



## ORIGINAL ARTICLE

# Descriptive analysis of the annual cost of treating spasticity with different types of botulinum toxin A<sup>☆</sup>

D. Hernández Herrero<sup>a,b,\*</sup>, J.C. Miangolarra Page<sup>c,d</sup>

<sup>a</sup> Servicio de Medicina Física y Rehabilitación, Hospital Universitario La Paz, Madrid, Spain

<sup>b</sup> Escuela Internacional de Doctorado, Universidad Rey Juan Carlos, Madrid, Spain

<sup>c</sup> Departamento de Medicina Física y Rehabilitación, Universidad Rey Juan Carlos, Madrid, Spain

<sup>d</sup> Servicio de Rehabilitación y Medicina Física del Hospital Universitario de Fuenlabrada, Fuenlabrada (Madrid), Spain

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## KEYWORDS

Botulinum toxin A;  
Spasticity;  
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## Abstract

**Introduction:** Botulinum toxin A is the first-line treatment for localised spasticity. However, the economic impact of this treatment is not fully known. This study aimed to describe the real costs of botulinum toxin A for the treatment of adult patients with spasticity at a spasticity clinic pertaining to a rehabilitation service, over a period of one year.

**Methods:** We retrospectively reviewed all medical procedures carried out during the year 2017. We collected data on the type of toxin used (incobotulinumtoxin A, onabotulinumtoxin A, or abobotulinumtoxin A), the number of units injected, the anatomical region, and the time elapsed between infiltrations. The costs of medication and indirect costs, such as staff and consumables, were also calculated.

**Results:** This is the first study to describe the real costs of botulinum toxin treatment of spasticity in adult patients in Spain. In 2017, 510 infiltration procedures were performed in 164 patients. The total cost of treating spasticity in our service was €116 789.70. The mean annual cost per patient was €603.64 for onabotulinumtoxin A, €642.69 for abobotulinumtoxin A, and €707.59 for incobotulinumtoxin A.

**Conclusions:** Our economic study of real clinical practice is consistent with the theoretical models published in the literature. The different characteristics of each toxin and the inability to establish an equivalence between the units of each drug prevents us from directly comparing these costs.

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\* Corresponding author.

E-mail address: [dhernandez.herrero@salud.madrid.org](mailto:dhernandez.herrero@salud.madrid.org) (D. Hernández Herrero).

**PALABRAS CLAVE**

Toxina botulínica A;  
Espasticidad;  
Análisis de costes;  
España

## Análisis descriptivo de coste de tratamiento de la espasticidad con diferentes tipos de toxina botulínica A, a lo largo de un año

**Resumen**

**Introducción:** La toxina botulínica A es el tratamiento de elección para la espasticidad localizada. Sin embargo, no se tiene un conocimiento real de su repercusión económica. El objetivo de este trabajo es describir los costes reales del tratamiento de la espasticidad en adultos con toxina botulínica A en una consulta de espasticidad de un Servicio de Rehabilitación, a lo largo de un año.

**Métodos:** Se ha realizado la revisión retrospectiva de todos los actos médicos llevados a cabo a lo largo del año 2017. Se han recogido el tipo de toxina utilizado (incobotulinumtoxin A, onabotulinumtoxin A, abobotulinumtoxin A), las unidades inyectadas, la región anatómica y el tiempo transcurrido entre infiltraciones. Se han obtenido los costes de la medicación y los costes indirectos, como los de personal o fungibles.

**Resultados:** Este es el primer trabajo que describe los costes reales del tratamiento de la espasticidad en adultos con toxina botulínica A en España. En 2017 se realizaron 510 actos de infiltración en 164 pacientes. El coste total de tratamiento de espasticidad en nuestro Servicio fue de 116.789,70 €. El coste medio anual por paciente fue 603,64 € para onabotulinumtoxin A, 642,69 € para AbotoxA y 707,59 € para incobotulinumtoxin A.

