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RAPID COMMUNICATION

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Reduction in expenditures on analgesics during one year of treatment of chronic tension headache with BoNT-A

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Abstract The aim of this study was to investigate the impact of the use of botulinum toxin type A (BoNT-A; BOTOX; Allergan, Inc.; Irvine, CA) as preventive treatment of chronic tension-type headache (CTH) on analgesic use and expenditure.
This was a prospective, single-center, 1-year, open-label study of the effect of BoNT-A treatment on acute analgesic use and expenditure in CTH patients.
A structured headache questionnaire, which included questions about medication costs, was completed by CTH patients attending a specialist headache clinic in Rome prior to BoNT-A injections. Repeat injections were administered every 3 months for up to 1 year. Patients were required to complete the questionnaire prior to each injections cycle. A pharmacoeconomic analysis was performed at each assessment to determine the effect of BoNT-A treatment on analgesic use and expenditure.
Three hundred questionnaire were distributed and 296 (98%) were completed. The study population consisted of 67.8% (201) females and 32.2% (95) males, with a mean age of 46.7±16.1 years.
The economic evaluation of the pharmacologic treatment of CTTH was conducted on the 101 (34.12%) patients who gave complete information on posology. Pharmacoeconomic data analysis focused on the whole group using analgesics compared to those who self-prescribed and those who turned to health specialists before and after treatment with BoNT-A.
Prior to treatment with BoNT-A the median monthly pharmaceutic expenditure per patient was euro (€) 24.30 for the whole group using analgesics, and € 34.93 and € 18.51 for the "self-prescribers" and the "prescribed by specialist" groups, respectively.
Median monthly pharmaceutic expenditure decreased significantly for the whole group ($p<0.001$), the "self-prescribers" ($p<0.01$), and the "prescribed by specialist" group ($p<0.002$) (3rd month: € 13.3, 9.3, 7.2, respectively; 6th month: € 8.9, 9.0, 4.1, respectively; 9th month: € 5.7, 12.4, 3.0, respectively; 12th month € 4.1, 9.8, 3.4, respectively).
BoNT-A treatment produced significant reductions in both analgesic use and expenditure. The data suggest that consultation with a specialist would be helpful in patients with CTTH.
Cooperative studies on cost analysis of chronic daily headaches, including both CTTH and chronic migraine, comparing the economic cost package borne by patient and community both before and after treatment with BoNT-A, are warranted. However, in the near future additional studies to compare clinical efficacy of BoNT-A in CTTH with its painkiller use/expenditure in the control of pain are needed in order to avoid any possible interference due to placebo effect.

Introduction

Tension headache (TH) is the most common forms of chronic headache, with a lifetime prevalence in the general population as high as 30% [1]. The socioeconomic burden of TH includes both direct costs associated with healthcare utilization and costs associated with missed work due to reduced efficiency or absence. The individual and socioeconomic burdens of TH are substantial. A study of a Danish population reported 870 workdays lost per 1000 people for migraine [2].

The cost of managing TH for both patients and the healthcare system is a critical issue in terms of drug consumption and the treatment of conditions resulting from analgesic overuse [3, 4]. Chronic tension headache (CTH; frequency of headache ≥15 days/month) substantially increases analgesic expenditure in headache disorders [5]. There are few effective preventive drugs for CTH. Botulinum toxin type A (BoNT-A) is a focally acting neurotransmitter from presynaptic nerve endings at the neuromuscular junction that results in muscle relaxation. Treatment with BoNT-A is a safe and efficacious treatment of CTH and migraine [6–8]. Although its mechanism of action in headache disorders is unknown, BoNT-A may have antinociceptive effects apart from its muscle-relaxing actions [9]. The aim of this study was to investigate whether preventive treatment of CTH with BoNT-A may have an impact on analgesic expenditure.

Materials and methods

Patients

The study enrolled CTH inpatients attending the Day Hospital of the Headache Centre (DHHC) of La Sapienza University, Sant'Andrea Hospital in Rome. No patient that had received BoNT-A for cosmetic reasons during the previous 3-month period was admitted into the study. The period of study ranged from March 2002 to March 2003.

The protocol was approved by Sant'Andrea Hospital's Institutional Ethics Committee. All patients who entered the study gave written informed consent.

