

Fabio Palazzo  
Francesco S. Mennini  
Laura Fioravanti  
Laura Piasini  
Gabriella Coloprisco  
Paolo Martelletti

## A one-year prospective costing study of botulinum toxin type A treatment of chronic tension headache

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F. Palazzo  
National Research Council,  
Institute for Population Research and Social  
Policies,  
Rome, Italy

F.S. Mennini • L. Fioravanti • L. Piasini  
CEIS Centre for Health Economics and  
Health Care Management,  
School of Economics,  
University of Rome Tor Vergata,  
Rome, Italy

G. Coloprisco • P. Martelletti (✉)  
Department of Internal Medicine,  
Regional Referral Headache Centre,  
2nd School of Medicine,  
University of Rome La Sapienza,  
Sant'Andrea Hospital,  
Via di Grottarossa 1035,  
I-00189 Rome, Italy  
e-mail: paolo.martelletti@uniroma1.it  
Tel.: +39-06-8034-5250/5684  
Fax: +39-06-8034-5323

**Abstract** The objective was to measure the cost of botulinum toxin type A (BTX-A) treatment of chronic tension-type headache. A prospective pharmaceutical costing analysis was completed in the Day Hospital of the Regional Referral Headache Centre at Sant'Andrea Hospital in Rome, chronic tension-type headache patients were treated from February 2003 to January 2004. Patients were treated with 100 U of BTX-A every three months for one year by using the Fixed Doses Fixed Sites procedure. The cost of treatment was based on drug acquisition costs, supplies and professional time needed to administer treatment. The average cost of conventional headache medications was € 853.43 before BTX-A treatment, and € 450.47 after. The cost of BTX-A treatment was € 642.00. Adding the cost of adjunctive conventional medications brought the

total cost of BTX-A treatment to € 1092.47. BTX-A treatment reduced use of conventional headache medications and expenditures although the net cost of treatment increased with BTX-A use.

**Key words** Chronic tension-type headache • Costs • Botulinum toxin type A

### Introduction

A retrospective analysis of the efficacy of botulinum toxin type A (BTX-A) treatment of chronic tension-type headache found that 85% of patients experienced at least some degree of pain relief and reduced their use of anal-

gesics as a result of BTX-A treatment [1]. BTX-A may be a promising alternative to conventional headache treatments. Concurrent to the retrospective analysis, we conducted a prospective costing study in the same patients to identify and measure all pharmaceutical expenditures involved in using BTX-A in the management of chronic tension-type headache.

## Methods

### Objective

The purpose of this analysis was to assess the cost of BTX-A in the treatment of chronic tension-type headache using the principles outlined by Sofio and colleagues [2].

### Design

The study was divided into two parts: part one was a one-year retrospective analysis of headache medication utilisation patterns after BTX-A treatment of chronic tension-type headache as previously described in part one [1]; and part two was a prospective analysis of treatment costs before and after BTX-A treatment. BTX-A was administered at the standard dosage of 100 units [U] every 90 days for a period of one year. The Fixed Doses Fixed Sites (FDfS) procedure has been followed in the administration of BTX-A.

### Participants

A group of 100 chronic tension headache patients were selected among the patients entering the Day Hospital of the Regional Referral Headache Centre at the Sant'Andrea Hospital in Rome in the period February 2003 to January 2004. The patients gave their informed consent to the study, which has previously been approved by the Local Ethics Committee.

### Outcome measures

The primary outcome measure was the cost of one year of headache treatment before and after administration of 4 BTX-A treatments. A secondary outcome measure was the loss of productivity in terms of annual working days lost as reported by appropriate questionnaires submitted to patients.

### Determining the cost of headache treatments

Included in the cost of headache treatment was the cost of BTX-A; the cost of supplies (surgical cotton, gloves, a syringe and alcohol); the professional time needed to administer treatment (determined by clinical experience as 20 min of clinician time and 40 min of nursing time); and the costs of conventional headache treatments instead of, or adjunctive to, BTX-A.

The costs of conventional headache medications were based on drug acquisition costs, the average cost of the first treatment profile (those patients that did not modify their initial therapy) and the incremental cost for subsequent modifications of treatment before and after administration of BTX-A. A direct survey of drug costs based on consumptions by single patients as reported through appropriate questionnaires was used [3].

