Neurol Sci (2010) 31:411–415
DOI 10.1007/s10072-010-0229-1

REVIEW ARTICLE

Is idiopathic intracranial hypertension without papilledema a risk factor for migraine progression?

Roberto De Simone · Angelo Ranieri · Chiara Fiorillo · Leonilda Bilo · Vincenzo Bonavita

Received: 12 October 2009 / Accepted: 20 January 2010 / Published online: 25 February 2010

Abstract The association of chronic migraine (CM) with an idiopathic intracranial hypertension without papilledema (IIHWOP), although much more prevalent than expected in clinical series of CM sufferers, is not included among the risk factors for migraine progression. We discuss the available evidence supporting the existence of a pathogenetic link between CM and idiopathic intracranial hypertensive disorders and suggest a causative role for IIHWOP in migraine progression.

Keywords Chronic migraine · Idiopathic intracranial hypertension · Idiopathic intracranial hypertension without papilledema · Medication overuse headache · Central venous stenosis · Review

Progression of migraine

Convergent clinical, functional and anatomical evidences indicate that migraine can progressively worsen leading to an almost daily condition [1–6]. Chronic migraine (CM) taxonomy has evolved in recent years. The current ICHD-II criteria for CM [7] have resulted unpractical because of their low sensitivity [8]. The new appendix criteria for CM issued in 2006 (ICDH-II R CM) [9] have proven to be as sensitive [10–12] as those proposed for transformed migraine (TM), a subtype of chronic daily headache (CDH), by Silberstein and Lipton [13]. The use of appendix criteria for CM has been strongly recommended to allow its extensive field testing considering a possible inclusion into the next classification revision. Still, in the present review we will refer also to clinical and epidemiological papers published before the release of appendix criteria of 2006. In such cases, we will use the terms CDH, TM, ICDH-II CM; according to the actual criteria set chosen by the authors for patients selection.

Population prevalence of TM with or without medication overuse is about 1–2% [14]. Therefore, this condition is emerging as a dramatic worldwide health problem, with a deep impact on both direct and indirect social costs [15–17]. Chronification of migraine is characterized by a progressive increase in headache frequency and duration, often parallel to the reduction in pain intensity and accompanying symptoms. The process goes on over months or years, ultimately leading to a continuous mild pain with superimposed exacerbations of moderate to severe migrainous pain. Several evidences support such an evolution [3–6].

A longitudinal survey [5] has shown that infrequent episodic headache sufferers (2–104 days per year) carry a 6% annual risk to progress to a frequent episodic pattern (105–179 days per year) and a 3% annual risk to develop a chronic condition. In the same study, a spontaneous return to a frequent or infrequent episodic pattern (<180 days per year) was observed in 57% and to <1 attack per week in 14% of chronic sufferers. These data suggest that some migraine patients are at a risk for a progressive headache worsening and that progression of migraine is a clinically dynamic and reversible event. These observations highlight

R. De Simone (✉) · A. Ranieri · L. Bilo
Headache Centre, Department of Neurological Sciences, University of Naples "Federico II", via Pansini, 5, 80131 Naples, Italy
e-mail: rodesimo@unina.it

C. Fiorillo · V. Bonavita
Istituto Di Diagnosi e Cura Hermitage Capodimonte, Naples, Italy

the need for a prompt identification of population at a risk and of factors associated with both the progression of migraine and the possible return to an episodic pattern.

Factors involved in migraine progression: focus on medication overuse

Non-modifiable risk factors associated with the progressive worsening of migraine include age, female sex, white race, low educational level, socioeconomic status and genetic factors. Among modifiable risk factors that include frequent migraine attacks, obesity, excessive use of acute medications, sleep disorders, caffeine overuse, stressful life events, depression and cutaneous allodynia [18, 19], medication overuse is the best known and the more investigated. Because discontinuation of overuse alone is followed by the return to an episodic pattern in about half of the patients [20], or by the restoration of responsiveness to prophylactic treatments in many of the non-responders [21], medication overuse headache (MOH) is recognized as causative factor for migraine progression. Consequently, it is classified as an autonomous entity among the secondary headaches. The new appendix criteria for MOH [9] eliminated the need for a return to an episodic pattern after a 2 months overuse discontinuation, so that a definite diagnosis can now be reached already at the first visit.

