



Topic: 8 - Headache

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No: 3149

Topic: 8 – Headache

Intracranial hypotension is a rare cause of orthostatic headache: A review of the etiology, treatment and prognosis of 13 cases

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The aim of this investigation is to examine the causes, clinical picture, treatment, and prognosis of spontaneous intracranial hypotension, a rare cause of orthostatic headache, among the cases presenting in our clinic.

Thirteen cases (5 males and 8 females), diagnosed with spontaneous intracranial hypotension in our clinic between January 1st, 2009 and October 30th, 2011, were included in this study.

The presenting symptoms, treatment, findings on cranial magnetic resonance imaging, cerebrospinal fluid pressure measured at lumbar puncture (in available patients), and healing period of the patients were recorded. Five patients with orthostatic headache and accompanying symptoms were treated with bed rest, increase in oral fluid intake, intravenous hydration, and caffeine, and experienced a complete recovery. Complete recovery was observed in two patients (15.3%) within 10 days, in another two (15.3%) within 15 days and in one patient (7.6%) within 21 days. Headaches and other clinical symptoms significantly regressed within 30 days in four patients (37.6%) who received similar treatment, but a mild headache persisted intermittently during follow-up in these individuals. As the headache had not resolved after 30 days, an epidural blood patch was applied in these four cases (37.6%) and the clinical picture completely improved within 10 to 15 days.

Spontaneous intracranial hypotension should primarily be suspected in cases complaining about postural headache and contrast-enhanced cranial imaging should be performed. The presence of cranial nerve paralysis and pyramidal tract signs should be considered. Conservative treatments should be considered initially, however if conservative treatments fail, epidural blood patches must be applied.

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Association of cholecystokinin receptor 1 gene polymorphism and migraine

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Background: Cholecystokinin (CCK) is one of the most abundant neurotransmitter peptides in the brain. CCK coexists with dopamine in dopaminergic neurons, and modulates the release of dopamine in the nucleus accumbens. The CCK system is believed to be involved in pain processing. The aim of the study was to investigate the prevalence of -81A/G (rs1799723), -128G/T (rs1800908) and 984T/C (rs1800857) polymorphisms of the CCK-AR gene in migraine patients and controls.

Method: 144 migraine patients (ICHD III), mean age = 41.6 ± 12.5 y.o. and 197 healthy controls living in Moscow and the Moscow Region were included. SNPs were genotyped by a PCR-RLFP technique: PCR with “GenPak™ PCR Core” (Isogene Lab., Ltd.) and restriction with HinfI for rs1799723 and rs1800908 and with PstI for rs1800857 (ferments by SibEnzyme Ltd.).

Results: C-allele frequency in 984T/C was significantly higher in migraine patients, 0.479 ± 0.030 compared with controls, 0.154 ± 0.026 ($\chi^2 = 85.44$, $p < 10^{-10}$; OR = 5.0, 95% CI = 3.50–7.13). The -81A/G and -128G/T minor allele's frequencies didn't differ between groups: -81G = 0.049 ± 0.018 in the migraine group and 0.045 ± 0.015 in the controls; -128T = 0.045 ± 0.017 in the migraine group and 0.025 ± 0.011 in the controls.

Conclusion: This study is the first to report a more positive association of the C-allele of the CCK-AR gene 984T/C polymorphism in patients with migraine than in control subjects.

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Can vision influence trigeminal nociception? A study of the effect of visual cortex activation on the nociceptive blink reflex

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Background: In migraine, the link between cortical phenomena and trigeminovascular activation is not clear and thus, headache as well.

Objective: To search in humans for a possible functional connection between the visual cortex and the trigeminal nociceptive system by studying the effect on the nociceptive blink reflex (nBR) of repetitive transcranial magnetic stimulation (rTMS) applied over the visual cortex, and to compare healthy volunteers (HV) and migraine without aura patients (MO).