**Conclusiones:** Nuestro estudio económico de actividad clínica real sigue una pauta similar a la descrita en los modelos teóricos publicados en la literatura. Las diferentes características de cada toxina y la imposibilidad de establecer una equivalencia entre las unidades de cada una de ellas impiden la comparación directa de estos costes.

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**Introduction**

Spasticity frequently appears over the course of upper motor neuron disease, causing pain, functional limitations, and difficulty attending to personal hygiene.<sup>1</sup>

Spasticity treatment includes a wide range of options, from physical medicine and rehabilitation techniques to surgery.<sup>2</sup> Regarding pharmacological treatment, spasticity may be treated with oral (tizanidine, baclofen, etc) or intrathecal drugs (baclofen). However, the treatment of first choice for focal spasticity is intramuscular botulinum toxin A (BoNT-A) injection.<sup>3,4</sup>

Three types of BoNT-A are available in Spain, from different pharmaceutical companies and with different characteristics, preventing direct comparison between them. All 3 types have been shown to be efficacious in the treatment of focal spasticity.<sup>5</sup> Incobotulinumtoxin A (IncotoxA; Xeomin®, Merz Pharmaceuticals) includes no complexin proteins (haemagglutinins) and does not require cold storage. Onabotulinumtoxin A (OnatoxA; Botox®, Allergan) and abobotulinumtoxin A (AbotoxA; Dysport®, Ipsen Biopharm), in contrast, must be stored under refrigeration.<sup>6</sup> The conversion ratio between IncotoxA and OnatoxA is 1:1, whereas the conversion ratio for IncotoxA and AbotoxA is 1:3.<sup>7</sup> This ratio was established by indirect methods, since no standardised tests are available to compare these products. Furthermore, AbotoxA seems to be more cost-effective.<sup>3</sup> Roze et al.<sup>8</sup> compared the cost of treating upper-limb spasticity based on the recommended doses of

OnabotA and AbotoxA in 19 countries, including Spain; in all cases, treatment with AbotoxA was found to be less costly.

One of the characteristics of this treatment is that infiltrations must be performed periodically, with medical appointments either scheduled in advance every 3-4 months, or offered on demand, when spasticity symptoms reappear and affect the patient's daily life.<sup>6</sup>

The dose injected at each session depends on the patient's clinical status at the consultation prior to treatment and on the effectiveness of previous treatments.<sup>1</sup> Therefore, a fixed maintenance dose cannot be established and doses usually change from session to session.

The need for periodic injections and the changes in dosage between sessions make it difficult to estimate the cost of treatment over time.

We aimed to calculate the costs of treatment with BoNT-A over one year in a spasticity unit for adults from the rehabilitation department of a tertiary hospital of the Spanish National Health System.

**Material and methods**

The study was approved by our hospital's ethics committee.

Our department has a spasticity unit that treats adult patients, providing outpatient consultations 2 days per week. We retrospectively reviewed the medical histories of all patients receiving treatment at the spasticity unit in 2017. The study included those patients treated with BoNT-A.

**Table 1** Distribution of patients by type of botulinum toxin A received and doses administered.

		OnatoxA	AbotoxA	IncotoxA
Patients	161	53	60	48
Women/men	67/94	26/27	20/40	21/27
Mean age (SD), years <sup>a</sup>	42 (21.4)	32 (19.3)	41 (21.8)	53 (17.6)
Upper limbs/lower limbs	81/133	21/42	31/51	29/40
Time between infiltrations during the study period				
Mean (SD), days <sup>b</sup>	134.77 (31.9)	143.60 (35.5)	133.39 (28.38)	127.10 (31.1)
Units used in each infiltration procedure				
All procedures conducted in 2017				
Average dose		308.95	914.23	425.97
SD		145.56	377.45	169.99
Max/min dose		900/30	1850/250	760/100
1st infiltration of the year				
No. patients		53	60	48
Average dose		273.77	879.75	387.71
SD		129.75	386.53	176.01
Max/min dose		650/30	1850/250	760/100
2nd infiltration of the year				
No. patients		42	54	35
Average dose		318.1	859.72	394.29
SD		147.02	373.19	158.82
Max/min dose		900/100	1500/250	700/100
3rd infiltration of the year				
No. patients		23	33	21
Average dose		343.91	917.42	410.24
SD		171.25	381.89	177.94
Max/min dose		900/100	1500/450	750/150
4th infiltration of the year				
No. patients		1	1	3
Average dose		300	1000	511.67
Max/min dose				675/310
Total per patient and year				
No. patients		53	60	48
Average dose		680.75	2174.75	886.67
SD		466.41	1160.34	595.68
Max/min dose		2300/30	4850/325	2500/250

