionized the treatment of dystonias, particularly, the focal forms. BT is produced by the bacterium *Clostridium botulinum*, and has seven immunologically distinct serotypes named by letters A to G. The active portion of the toxin is a peptide comprised of a heavy chain of 100 kDa and a light chain of 50 kDa that prevent the release of acetylcholine in nerve terminals, producing denervation of the motor terminals [19]. BT is isolated, purified and bottled in small vials. There are four toxins available commercially in the United States: three type A and one type B. In 1989, Botox® (Allergan) was approved by the US Food and Drug Administration (FDA) for the treatment of blepharospasm, hemifacial spasm and strabismus. Since then, the FDA approved three other formulations: Dysport® (Ipsen), Myobloc® (US Mundial Meds) and Xeomin® (Merz Pharmaceuticals). In 2009, new BT generic names were assigned to the commercially available toxins: onabotulinumtoxin A (Botox®), abobotulinumtoxin A (Dysport®), incobotulinumtoxin A (Xeomin®), rimabotulinumtoxin B (Myobloc®). In Brazil, some formulations of botulinum toxin type A are available and their brand names are: Botox®, Dysport®, Xeomin®, Prosigne® and Botulift®.

The therapeutic clinical use of BT started with Dr. Alan Scott for the treatment of strabismus. The first application in Brazil occurred in 1987, in the city of Fortaleza, with a number of cases treated by Dr. Wagner Horta under the supervision of Prof. Dr. Andrew Lees. In 1991, after the technical opinion of Dr. Nasser Allam, BT was approved by regulatory agencies of the Ministry of Health. Between 1991 and 1994, several treatment centers started using BT in Brazil. Since 1994, BT has been incorporated in the list of special drugs and, in 1996, SUS began the distribution of BT for the entire national territory.

2. Results

According to DATASUS data [20], in 2009, the total number of patients with dystonia treated with BT distributed by SUS was 9057. It increased to 10,497 patients in 2013 and dropped to 9931 in 2014. Comparing 2009 and 2014 the number of treated patients increased approximately 9% (Fig. 1).

The distribution of BT is not homogeneous in Brazil, certain regions, particularly the North, show lower distribution of the product (Fig. 2).

3. Discussion

Because dystonia is a sustained muscle contraction leading to twisting posture, BT enables partial or complete correction of these abnormal postures, the stereotyped movements and pain, when present [21].

The inclusion of BT in the therapeutic arsenal, in addition to functional improvement, provided the decreased use of medications (reducing side effects) and surgical indications (Mackenzie and rhizotomy surgery), thus optimizes the dystonic patient treatment costs.

Another relevant factor is the prevention of deformities resulting long-term dystonic postures or other complications such as cervical fractures and hernias, which may be associated to cervical dystonia [22]. Treatment with BT provides the return to work activities and everyday life, improves socialization, self-esteem and quality of life [23–26].

As previously stated BT has proven benefit in the treatment of dystonia, which is a rare disease and its prevalence is 16 cases per 100,000 inhabitants, according to a meta-analysis published in 2012 [27]. Based on data from the Brazilian Institute of Geography and Statistics (IBGE) of 2013, in which the Brazilian population is around 201 million, the estimated number of patients with dystonia in Brazil would be 32,160 [28]. In 2013, BT was distributed for 10,497 patients with dystonia in the country. Subsequently, only 32% of patients with this condition received BT from the public health facilities.

From 2009 to 2014, the increment of patients benefited with BT was approximately 9%. Based on the estimated incidence of 1.07 new cases of dystonia per 100 thousand inhabitants [27] in the Brazilian population, we would expect a projection around 2 thousand new cases per year. Over five years, we would have 10 thousand new cases of dystonia in general, a much higher number than the increase in treated cases, according to data provided by DATASUS.

Analyzing the DATASUS data, we also observed that the distribution of BT is not homogeneous in Brazil despite differences in population density. Certain regions, particularly the North, show a low distribution of the product.

It is identified that although the number of patients benefited from public treatment, there is a repressed demand. Among the possible causes for this situation, the first would be the lack of referral centers with qualified professionals to treat patients. Second, would be the difficulty of diagnosis and referral of this population to application centers. Moreover, the need for continued treatment of such patients, who are not discharged from outpatient clinics, saturates the ability of new medical assistance.