### Statistical analysis

Intervals of reliability of 90%, 95% and 99% were calculated to express the interval of reliability of the sample-group estimate. The interval of reliability is a key parameter when the sample-group variability – a consequence of the limited number of cases observed – can potentially influence the interpretation of the results.

## Results

BTX-A treatment cost € 141.00 per treatment. At four treatments per year, the cost of one year of BTX-A treatment based on acquisition expenditures was € 564.00. Additional costs, as described in Methods, amounted to € 78 per patient (€ 19.50 4 administrations). Therefore, the total annual cost of BTX-A treatment per patient was € 642.00.

Before the administration of BTX-A, the average cost of conventional headache medications was determined to be € 853.43, with a minimum cost of € 87.70 and a maximum cost of € 3010.85.

Intervals of reliability were determined as follows: at 90% the limit figures were € 737.18 and € 969.67; at 95% the limit figures were € 714.50 and € 992.36; at 99% the limit figures were € 671.97 and € 1034.89.

The average cost of conventional headache medications dropped to € 450.47 after administration of BTX-A (min € 45.34 and max € 1354.76).

Intervals of reliability were determined as follows: at 90% the limit figures were € 395.72 and € 505.23; at 95% the limit figures were € 385.03 and € 515.91; at 99% the limit figures were € 365.00 and € 535.94.

The average cost of the first treatment regimen and the additional cost for subsequent modifications of the treatment regimen (with respect to the initial regimen) were calculated. Only 16 patients followed the initial treatment regimen with no subsequent modifications, at an average cost of € 666.65. A total of 14 patients modified the initial regimen once with an average additional cost of € 395.75; 28 patients modified the initial regimen twice with an aver-

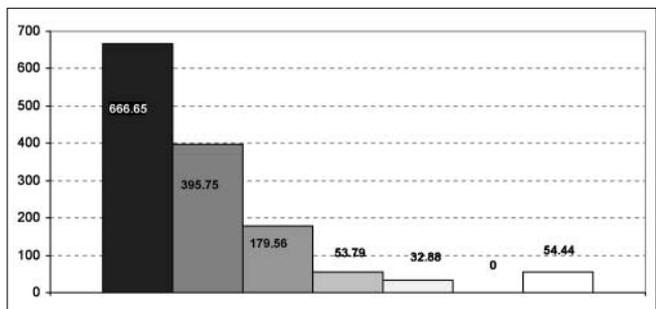


Fig. 1 Average additional cost per treatment episode (€)



**Table 1** Number of working days lost annually

Working activities	Male					Female				
	People	Before		After		People	Before		After	
		Total	Average	Total	Average		Total	Average	Total	Average
Workers	1	10	10.0	8	8.0	5	59	11.8	32	6.4
Public salaried employees	8	92	11.5	67	8.4	22	227	10.3	141	6.4
Private salaried employees	6	57	9.5	34	5.7	26	243	9.3	137	5.3
Self-employed	3	14	4.7	9	3.0	7	38	5.4	16	2.3
Students	1	13	13.0	9	9.0	3	39	13.0	23	7.7
Housewife	0					18	225	12.5	131	7.3
Total	19	186	9.8	127	6.7	81	831	10.3	480	5.9

Another important aspect was comparison in terms of loss of productivity calculated through annual working days lost for each working category. Even this analysis was possible only using appropriate questionnaires submitted to patients.

Before BTX-A treatment, the average number of days of work lost per year caused by chronic tension headache were 9.8 days for males and 10.3 days for females. After BTX-A treatment, the average number of lost working days was reduced to 6.7 days per year for males and 5.9 days for females (Table 1).

## Discussion

The results of this economic evaluation revealed a cost of € 853.43 for one year of chronic tension-type headache treatment using conventional medications. After one year of BTX-A treatment, the annual cost of conventional medications fell to € 450.47. The cost of one year of BTX-A treatment was determined to be € 642.00, a figure that includes drug costs, supplies and the time used by medical personnel in administering treatment. The cost of one year of BTX-A treatment of chronic tension-type headache with adjunctive conventional medications was € 1092.47.

BTX-A treatment led to an important reduction of annual lost working days, from an average of 10.1 days to 6.3 days (average of both sexes).

The overuse of various analgesic drugs can lead to the development of a secondary headache disorder, medication overuse headache (MOH), as described in the recently revised 2004 International Headache Society classification [4]. MOH represents an obstacle for the success of any headache treatment regimen and remains a major cause of incremental cost increases for drug expenditures for the treatment of chronic tension headache [3, 5].