SD: standard deviation.

<sup>a</sup> Age at the time of the first infiltration of the study period. ANOVA:  $P > .000$ ; OnatoxA vs AbotoxA:  $P = .05$ ; OnatoxA vs IncotoxA:  $P = .000$ ; AbotoxA vs IncotoxA:  $P = .004$ .

<sup>b</sup> ANOVA:  $P = .013$ ; OnatoxA vs AbotoxA:  $P = .146$ ; OnatoxA vs IncotoxA:  $P = .012$ ; AbotoxA vs IncotoxA:  $P = .706$ .

Our spasticity unit administers all 3 types of BoNT-A (OnatoxA, IncotoxA, and AbotoxA); the specific treatment selected depends on the judgement and experience of the 2 physicians leading the unit. BoNT-A is used in accordance with Spanish Royal Decree-Law 16/2012 on resource optimisation. Due to its form of presentation, the entire vial must be reconstituted at once; therefore, if the whole dose is not administered, the remaining drug is stored appropriately for subsequent use in another patient.<sup>9</sup>

BoNT-A is administered by ultrasound-guided injection at the consultation. At our unit, the mean duration of

consultations is 25 minutes for patients with upper-limb spasticity and 30 minutes for those with lower-limb spasticity (this includes examination, patient transfer, undressing and dressing, and BoNT-A infiltration). Treatment is administered by a specialist, the head of a hospital department in all cases (this has been considered in the cost estimation), with the assistance of a nurse. During the study period (2017), 2 specialists were responsible for administering all treatments at the spasticity unit.

We reviewed patient's medical histories to gather data on the type of BoNT-A used, dose, date of infiltration, and

**Table 2** Cost of the 3 types of botulinum toxin A used in our study.

	OnatoxA	AbotoxA	IncotoxA
Price per vial	€88.673	€147.763	€79.803
Units per vial	100	500	100
Price per unit	€0.88673	€0.295526	€0.79803

the anatomical region treated. Two anatomical regions were considered: upper limbs and lower limbs.

From an administrative viewpoint, the unit schedules periodical consultations (approximately every 4 months) with patients receiving BoNT-A. The number of units of BoNT-A infiltrated in each consultation depends on the patient's clinical status, examination results at the time of infiltration, and patients' and their relatives' degree of satisfaction with the outcomes of the previous infiltration procedure.

We also obtained information from the hospital's purchasing department on the prices of the different types of BoNT-A used at our centre.

The calculation of annual cost included the salaries of the healthcare professionals involved in the treatment and the cost of expendable materials (needles, syringes, etc). We did not account for such indirect costs as equipment depreciation or other general costs (water, electricity, etc). As in previous studies, these costs were not considered in the comparison of the different types of BoNT-A, since the procedure is similar regardless of the type of BoNT-A administered and the associated costs present no significant differences.

The costs of the physician and nurse are based on the salary table published by the Madrid regional health ministry in the Official Gazette of the Community of Madrid for 2017,<sup>10</sup> and a total of 1465 working hours per year.

Microsoft® Excel was used for data collection and handling and cost calculation. Statistical analysis was performed with Stata, version 15. We used ANOVA to compare quantitative data between the 3 groups, and the *t* test with Bonferroni correction for a posteriori pairwise comparisons.