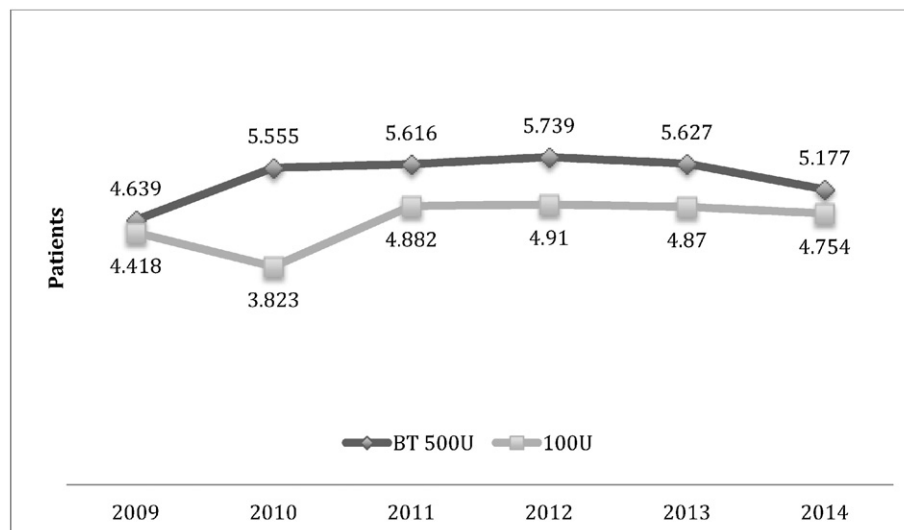


Fig. 1. Number of patients with dystonia treated with Botulinum toxin type A (BT 500U = botulinum toxin type A 500U per vial, BT100U = botulinum toxin type A 100U per vial).

PERIOD	NOV 2008- OCT 2009		NOV 2009- OCT 2010		NOV 2010- OCT 2011		NOV 2011- OCT 2012		NOV 2012- OCT 2013		NOV 2013- OCT 2014	
BT	500U	100U	500U	100U	500U	100U	500U	100U	500U	100U	500U	100U
AC	16	95	34	23	0	27	16	6	29	23	29	2
AL	137	83	129	30	105	27	78	68	86	87	213	109
AM	68	74	86	48	126	87	144	129	140	157	112	187
AP	0	8	0	0	1	3	0	8	3	7	2	4
BA	405	140	717	219	501	353	608	310	309	419	4	85
CE	90	374	162	326	37	539	9	572	5	532	126	597
DF	76	189	128	205	139	189	129	224	200	243	220	282
ES	137	350	373	261	292	407	189	577	314	557	589	248
GO	237	370	314	327	393	417	609	354	745	440	783	566
MA	0	62	0	73	22	81	23	111	20	141	38	152
MG	831	584	989	511	1414	585	1747	622	2103	704	2480	796
MS	104	169	79	146	62	147	70	100	219	166	195	116
MT	116	44	235	44	238	39	291	31	285	86	270	70
PA	61	98	70	95	29	180	96	197	107	192	87	188
PB	349	54	342	151	320	168	380	134	328	144	335	180
PE	193	343	267	397	347	326	510	318	847	158	716	134
PI	126	56	119	90	90	163	34	208	71	153	81	165
PR	111	158	364	284	463	363	594	3332	789	409	712	519
RJ	148	377	234	124	306	665	249	635	482	469	701	182
RN	2	286	0	283	0	319	25	203	78	325	179	310
RO	42	49	83	54	173	54	181	48	151	63	184	81
RS	5	871	5	899	1	988	7	1037	9	955	37	1035
SC	310	1050	763	47	924	497	1284	602	1119	507	1264	797
SE	7	113	15	119	42	104	45	83	92	61	55	82
SP	4653	1321	4788	1179	5201	1304	5658	1251	6332	994	6488	1023
TO	1	20	1	26	2	27	6	15	22	24	12	19
RR	0	0	4	0	2	1	0	48	0	0	2	0
Brazil	8,244	7336	10,298	5,961	11,214	8,058	12,982	8,172	14,881	8,007	15,910	7,926
Total	14,911		15,512		18,505		20,623		21,977		22,872	

Fig. 2. Quantity of BT bottles distributed for each Brazilian state.