Interestingly, MOH only occurs in subjects with a previously episodic primary headache. Among 103 patients presenting to a rheumatology-monitoring clinic with a daily use of analgesics, 8 subjects (7.6%) developed a chronic headache and all of them had a previous episodic migraine [22]. However, episodic migraine prevalence in the rheumatologic patients who did not develop a chronic headache after a prolonged daily use of analgesics was much higher (40%), indicating that not all migraine subjects exposed to medication overuse actually progress towards a chronic form. On the other hand, according to existing population data, up to two-third [23, 24] of chronic headache sufferers do not overuse acute medications. Primary headaches progression sustained by medication overuse is not limited to migraine, but extended to the whole CDH spectrum [25]. This is in agreement with the medication overuse putative mechanism of action, attributed to a reversible central sensitisation of pain processing pathways mainly involving the thalamocortical level [26].

Thus, medication overuse remains the more common and the best-known factor associated with the chronic transformation of pain in episodic migraine subjects but it cannot be easily considered neither a sufficient nor a necessary factor for migraine progression.

Idiopathic intracranial hypertension (IIH) with and without papilledema

Idiopathic intracranial hypertension [27] is an infrequent and enigmatic condition almost always encountered in overweight or obese women of childbearing age. IIH is characterized by headache, often on a daily basis, papilledema, transient visual obscuration, diplopia and tinnitus. Symptoms arise from a hypertensive intracranial status which is not associated with any detectable cause. IIH may run without papilledema (IIHWOP) in some patients [28, 29], but its prevalence on general population is not known.

Stenosis of large intracranial venous sinuses can be found at magnetic resonance venography in almost all affected subjects and is considered as a reliable radiologic marker of intracranial hypertension with a high specificity (93%) and sensitivity (93%) [30]. There is evidence [31] of a venous pressure gradient across the stenosis with a potential effect in increasing the cerebrospinal fluid (CSF) pressure [32]. Conversely, the venous pressure gradient normalizes soon after sub occipital CSF subtraction [31] and the stenosis may reduce or resolve after a single 20-ml CSF subtraction with lumbar puncture [33] or after continuous CSF diversion procedures, such as lumboperitoneal shunt [34, 35]. These findings suggest that venous flow disturbances in IIH are more probably the effect of CSF hypertension, not its cause [36]. However, the placing of a self-expanding stent at the venous stenosis level is followed by the immediate and longstanding resolution of symptoms in most of the cases [37]. Thus, on one hand, an acute or continuous CSF subtraction may reduce the stenosis degree; on the other hand, the stenting of segmental venous narrowing at transverse sinus level may revert the CSF hypertensive status. Taken together, these findings indicate that, in IIH patients, sinus venous stenosis and CSF hypertension may influence each other in a circular way whose starting point may only arbitrarily be indicated. Since the CSF pressure is higher than central venous pressure (at least in clinostatic position), if a large central vein were not sufficiently rigid then it would be compressed as a consequence of transmural pressure gradient. Consequently, it can be speculated that in subjects harboring one ore more collapsible segments of central veins and exposed to an unknown CSF raising factor, the subsequent segmental venous narrowing and the related further CSF pressure rising may engage a positive feedback loop. This loop is self-limiting: once the maximum stretching of the venous wall is reached no further venous narrowing could parallel CSF pressure rising, leading to a relatively stable new balance at higher values of CSF and venous blood pressures [33]. The hypothesis of a causative "self-limiting venous collapse" in IIH pathogenesis that we proposed on the basis of clinical observations [33] is

supported by a series of independent and about simultaneous mathematic modeling studies [38, 39]. In subjects carrying one or more collapsible segment of large central venous collectors, the hypothesis of a self-limiting venous collapse may account at least for the maintenance of a hypertensive intracranial status induced by a different cause. It also gives full explanation of the relatively good prognosis of "benign" intracranial hypertension as compared to cerebral venous thrombosis, in which a venous hypertension is sustained by an endoluminal obstruction, a mechanism lacking any self-limiting property. Moreover, the proposed mechanism may explain the not infrequent long-term remissions observed in IIH patients after single or serial CSF subtraction by LP. In fact, the acute subtraction of even a small CSF volume, could account for a venous expansion that may in turn reduce CSF pressure, ultimately leading to the restoration of the previous relatively stable balance at physiologic CSF and venous pressure values.