## Results

In 2017, a total of 763 medical procedures were performed at the spasticity unit. Of these, 253 were intrathecal

baclofen pump refills and 510 were BoNT-A infiltrations. A total of 169 patients received treatment with BoNT-A. We excluded 5 patients: 2 who received treatment with BoNT-A for other indications and 3 who received different types of BoNT-A for unknown reasons. Of the 164 patients included, 138 received infiltrations in the lower limbs and 84 in the upper limbs. In 129 medical procedures, 55 patients received BoNT-A in both the upper and the lower limbs.

**Table 1** describes our patient sample and the doses administered for each type of BoNT-A.

**OnatoxA:** 53 patients. Mean of 2.2 sessions during the study period. The mean time between infiltrations was 143.6 days. The mean number of units administered in each session was 308.95. The mean total number of units administered to each patient over one year was 680.75.

**AbotoxA:** 60 patients. Mean of 2.4 sessions during the study period. The mean time between infiltrations was 133.4 days. The mean number of units administered in each session was 914.23. The mean total number of units administered to each patient over one year was 2174.75.

**IncotoxA:** 48 patients. Mean of 2.4 sessions during the study period. The mean time between infiltrations was 127.1 days. The mean number of units administered in each session was 425.97. The mean total number of units administered to each patient over one year was 889.67.

**Table 2** lists the costs associated with the 3 types of BoNT-A, whereas **Table 3** presents the cost of healthcare professionals' salaries. For each infiltration procedure, we considered the costs of the following expendable materials: 2 syringes ( $2 \times \text{€}0.027$ ), 2 needles ( $2 \times \text{€}0.06$ ), and 1 serum vial ( $\text{€}0.723$ ), resulting in a total cost of  $\text{€}0.90$  in expendable materials per procedure.

**Table 4** summarises the costs of using BoNT-A in 2017.

The mean cost of treatment per patient in 2017 was  $\text{€}603.64$  for OnatoxA,  $\text{€}642.69$  for AbotoxA, and  $\text{€}707.59$  for IncotoxA.

Overall, the mean cost of treatment with BoNT-A in our unit is  $\text{€}643.29$ , whereas the annual cost of the drug is  $\text{€}104\,519.09$ .

**Table 5** shows data on patients who received the same dose throughout the year. This is an indirect indicator that the optimal dose has been achieved; it is therefore to be expected that the optimal dose will be maintained over time, unless the patient's clinical status worsens. This was the case in 49% of the patients receiving OnatoxA, 43.3% of those receiving AbotoxA, and 45.8% of those treated with IncotoxA. The annual cost of treatment in these patients

**Table 3** Healthcare staff costs calculated based on the salary table published in the Official Gazette of the Community of Madrid for 2017.

	Annual salary	Salary per minute	Direct cost applicable	
			Upper limbs (25 min)	Lower limbs (30 min)
Head of department	€48 170.16	€0.54	€13.5	€16.2
Nurse	€25 150.08	€0.286	€7.15	€8.58

**Table 4** Cost of treatment with botulinum toxin A for spasticity per patient and year, depending on the maximum and minimum doses used.

	OnatoxA	AbotoxA	IncotoxA
<i>Mean dose per session</i>			
Units	308.95	914.22	425.97
Cost	€273.95	€270.17	€339.94
<i>Total per patient and year</i>			
Units	680.75	2174.75	886.67
Cost	€603.64	€642.69	€707.59
<i>Maximum dose</i>			
Units	900	1850	760
Cost	€798.06	€546.72	€606.50
<i>Minimum dose</i>			
Units	30	250	100
Cost	€26.60	€73.88	€79.80

**Table 5** Cost of treatment in patients receiving the same dose throughout the whole study period.

	OnatoxA	AbotoxA	IncotoxA
No. patients	26	26	22
<i>Mean annual dose per patient</i>			
Units	778.46	2174.81	1023.81
Cost	€690.28	€642.71	€817.03
<i>Mean annual dose per session</i>			
Units	297.65	856.74	413.46
Cost	€263.94	€253.19	€329.95

was €690.28, €642.71, and €817.03, respectively. In the subgroup of patients receiving the same dose during the whole study period, the mean total cost of treatment was €711.25.

