J Headache Pain (2006) 7:317–319
10.1007/s10194-006-0341-z

SPOTLIGHT

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# The road ahead for chronic headache patients

Published online: 25 October 2006

Unkind, almost abrasive, judgements regarding the value of prophylaxis therapy with botulinum neurotoxin type A (BoNTA; BOTOX) in chronic headache continue to appear in journals in this field [1–3]. In view of the increasingly widespread use of this new therapeutic opportunity, the controversy is raging. Semantic discussion about the interpretation of frequent new reports assessing BoNTA's efficacy, both in open or double-blind studies [4–10], has created factions for and against, both with proponents of high rank [2, 11].

On the other hand, the international medical community is going through a phase of great expectations for a therapeutic possibility that could fill the enormous void in prophylaxis in chronic forms of headache. In fact, except for topiramate, this area presents molecules discovered on average 25–30 years ago, with a limited efficacy in time and often unacceptable side effects.

I believe a remark on the reasons should be made.

First of all, the treatment of chronic daily headache (CDH) is still inadequate. Effective, well tolerated prevention represents the ultimate goal for complete rehabilitation of CDH patients. Medication overuse headache is often superimposed on CDH, causing the re-prophylaxis phase schedule after detoxification to be inadequate and providing short-term relief given by the few existing "old-fashioned" prophylaxis drugs. The number of patients with CDH, including all the clinical forms mentioned in the definition, is growing. With respect to chronic tension-type headache, chronic migraine, transformed migraine, hemicrania continua and new daily persistent headache, as the various facets of CDH, the therapeutic armamentarium is still based on old drugs: antidepressants (tricyclics) and non-steroidal anti-inflammatory drugs (NSAIDs); and the new entry topiramate. Nothing more. There is an evident paucity of EBM-based current treatments used in CDH prevention. Both topiramate and BoNTA seem to represent – in terms of efficacy – the most convincing options in the operational therapeutic scenario of CDH. Nevertheless, the incidence of adverse events (AEs) should always be considered in the therapeutic choice of these chronic disorders, which are often complicated with MOH.

A retrospective analysis of both open and double-blind studies on the efficacy of BoNTA in CDH, with or without MOH, showed conflicting results. Negative results in such trials appear to be explained with a bias in the selection of CDH patients with MOH.

BoNTA's prevention mechanism for CDH is not completely known, and probably not only based on neuromuscular junction Ach inhibition. BoNTA may have a distinct antinociceptive mechanism or inhibition of CGRP release, SP and other neuropeptides at trigeminal levels, as suggested by studies on animal models [12]. Also, scientific evidence on BoNTA mechanisms of action supports its efficacy on migraine through suppressive activity on pain, flare and hyperalgesia induced by capsaicin injection in the forehead [13].

Furthermore, it is necessary to mention a series of pharmacoeconomic analyses, which find the assumption that BoNTA therapy represents a high-cost alternative compared to traditional treatments to be untrue.

Recently, an analysis of BoNTA's efficacy as a preventive treatment for chronic tension-type headache (CTTH) has illustrated its impact on headache pharmaceutical utilisation and costs.

A retrospective chart review on the efficacy of BTX-A preventive treatment in a large series of CTTH patients has been followed by a one-year prospective analysis of headache pharmaceutical utilisation and costs before and after BoNTA treatment. A direct survey of pharmaceutical consumption per patient has been carried out with appropriate questionnaires [14, 15]. Pharmaceutical average costs and incremented (additional) average costs criteria were used for the periods before and after BoNTA treatment.

The retrospective chart review revealed that BoNTA treatment resulted in 26% of patients with a total absence of pain and substantial reduction in pharmaceutical use; 37% of patients reported significant pain reduction and significant reduction in pharmaceutical use; 22% of patients reported some pain reduction and a slight reduction in pharmaceutical use; and 15% of patients reported no effect or "possible" worsening of pain and no reduction in pharmaceutical use [15]. A subsequent one-year prospective analysis revealed that after BoNTA treatment there was a 45% reduction in the consumption of analgesics/antimigraine drugs, a 35% reduction of NSAIDs and a 100% reduction of other off-label prophylactic agents. The average costs of medications had been reduced from € 853.43 before BoNTA treatment to € 450.47 afterwards [16]. The overall conclusion of these studies displayed, together with BoNTA's efficacy for CTH, a substantial reduction of headache medication utilisation and costs. This completely contradicts the high-cost hypothesis for this innovative therapy.

We can reasonably affirm that BoNTA is efficacious, safe and convenient, especially in CDH patients not affected by drug abuse following the acute treatment of headache itself.

Therefore, from a pragmatic EBM perspective, we must consider a non-hostile attitude towards this new advancing therapeutic opportunity to be ethically correct, based on the homogeneous and widespread demand of an increasing number of patients [17]. Contrasting information could produce uncertainty in the headache scientific body, which reached its credibility with difficulty that becomes sometimes still threatened by dangerous rifts. A negative attitude should be avoided, at least until BoNTA's registration phase is complete and a final consensus has been reached.

All these data and considerations demand that we do not deny our CDH patients a new pathway, which seems to lead to an innovative and efficacious prophylaxis therapy [18].

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