In contrast, there is evidence of the persistence of the sinus venous stenosis at the RM venography in a small series of IIH/IIHWOP patients exhibiting a normalized intracranial pressure at follow-up while on medical treatment (acetazolamide and weight loss) [40]. However, according to the findings of an intracranial pressure monitoring study on 10 IIHWOP subjects presenting with a CDH [41], the CSF pressure may exhibit intraday, high amplitude, pulsatile course in such patients. While the opening pressure was found within normal limits in half of the cases and the mean resting CSF pressure (recorded along a 2–3 days of continuous CSF pressure monitoring) was only 118 $\pm$ 17 mm H_2O, slow waves of pathologically high CSF pressures (mean peak = 560 mm H_20) could be recorded in all patients, mainly at night. All cases in this series reported a dramatic improvement after shunt surgery. Thus, a single LP may fail to identify the possible persistence of CSF hypertension. Consequently, the finding of stenosis persistence in subjects with normalization of CSF pressure documented by a single LP does not argue against the possible role of venous flow disturbances in IIH pathogenesis.

Based on the reported observation, it can be hypothesized that in subjects harboring one ore more collapsible segments of central veins a "self-limiting venous collapse" may promote the development of a relatively stable CSF hypertension status, ultimately leading to the clinical picture of IIH with or without papilledema.

Is IIHWOP pathogenetically involved in progression of migraine?

Clinical presentation of IIHWOP may be limited to a mild to moderate continuous headache, thus resembling a chronic tension-type headache [42]. However, in most cases, superimposed recurrences of severe migrainous pain are reported, leading to a picture indistinguishable from that of TM [43]. According to the results of the first systematic study on the coexistence of IIHWOP in chronic headache sufferers [44] obesity and pulsatile tinnitus predicted the CSF hypertension while the headache profiles of CDH patients with IIHWOP did not differ from that of chronic headache sufferers without evidence of raised CSF pressure. As a consequence, IIHWOP is frequently misdiagnosed as TM/CM. In a clinical series of 85 TM patients diagnosed with chronic migrainous headache, Mathew et al. [43] found a 14% prevalence of IIHWOP. More recently, an IIHWOP has been diagnosed in 10% of 62 CM patients (diagnosed with either ICHD-II or ICDH-II R criteria for CM) referring to a Headache Centre [45]. In this paper, the MR venography of the subgroup with IIHWOP was reported as "normal" in all cases. This raised a criticism to the paper in which the possible use of a suboptimal imaging technique was hypothesized [46]. In their replay, the authors admitted that bilateral venous abnormalities were actually present in their series, but also in patients without IIHWOP. Unfortunately, they did not provide the prevalence data of the venous changes in the two groups. There is evidence that, in migraine patients, sinus venous stenosis predicts the presence of IIHWOP [47]. Unexpectedly, all migraine patients carrying bilateral transverse sinus stenosis in this series were episodic, a finding attributed by the authors to different methods to select patients for the diagnostic LP. IIH and CM share some relevant risk factors as: female gender, obesity and sleep disturbances [18, 48, 49]. Topiramate a drug with growing evidences of efficacy in CM [50, 51] shares with acetazolamide the inhibition of carbonic anhydrase isoenzyme [52]. Acetazolamide reduces intracranial hypertension and is widely used in IIH treatment [53]. Topiramate has been found effective in IIH treatment [54–56]. In a recent study, topiramate resulted as effective as acetazolamide in IIH treatment [56] suggesting that the efficacy shown by this drug in CM treatment could be related, at least partially, by an acetazolamide-like CSF pressure lowering effect.

IIH may occur without headache in non-migrainous individuals or in the course of a well-known migraine protective factor as pregnancy [57] suggesting that a CM-like clinical presentation of IIHWOP could require a migrainous predisposition. Thus, it can be speculated that, in non-migrainous subjects, IIHWOP may be associated with a mild to moderate tension-type pain, or may even run un-associated to any symptom or sign. This consideration rises the question of a possible relevant underestimation of IIHWOP prevalence in general population.

The reported observations suggest a pathogenetic link between IIH with or without papilledema and migraine

(and, possibly, other primary headaches). At least in some patients, the co-morbidity between IIH and migraine significantly increases the clinical complexity of the syndrome [58] and may promote the isolated worsening of headache frequency and duration, ultimately leading to a CM-like clinical picture. A similar mechanism could be involved in the progression of other primary headaches, namely, of chronic tension-type headache. Analogously to MOH, the pain progression linked to IIH could require a primary headache background.