Table 6 presents the total annual cost of treatment, including personnel and expendable material costs. In 2017, the total cost of spasticity treatment with BoNT-A in our unit was €116 789.70, which represents 5.23% of the unit's total annual budget for 2017.

## Discussion

To our knowledge, this is the first study into the real costs of spasticity treatment for adults to be conducted in Spain.

According to a previous study,<sup>11</sup> the annual cost of treatment with BoNT-A in Spain in 2013 ranged from €265 to €2120 per patient, depending on the indication, dose, and type of BoNT-A used. Costs were established according to

diagnosis, theoretical mean dose, and muscles infiltrated with the 3 types of BoNT-A analysed. The cost of treatment for upper-limb spasticity in adult patients in that study was €291.43 for OnatoxA at initial doses, €702.08 for OnatoxA at average doses, and €1271.69 for AbotoxA at maximum doses, for the least costly procedures. In the case of children with cerebral palsy, costs amounted to €331.17 for initial and average doses and €529.87 for maximum doses; in all cases, OnatoxA was the least costly drug. Our study considered the real doses administered. AbotoxA is less costly than the other 2 types of BoNT-A, taking into account individual infiltration procedures, and OnatoxA is the least costly if we consider the whole treatment period. However, the study by de Andrés-Nogales et al.<sup>11</sup> is not comparable to our own since it presents only theoretical data, whereas our study presents data on the real doses used in clinical practice.

Roze et al.<sup>8</sup> studied the theoretical cost of treatment for upper-limb spasticity in 19 countries; AbotoxA was found to be the least costly option in 18 of these. This finding is consistent with our results: in our study, AbotoxA was less costly than OnatoxA and IncotoxA for each individual session, although this was not the case for the whole treatment period.

Tapias et al.<sup>5</sup> analysed the cost of treatment with BoNT-A for pes equinus in children with cerebral palsy. They only compared OnatoxA and AbotoxA, and concluded that the latter was the less costly treatment (€631.23 vs €839.56). IncotoxA was not included in the comparison since the drug is not indicated for children. These results stand in contrast with our own. This may be due to the fact that while the retrospective study by Tapias et al.<sup>5</sup> was based on real doses, it analysed a single problem (pes equinus in cerebral palsy), whereas our patients were adults with spasticity of various aetiologies. Furthermore, the study by Tapias et al. did not apply the Spanish Royal Decree-Law 16/2012 on resource optimisation, which allows the same vial to be used for different patients. In a similar study including the same type of patients (children with cerebral palsy), Houltram et al.<sup>12</sup> calculated that treatment with BoNT-A cost \$595 for hemiplegia and \$1045 for diplegia, and was effective and safe, with only a slight increase in direct medical costs per patient per year.

Ward et al.<sup>13</sup> studied a decision tree model based on the Delphi method in the United Kingdom, and compared the outcomes of oral therapy, BoNT-A alone, and BoNT-A as a second-line treatment after oral therapy. The cost of BoNT-A as a first-line treatment was estimated at £942; the authors concluded that first-line BoNT-A is effective for the treatment of post-stroke spasticity. The study also calculated a mean time of 30 minutes per patient contact, with a cost of £54.50 for physician care and £19.50 for nurse care. Patient contact times were similar to those observed in our unit, although physician care is considerably more costly in the study by Ward et al.<sup>13</sup> (£54.50 vs €16.20). Furthermore, while Ward et al. report a mean of 4 sessions per year, patients in our sample were attended a mean of 2.32 times per year.