This article provides a brief overview of the dispensation of BT to the treatment of dystonic patients in Brazil during the years of 2009 to 2014. Because the only source available for the analysis of the dispensation of BT by SUS is provided by DATASUS, several limitations should be addressed. Firstly, all the data obtained are observational so the panel could not make further analysis of factors leading to low demand of BT. Secondly, although it could be intuitive to conclude that the provision of BT to North and Northeast regions of Brazil should be attributed to lower Human Development Index, lower number of physicians in those states or limitations of dystonic patients to have adequate assistance, such correlation is no direct. Further studies should be conducted to ascertain the discrepancy of BT distribution in Brazil. Thirdly, it would be interesting to compare the proportion of patients treated with BT in United Kingdom or others countries in which all costs are borne by their National Healthcare Services, but data referring such dispensation are not promptly accessible for comparisons. Finally, the number of patients with dystonia benefited from BT provided by SUS could be overestimated because in some cases the request of BT could be used for conditions other than dystonia (e.g. spasticity).

Therefore, our recommendations for better distribution of BT and increase the number of dystonic patients who could be benefited from the treatment are:

- Increasing the number of qualified centers for diagnosis and treatment of movement disorders.
- Stimulate the development of qualified professionals for diagnosis and treatment of movement disorders.
- Encourage the development of informative educational programs to health professionals and to the community in general to identify movement disorders.

Conflicts of interest

The authors declare that there are no conflicts of interest.

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References

- [1] A. Albanese, K. Bhatia, S.B. Bressman, et al., Phenomenology and classification of dystonia: a consensus update, *Mov. Disord.* 28 (7) (2013) 863–873.
- [2] P.G. Costa, L. Aoki, F.P. Saraiva, et al., Botulinum toxin in the treatment of facial dystonia: evaluation of its efficacy and patients' satisfaction along the treatment, *Arq. Bras. Oftalmol.* 68 (4) (2005) 471–474.
- [3] R. Laskawi, The use of botulinum toxin in head and face medicine: an interdisciplinary field, *Head Face Med* 4 (2008) 5.
- [4] C.H. Camargo, H.A. Teive, N. Becker, et al., Botulinum toxin type A and cervical dystonia: a seven-year follow-up, *Arq. Neuropsiquiatr.* 69 (5) (2011) 745–750.
- [5] A. Brashear, The safety and tolerability of botulinum toxins for the treatment of cervical dystonia, *Expert Opin. Drug Saf.* 4 (2) (2005) 241–249.
- [6] J.P. De Mattos, A.L. De Rosso, S. Novis, Dystonias: clinical and therapeutic aspects in 64 patients, *Arq. Neuropsiquiatr.* 54 (1) (1996) 30–36.
- [7] L. Silveira-Moriyama, L.R. Goncalves, H.F. Chien, et al., Botulinum toxin in the treatment of blepharospasm: a 10-year experience, *Arq. Neuropsiquiatr.* 63 (2 A) (2005) 221–224.
- [8] S.A. Novis, J.P. De Mattos, A.L. De Rosso, Botulinum toxin in blepharospasm, in hemifacial spasm, and in cervical dystonia: results in 33 patients, *Arq. Neuropsiquiatr.* 53 (3-A) (1995) 403–410.
- [9] C.R. Rieder, P. Schestatsky, M.P. Socal, et al., A double-blind, randomized, crossover study of prosigne versus botox in patients with blepharospasm and hemifacial spasm, *Clin. Neuropharmacol.* 30 (1) (2007) 39–42.
- [10] C.H. Camargo, H.A. Teive, N. Becker, et al., Cervical dystonia: clinical and therapeutic features in 85 patients, *Arq. Neuropsiquiatr.* 66 (1) (2008) 15–21.