Putative pathogenetic link between IIHWOP and migraine progression

Putative mechanisms linking IIH and migraine progression could involve a raised central venous pressure above the sinus venous stenosis. Congestion of large venous sinuses, most probably due to its high nociceptive innervation, may aggravate a running migrainous pain [59, 60]. Thus, it can be speculated that, in individuals carrying this co-morbidity, a mild but persistent central venous hypertension could promote a continuous nociceptive firing, leading to the sensitisation of pain processing pathways and ultimately to the progressive increase of attacks frequency and duration.

Conclusions

A number of evidences suggest that in migraine subjects carrying one or more collapsible segment of central venous sinus, the development of a co-morbid IIHWOP could represent an important risk factor for the progression of migraine. Since IIHWOP is not routinely excluded in diagnostic work up for chronic headache, its co-morbidity in migrainous patients is probably underdiagnosed (and undertreated). A similar mechanism could be involved in progression of pain in other primary headaches. We suggest that IIHWOP should be suspected in every CM patients with evidence of venous flow disturbances at MR venography. Studies addressing the IIHWOP prevalence in general population and in CM sufferers with or without medication overuse are urgently needed.

References

1. Bigal ME, Lipton RB (2008) Concepts and mechanisms of migraine chronification. Headache 48:7–15
2. Bigal ME, Lipton RB (2008) Clinical course in migraine conceptualizing migraine transformation. Neurology 71:848–855
3. Mathew NT, Reuveni U, Perez F (1987) Transformed or evolutive migraine. Headache 27:102–106
4. Mathew NT (1993) Transformed migraine. Cephalalgia 13:78–83
5. Scher AI, Stewart WF, Ricci JA, Lipton RB (2003) Factors associated with the onset remission of chronic daily headache in a population-based study. Pain 106:81–89
6. Bigal ME, Rapoport AM, Sheftell FD, Tepper SJ, Lipton RB (2005) Chronic migraine is an earlier stage of transformed migraine in adults. Neurology 65:1556–1561
7. Headache Classification Committee of the International Headache Society (2004) The International Classification of Headache Disorders: 2nd edition. Cephalalgia 2004;24 (Suppl 1):9–160
8. Bigal ME, Tepper SJ, Sheftell FD, Rapoport AM, Lipton RB (2004) Chronic daily headache: correlation between the 2004 and the 1988 International Headache Society diagnostic criteria. Headache 44:684–691
9. Headache Classification Committee (2006) New appendix criteria open for a broader concept of chronic migraine. Cephalalgia 26:742–746
10. Bigal ME, Rapoport AM, Sheftell FD, Tepper SJ, Lipton RB (2007) The International Classification of Headache Disorders revised criteria for chronic migraine-field testing in a headache specialty clinic. Cephalalgia 27:230–234
11. Sancisi E, Cevoli S, Pierangeli G, Zanigni S, Grimaldi D, Nicodemo M, Cortelli P, Montagna P (2007) Application of ICHD-II and revised diagnostic criteria to patients with chronic daily headache. Neurol Sci 28:2–8
12. D'Amico D, Tullo V, Proietti Cecchini A, Usai S, Mea E, Bussone G (2008) Application of revised criteria for chronic migraine and medication overuse headache in a tertiary headache centre. Neurol Sci 29:S158–S160
13. Siberstein SD, Lipton RB, Solomon S, Mathew NT (1994) Classification of daily and near-daily headaches: proposed revisions to the IHS criteria. Headache 34:1–7
14. Scher AI, Stewart WF, Liberman J, Lipton RB (1998) Prevalence of frequent headache in a population sample. Headache 38:497–506
15. Leonardi M, Steiner TJ, Scher AT, Lipton RB (2005) The global burden of migraine: measuring disability in headache disorders with WHO's classification of functioning, disability and health (ICF). J Headache Pain 6:429–440
16. Edmeads J, Mackell JA (2002) The economic impact of migraine: an analysis of direct and indirect costs. Headache 42:501–509
17. Munakata J, Hazard E, Serrano D, Klingman D, Rupnow MF, Tierce J et al (2009) Economic burden of transformed migraine: results from the American migraine prevalence and prevention (AMPP) study. Headache 49:498–508
18. Silberstein S, Diener HC, Lipton R, Goadsby P, Dodick D, Bussone G et al (2008) Epidemiology, risk factors, and treatment of chronic migraine: a focus on topiramate. Headache 48:1087–1095
19. Bigal ME, Lipton RB (2009) What predicts the change from episodic to chronic migraine? Curr Opin Neurol 22:269–276
20. Zeeberg P, Olesen J, Jensen R (2006) Probable medication-overuse headache: the effect of a 2-month drug-free period. Neurology 66:1894–1898
21. Zeeberg P, Olesen J, Jensen R (2006) Discontinuation of medication overuse in headache patients: recovery of therapeutic responsiveness. Cephalalgia 26:1192–1198
22. Bahra A, Walsh M, Menon S, Goadsby PJ (2003) Does chronic daily headache arise de novo in association with regular use of analgesics? Headache 43:179–190
23. Castillo J, Munoz P, Guitera V, Pascual J (1999) Kaplan Award 1998: epidemiology of chronic daily headache in the general population. Headache 39:190–196
24. Colás R, Muñoz P, Temprano R, Gómez C, Pascual J (2004) Chronic daily headache with analgesic overuse: epidemiology and impact on quality of life. Neurology 62:1338–1342