**Table 6** Total annual cost of treatment.

	OnatoxA	AbotoxA	IncotoxA	Total
No. sessions for upper-limb spasticity	47	79	67	193
No. sessions for lower-limb spasticity	97	127	93	317
Cost of healthcare professionals				
Physician	€2205.9	€3123.9	€2411.1	€7740.09
Nurse	€1139.21	€1654.51	€1276.99	€4070.71
Cost of expendable materials	€129.6	€185.4	€144	€459
Cost of botulinum toxin A	€31 993.22	€38 561.71	€33 964.16	€104 519.09
Total	€35 467.93	€43 525.52	€37 796.25	€116 789.70

Schnitzler et al.<sup>4</sup> estimated the cost of BoNT-A treatment in France at €1559 per year and €652.23 per session. They used OnatoxA and AbotoxA, making no distinction between the 2 drugs. Cost estimations include the price of BoNT-A and also such indirect costs as staffing and equipment costs. In that study, healthcare staff costs (€57 046/year for physicians) are similar to our estimates (€13.5/session for upper-limb spasticity and €16.2/session for lower-limb spasticity). It should be noted that France and Spain have different healthcare funding systems.

The studies available in the literature also present differences in the infiltration schedule. In our study, we scheduled periodic consultations at our unit, with a mean time between infiltrations of 134.77 days. Although the different types of BoNT-A presented statistically significant differences, these cannot be considered clinically significant, given the consultation scheduling system used at our unit. Sanz-Granda et al.<sup>6</sup> compared the outcomes of 2 different forms of scheduling (fixed vs flexible intervals) for the treatment of blepharospasm and cervical dystonia, and concluded that IncotoxA at flexible intervals was more cost-effective than OnatoxA at fixed intervals. The study conducted by Arroyave et al.<sup>14</sup> in children with cerebral palsy in Mexico established a period between infiltrations ranging from 84 to 138 days.

In the assessment of outcomes by type of BoNT-A and mean age, although statistical analysis yielded significant differences, these results are not valid from a clinical viewpoint due to the design of the study. Many patients had been receiving treatment before the study period, some since childhood, and the type of BoNT-A used frequently remained unchanged, which prevents us from establishing an association between age and type of BoNT-A. Furthermore, IncotoxA is not indicated for children, which may also explain the higher mean age in the group of patients treated with this type of BoNT-A.

Our study has a number of limitations.

Firstly, it is a retrospective study. Secondly, the decision to administer one type of toxin or another is based on the experience and subjective judgement of the physicians

responsible for the treatment. Dose adjustment between sessions is based on treatment effectiveness, which is determined by clinical practice. We assumed that the 3 types of BoNT-A were equally effective and that dose adjustments in a single patient were due to fluctuations in clinical status rather than to underdosing.

Furthermore, the different types of BoNT-A used have different properties, composition, and storage requirements, and no study has established equivalence between units; it is therefore not possible to establish direct comparisons between drugs, even in terms of costs.<sup>15</sup>

Our department has a unit specialising in the management of adult patients with spasticity, with consultations held 2 days per week; this enables resource optimisation as vials can be used more efficiently. However, departments attending patients at normal consultations, rather than at specialised units, are more likely to waste units of BoNT-A due to the drug's stringent storage requirements.

Randomised, prospective studies should be designed to evaluate the efficacy of this treatment with spasticity and quality of life scales. This would allow us to draw conclusions on the cost of spasticity treatment with BoNT-A in clinical practice with a view to making informed decisions about the most suitable intervention in each case.<sup>16</sup>

## Conclusions

The use of BoNT-A for the treatment of spasticity in adult patients in our department shows a similar trend to those of previous studies: AbotoxA seems to be the least costly drug for individual sessions, whereas OnatoxA is the least costly over a one-year treatment period. Differences in pricing, the wide range of indications, and the inability to establish direct comparisons between the 3 types of BoNT-A analysed prevent us from recommending any specific drug solely based on economic criteria.

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## Conflicts of interest

Dr Hernández has received travel expenses from Allergan, Ipsen, and Merz for attending congresses and courses, although he has received no compensation for participating in this study that might constitute a conflict of interest.

Dr Miangolarra Page has no conflicts of interest to declare.

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