Study design

This was a prospective, single-center, 1-year, open-label pharmacoeconomic study of the effects of BoNT-A treatment on analgesic expenditure in the management of CTH.

Upon admittance to DHHC, patients were administered an anonymous headache questionnaire dealing specifically with analgesic use and expenditure. Thereafter, patients were injected with 75–100 U BoNT-A (Botox; Allergan, Irvine, USA) at the referred pain sites. We followed the dosing guide per single muscles as suggested by basic Siberstein [8] and the protocol "fixed sites fixed doses" (FSFD) with a maximun BoNT-A dosage of 100 U per session. BoNT-A was reconstituted and diluted in sterile saline at a concentration of 100 U/ml. The starting dose was 75 U for all patients. Injections were administered every 3 months for up to 1 year. Patients were required to complete the headache questionnaire prior to each injection cycle.

The use of analgesics and the associated costs were calculated at baseline and during the treatment period on the basis of data from the questionnaire. Statistical analysis was performed using Student's *t* test for paired data.

Results

Three hundred questionnaires were distributed and 296 (99%) were completed. The study population consisted of

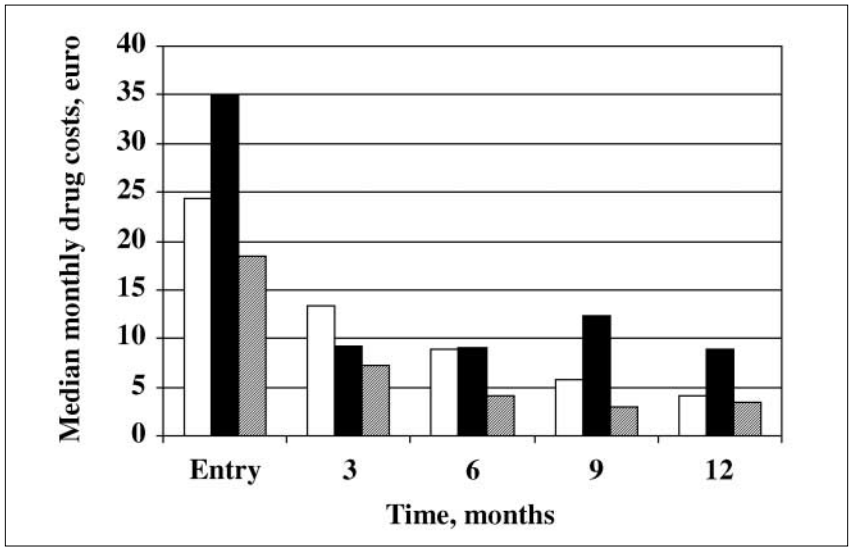

Fig. 1 Median monthly drug expenditures for 101 patients with chronic tension headache, by study group. □, whole group of CTH patients; ■, self-prescribers; ▨, prescribed-by-specialists group