25. Silberstein SD, Lipton RB, Sliwinski M (1996) Classification of daily and near-daily headaches: field trial of revised IHS criteria. Neurology 47:871–875
26. Obermann M, Nyhuis P et al (2006) Central sensitization of the trigeminal and somatic nociceptive systems in medication overuse headache mainly involves cerebral supraspinal structures. Cephalalgia 26:1106–1114
27. Friedman DI, Jacobson DM (2002) Diagnostic criteria for idiopathic intracranial hypertension. Neurology 59:1492–1495
28. Lipton HL, Michelson PE (1972) Pseudotumor cerebri syndrome without papilledema. J Am Med Assoc 220:1591–1592
29. Marcelis J, Silberstein SD (1992) Idiopathic intracranial hypertension without papilledema. Arch Neurol 48:392–399
30. Farb RI, Vanek I, Scott JN, Mikulis DJ, Willinsky RA, Tomlinson G, terBrugge KG (2003) Idiopathic intracranial hypertension: the prevalence and morphology of sinovenous stenosis. Neurology 60:1418–1424
31. King JO, Mitchell PJ, Thomson KR, Tress BM (2002) Manometry combined with cervical puncture in idiopathic intracranial hypertension. Neurology 58:26–30
32. Karakalios DG, Rekate HL, Khayata MH, Apostolides PJ (1996) Elevated intracranial venous pressure as a universal mechanism in pseudotumor cerebri of varying etiologies. Neurology 46:198–202
33. De Simone R, Marano E, Fiorillo C, Briganti F, Di Salle F, Volpe A, Bonavita V (2005) Sudden re-opening of collapsed transverse sinuses and longstanding clinical remission after a single lumbar puncture in a case of idiopathic intracranial hypertension: pathogenetic implications. Neurol Sci 25:342–344
34. Higgins JNP, Pickard JD (2004) Lateral sinus stenosis in idiopathic intracranial hypertension resolving after CSF diversion. Neurology 62:1907–1908
35. Baryshnik DB, Farb RI (2004) Changes in the appearance of venous sinuses after treatment of disordered intracranial pressure. Neurology 62:1445–1446
36. Rohr A, Dörner L, Stingele R, Buhl R, Alfke K, Jansen O (2007) Reversibility of venous sinus obstruction in idiopathic intracranial hypertension. AJNR Am J Neuroradiol 28:656
37. Brazis PW (2008) Clinical review: the surgical treatment of idiopathic pseudotumour cerebri (idiopathic intracranial hypertension). Cephalalgia 28:1361–1373
38. Stevens SA, Lakin W, Thakore N, Penar PL, Tranmer B (2005) A modeling study of idiopathic intracranial hypertension. In: Ursino M (ed) Modelling in medicine and biology VI, WIT Press, Southampton
39. Stevens SA, Stimpson J, Lakin WD, Thakore NJ, Penar PL (2008) A model for idiopathic intracranial hypertension and associated pathological ICP wave-forms. IEEE Trans Biomed Eng 55(2 Pt 1):388–398
40. Bono F, Giliberto C, Mastrandrea C, Cristiano D, Lavano A, Fera F, Quattrone A (2005) Transverse sinus stenosis persist after normalization of the CSF pressure in IIH. Neurology 65:1090–1093
41. Torbey MT, Geocadin RG, Razumovsky AY, Rigamonti D, Williams MA (2003) Utility of CSF pressure monitoring to identify idiopathic intracranial hypertension without papilledema in patients with chronic daily headache. Cephalalgia 24:495–502
42. Bono F, Messina D, Giliberto C, Cristiano D, Broussard G, D'Asero S, Condino F, Mangone L, Mastrandrea C, Fera F, Quattrone A (2008) Bilateral transverse sinus stenosis and idiopathic intracranial hypertension without papilledema in chronic tension-type headache. J Neurol 255(6):807–812