- [11] R. Bhidayasiri, F. Cardoso, D.D. Truong, Botulinum toxin in blepharospasm and oromandibular dystonia: comparing different botulinum toxin preparations, *Eur. J. Neurol.* 13 (Suppl. 1) (2006) 21–29.
- [12] H.A. Teive, L.E. Kluppel, R.P. Munhoz, et al., Jaw-opening oromandibular dystonia secondary to Wilson's disease treated with botulinum toxin type A, *Arq. Neuropsiquiatr.* 70 (6) (2012) 407–409.
- [13] D.J. Silva, O. Vilela-Filho, J.E.S. Cavalcante, Tratamento de discinesia bucoorolingual tardia com toxina botulinica tipo A (TOXBA): registro de caso com vídeo. XX Congresso Brasileiro de Neurologia, 2002, Florianópolis, *Arq. Neuropsiquiatr.* 60 (Suppl. 1) (2002) 232.
- [14] M.S. Benninger, G. Gardner, C. Grywalski, Outcomes of botulinum toxin treatment for patients with spasmodic dysphonia, *Arch. Otolaryngol. Head Neck Surg.* 127 (9) (2001) 1083–1085.
- [15] A.C. Gama, L.N. Menezes, A.A. Maia, et al., Voice related quality of life after botulinum toxin injection for spasmodic dysphonia, *Rev. Laryngol. Otol. Rhinol.* 131 (1) (2010) 39–44 (Bord).
- [16] F.M. Maia, A.K. Kanashiro, H.F. Chien, et al., Clinical changes of cervical dystonia pattern in long-term botulinum toxin treated patients, *Parkinsonism Relat. Disord.* 16 (1) (2010) 8–11.
- [17] J.W. Brans, R. Lindeboom, M. Aramideh, et al., Long-term effect of botulinum toxin on impairment and functional health in cervical dystonia, *Neurology* 50 (5) (1998) 1461–1463.
- [18] I.M. Skogseid, J. Roislien, B. Claussen, et al., Long-term botulinum toxin treatment increases employment rate in patients with cervical dystonia, *Mov. Disord.* 20 (12) (2005) 1604–1609.
- [19] D. Dressler, F.A. Saberi, E.R. Barbosa, Botulinum toxin: mechanisms of action, *Arq. Neuropsiquiatr.* 63 (1) (2005) 180–185.
- [20] Datasus, 2014 cited October 2014. Available from: <http://www2.datasus.gov.br/DATASUS/index.php>.
- [21] N. Allam, J.P. Brasil-Neto, G. Brown, et al., Injections of botulinum toxin type a produce pain alleviation in intractable trigeminal neuralgia, *Clin J Pain* 21 (2) (2005) 182–184.
- [22] M. Spitz, L. Goncalves, L. Silveira, et al., Myelopathy as a complication of cervical dystonia, *Mov. Disord.* 21 (5) (2006) 726–727.
- [23] R.W. Werle, S.Y. Takeda, M.B. Zonta, et al., The physical, social and emotional aspects are the most affected in the quality of life of the patients with cervical dystonia, *Arq. Neuropsiquiatr.* 72 (6) (2014) 405–410.
- [24] M.R. Queiroz, H.F. Chien, E.R. Barbosa, Quality of life in individuals with cervical dystonia before botulinum toxin injection in a Brazilian tertiary care hospital, *Arq. Neuropsiquiatr.* 69 (6) (2011) 900–904.
- [25] K.D. Sethi, R. Rodriguez, B. Olayinka, Satisfaction with botulinum toxin treatment: a cross-sectional survey of patients with cervical dystonia, *J. Med. Econ.* 15 (3) (2012) 419–423.
- [26] S. Ochudlo, P. Bryniarski, G. Opala, Botulinum toxin improves the quality of life and reduces the intensification of depressive symptoms in patients with blepharospasm, *Parkinsonism Relat. Disord.* 13 (8) (2007) 505–508.
- [27] T.D. Steeves, L. Day, J. Dykeman, et al., The prevalence of primary dystonia: a systematic review and meta-analysis, *Mov. Disord.* 27 (14) (2012) 1789–1796.
- [28] Instituto Brasileiro de Geografia e Estatística, ftp://ftp.ibge.gov.br/Estimativas_de_Populacao/Estimativas_2013/populacoes_estimativas_BR_UF_TCU_31_10_2013.pdf (Accessed on May 5th 2015).