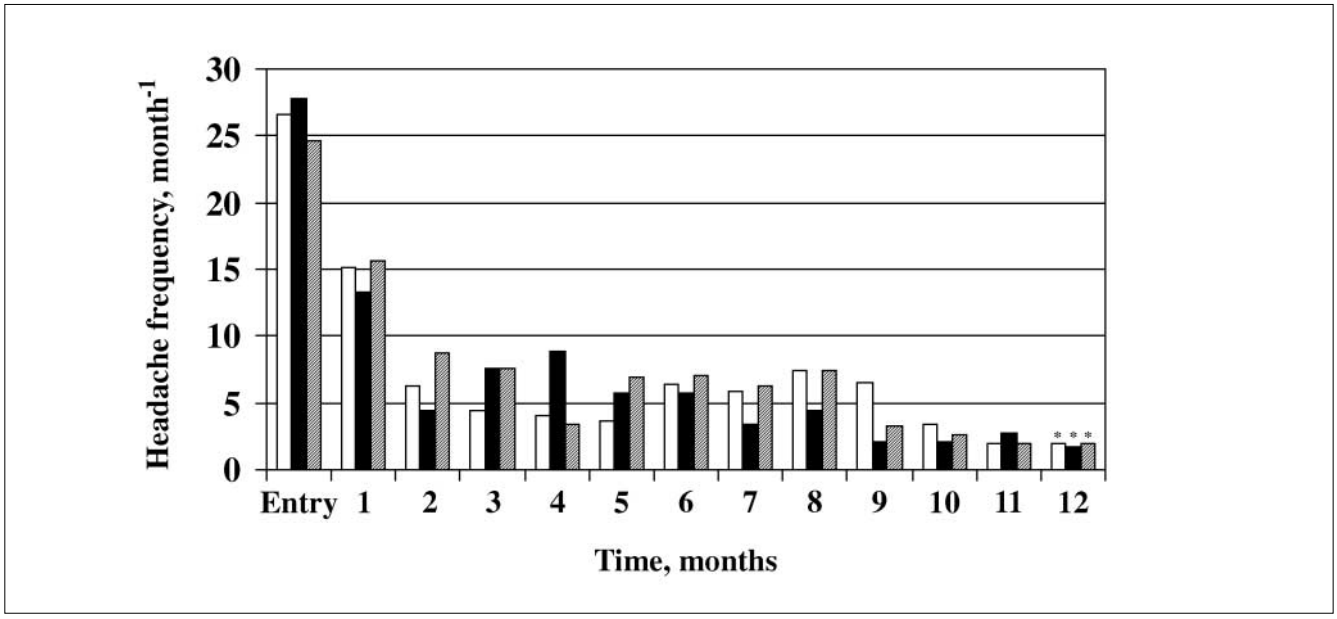

Fig. 2 Clinical efficacy of BoNT-A as preventive treatment in 101 CTH patients, by study group. Frequency of headache per month was calculated from the patients' headache diaries. □, whole group; ■, self-prescribers group; ▨, prescribed-by-specialists group. *p<0.05 for all groups at 12 months vs. study entry

201 women (67.9%) and 95 men (32.1%), with a mean age of 46.7 years (SD=16.1 years). The pharmacoeconomic effect of preventive BoNT-A treatment for CTH was conducted on the 101 patients (34.1%; 77 women; mean age 43.7 years; SD=13.5 years) who gave complete information on posology and completed the entire 1-year treatment period. The 101 patients were subdivided into 2 groups on the basis of how they obtained analgesics: 57 (56.4%) patients self-prescribed analgesiscs while 44 patients (43.6%) turned to medical specialists for prescriptions.

The mean distribution of costs for analgesics was strongly skewed to the right due to a few expensive treatments, therefore, only the median is reported. Pharmacoeconomic analysis focused on the whole group using analgesics (n=101), as well as on the "self-prescribers" and "prescribed-by-specialists" groups. Prior to treatment with BoNT-A, the median monthly drug expenditures per patient were euro (€) 24.30 for the whole group using analgesics, and € 34.93 and € 18.51 for self-prescribers and the prescribed-by-specialists groups, respectively (Fig. 1). Median monthly drug expenditure decreased significantly relative to baseline at each assessment point for the whole group (p<0.001), for self-prescribers (p<0.01), and for the prescribed-by-specialist group (p<0.002).

The evaluation of clinical efficacy of BoNT-A treatment in these CTH patients by comparing data from headache diaries revealed a parallel decrease in headache frequency during the 1-year treatment period (Fig. 2).

Discussion

BoNT-A treatment produced decreases in analgesic use that resulted in significant reductions in analgesic expenditure. Reductions appeared to be cumulative over the 12-month period of observation and matched with a reduction in headache frequency assessment during the 1-year treatment period. This open, non-controlled study suggests that BoNT-A reduces overall CTH clinical symptoms and that in these groups of CTH patients the consultation with a specialist helps to reduce overall analgesic expenditure and use during BoNT-A treatment.

Cooperative studies on cost analysis, including assessment of quality of life, disability and indirect costs of chronic daily headaches, including both CTH and chronic migraine, comparing the economic cost borne by the patient and the community both before and after treatment with BoNT-A, are warranted. Additionally, a better harmonization in the utilization of this promising therapeutic class, as previously suggested for migraine acute therapy [10], is necessary.

This financial study shall be accompanied by an economic evaluation to measure the broader expenses incurred by public and private services in the management of CTH. Additionally, a more complete picture of the impact of BoNT-A therapy on CTH should be established by coupling pharmacoeconomic and quality of life assessments. However, despite these encouraging results, the definitive inclusion of BoNT-A as preventive treatment for CTH must be established after the completion of double-blind, placebo-controlled studies in a large series of CTH patients.

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