43. Mathew NT, Ravishankar K, Sanin LC (1996) Coexistence of migraine and idiopathic intracranial hypertension without papilledema. Neurology 46:1226–1230
44. Wang SJ, Silberstein SD, Patterson S, Young WB (1998) Idiopathic intracranial hypertension without papilledema: a case–control study in a headache center. Neurology 51(1):245–249
45. Vieira DS, Masruha MR, Gonçalves AL, Zukerman E, Senne Soares CA, Naffah-Mazzacoratti Mda G, Peres MF (2008) Idiopathic intracranial hypertension with and without papilloedema in a consecutive series of patients with chronic migraine. Cephalalgia 28:609–613
46. Bono F, Quattrone A (2009) Idiopathic intracranial hypertension without papilloedema in headache sufferers. Cephalalgia 29(5):593 (author reply 594)
47. Bono F, Messina D, Giliberto C, Cristiano D, Broussard G, Fera F et al (2006) Bilateral transverse sinus stenosis predicts IIH without papilledema in patients with migraine. Neurology 67:419–423
48. Wall M (2008) Idiopathic intracranial hypertension (pseudotumor cerebri). Curr Neurol Neurosci Rep 8:87–93
49. Marcus DM, Lynn J, Miller JJ, Chaudhary O, Thomas D, Chaudhary B (2001) Sleep disorders: a risk factor for pseudotumor cerebri? J Neuroophthalmol 21:121–123
50. Diener HC, Bussone G, Van Oene JC, Lahaye M, Schwalen S, Goadsby PJ et al (2007) Topiramate reduces headache days in chronic migraine: a randomized, double-blind, placebo-controlled study. Cephalalgia 27:814–823
51. Diener HC, Dodick DW, Goadsby PJ, Bigal ME, Bussone G, Silberstein SD, Mathew N, Ascher S, Morein J, Hulihan JF, Biondi DM, Greenberg SJ (2009) Utility of topiramate for the treatment of patients with chronic migraine in the presence or absence of acute medication overuse. Cephalalgia 29:1021–1027
52. Dodgson SJ, Shank RP, Maryanoff BE (2000) Topiramate as an inhibitor of carbonic anhydrase isoenzymes. Epilepsia 41(Suppl 1):S35–S39
53. Johnson LN, Krohel GB, Madsen RW, March GA Jr (1998) The role of weight loss and acetazolamide in the treatment of idiopathic intracranial hypertension (pseudotumor cerebri). Ophthalmology 105:2313–2317
54. Pagan FL, Restrepo L, Balish M, Patwa HS, Houff S (2002) A new drug for an old condition. Headache 42:695–696
55. Palacio E, Rodero L, Pascual J (2004) Topiramate-responsive headache due to idiopathic intracranial hypertension in Behcet syndrome. Headache 44:436–437
56. Celebisoy N, Gökçay F, Sirin H, Akyürekli O (2007) Treatment of idiopathic intracranial hypertension: topiramate vs acetazolamide, an open-label study. Acta Neurol Scand 116:322–327
57. De Simone R, Marano E, Bilo L, Briganti F, Esposito M, Ripa P et al (2006) Idiopathic intracranial hypertension without headache. Cephalalgia 26:1020–1021
58. Bonavita V, De Simone R (2008) Towards a definition of comorbidity in the light of clinical complexity. Neurol Sci 29(Suppl 1):S99–S102
59. Doepp F, Schreiber SJ, Dreier JP, Einhäupl KM, Valdueza JM (2003) Migraine aggravation caused by cephalic venous congestion. Headache 43:96–98
60. Chou CH, Chao AC, Lu SR, Hu HH, Wang SJ (2004) Cephalic venous congestion aggravates only migraine-type headaches. Cephalalgia 24:973–979