BTX-A treatment has been shown to be safe and efficacious in the treatment of a variety of headache types [6–11], and, in several trials, reductions in analgesic use and expenditures have been demonstrated [11, 12]. The results of this trial suggest that BTX-A treatment results in a marked reduction in the use and expenditures associated with conventional headache treatments and may, therefore, impact the incidence of MOH.

Further studies are needed to measure the overall global burden of headache [13] and its socioeconomic impact [14] as it applies to chronic tension headache. There is also a dearth of literature focussed on the impact of chronic tension headache on quality of life and working activities. Most of the headache studies that focused on quality of life or loss of productivity relate to the burden of migraine headache [15–20]. Studies assessing the potential impact of BTX-A treatment on the economic, societal and quality of life burden of chronic tension headache would be of great interest.

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## References

- Mennini FS, Fioravanti L, Piasini L, Palazzo F, Coloprisko G, Martelletti P (2004) A one year retrospective economic evaluation of botulinum toxin type A treatment of chronic tension headache. *J Headache Pain* (*in press*)
- Sofio AD, Mazzuca F, Mennini FS (2003) General disease costing principles. *J Headache Pain* 4:S55–S58
- Coloprisko G, De Filippis S, Santi PG, Fiore G, Rodio A, Martelletti P (2003) Reduction in expenditure on analgesics during one year of treatment of chronic tension headache with BoNT-A. *J Headache Pain* 4:88–91

4. – (2004) The international classification of headache disorders, 2nd edn. Headache Classification Subcommittee of the International Headache Society. *Cephalalgia* 24:S1–S150
5. Iannazzo S, Cattaruzza MS, De Filippis S et al (2003) Analgesic therapy for headache: consumption, appropriateness and costs. *J Headache Pain* 4:S84–S87
6. Dodick DW (2003) Botulinum neurotoxin for the treatment of migraine and other primary headache disorders: from bench to bedside. *Headache* 43[Suppl 1]:25–33
7. Blumenfeld A (2003) Botulinum toxin type A as an effective prophylactic treatment in primary headache disorders. *Headache* 43:853–860
8. Silberstein S, Mathew N, Saper J, Jenkins S, for the BOTOX® Migraine Clinical Research Group (2000) Botulinum toxin type A as a migraine preventive treatment. *Headache* 40:445–450
9. Troost BT (2004) Botulinum toxin type A (BOTOX®) in the treatment of migraine and other headaches. *Expert Rev Neurother* 4:27–31
10. Smuts J, Baker M, Smuts H (1999) Prophylactic treatment of chronic tension-type headache using botulinum toxin type A. *Eur J Neurol* 6[Suppl 4]:S99–S102
11. Barrientos N, Chana P (2003) Botulinum toxin type A in prophylactic treatment of migraine headaches: a preliminary study. *J Headache Pain* 4:146–151
12. Schim J (2004) Effect of preventive treatment with botulinum toxin type A on acute headache medication usage in migraine patients. *Curr Med Res Opin* 20:49–53
13. Olesen J, Leonardi M (2003) The burden of brain diseases in Europe. *Eur J Neurol* 10:471–477
14. Marini A, Colombo GL, Pana A et al (2002) Social cost of diseases: methods and impact in health system. *Ig Sanita Pubbl* 8:315–316
15. Dahlof CG (2003) Measuring disability and quality of life in migraine. *Drugs Today* 39[Suppl D]:17–23
16. Fairclough DL, Gagnon D, Papadopoulos G (2004) Planning analyses of quality-of-life studies: a case example with migraine prophylaxis. *J Biopharm Stat* 14:31–51
17. Terwindt G, Ferrari MD, Launer LJ (2003) The impact of headache on quality of life. *J Headache Pain* 4:S35–S41
18. Prasad M, Wahlquist P, Shikar R, Shih YC (2004) A review of self-report instruments measuring health-related work-productivity: a patient-reported outcome perspective. *Pharmacoeconomics* 22:225–244
19. Stewart WF, Ricci JA, Chee E, Morganstein D, Lipton R (2004) Lost productive time and cost due to common pain condition in the US workforce. *JAMA* 290:2443–2454
20. Loeppke R, Hymel PA, Lofland JH et al (2003) Health-related workplace productivity measurement: general and migraine specific recommendations from the ACOEM Expert Panel. *J Occup Environ Med* 45:349–359