Methods: Fifteen bilateral nBR responses were recorded by stimulating the right supraorbital nerve in 22 HS and 13 MO before and after 1 Hz (15 min train) or 10 Hz (20 trains with a 15 s intertrain interval) rTMS. For comparison, we also performed the same study in HV after an 8 Hz visual flash stimulation.

Objective: To ascertain the effect of perioperative BP on the development of PDPH in the patients who received surgery under spinal anesthesia.

Patients and methods: We evaluated the presence of PDPH in all consecutive 199 patients (122 males, 77 females, age: 15–76 years) who received elective knee surgery under spinal anesthesia between September 2012 and February 2013. The spinal anesthesia was performed by the same anesthesiologist with 25-G Quincke needle. Data regarding previous history of headache, pre- and post-operative BP, highest and lowest BP during operation as well as demographic features were analysed.

Results: The overall incidence of PDPH was 9.0%. It was higher in female than in male (15.6% vs 4.9%, $p = 0.02$). Age, history of hypertension or recurrent headache was not different between patients with and without PDPH. The duration of operation or spinal anesthesia was not different between the two groups. BP variables were expressed as pre- and post-operative mean arterial pressure (MAP), the highest and the lowest MAP during operation, and their differences were not different either.

Conclusion: PDPH after knee surgery under spinal anesthesia occurred more frequently in female patients, and was not influenced by their perioperative BP states.

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Memory improvement after spreading depression by NMDA blocker as memory destructor

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Spreading depression (SD) is transient neural hyperexcitability followed by depolarization wave, which propagates through the brain and modulate electrical gradient and synaptic activity. Data have shown that SD wave distributes coincidence between neural activity and behavioral activity. Neural activity and electrical potential effect on memory retrieval have been demonstrated. Inhibitory effect of NMDA receptors in SD procedure can control memory impairment caused by SD. However, the negative effect of NMDA receptor blockage on memory has been proven in previous studies. In the present study the effect of NMDA receptors blockage (MK801) used to evaluate its efficiency in subsiding of SD negative influence on memory. Wistar rats (60–80 g) were randomly chosen in 6 groups and (NMDA blocker 0.63–1 mg/kg) were administrated after 3 mol/L KCl injection for induction of repetitive SD in rat. The groups were evaluated by T-maze test and SD groups were compared with control groups, including (NMDA blocker 1–0.63 mg/kg controls) and sham group. T-maze data have showed that repeated SD could significantly alter memory retrieval performance. However, in the second week memory enhancement was induced by SD induction. Repeated SD induction during other weeks indicated impairment in memory. Application of NMDA blocker showed significantly enhanced memory retrieval and could potentially control memory impairment after SD. The studies indicated that NMDA blocker may decrease memory performance, on the other hand the effect of MK801 on inhibition of SD propagation may somehow weaken memory improvement due to its memory destruction effects.

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Prevalence of migraine among medical students in Kuwait University

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Background: Prevalence of migraine among medical students is of particular interest as they are subjected to lots of tests and stresses that may precipitate migraine attacks.

Objectives: To determine the prevalence of migraine among medical students in Kuwait University.

Methods: This cross-sectional and descriptive study, which included students registered to Medical Faculty at Kuwait University in the academic year of 2012–2013. Out of 808 registrants, 621 students accepted to participate in the study. Participants who had two or more headaches in the last 3 months were subjected to two preliminary questions and participants with at least one positive response were asked to perform the validated ID-Migraine™ test. The frequency of headache per month and severity of headache by Numeric Rating Scale (NRS) were reported.

Results: Migraine was detected in 173 subjects (27.9%) based on the ID-Migraine™ test. The mean age of the migraine students was 20.17 ± 2.29 (16–25 years). Thirty-seven were male (21.4%) and 136 were female (78.6%). Migraine was significantly more frequent in the last 2 grades (35.5% and 44%, $p < 0.000$). The frequency and the severity of headache were significantly increased during the last 2 grades (5.55 ± 1.34 and 7.23 ± 1.27 , $p < 0.000$) (6.00 ± 0.76 and 6.68 ± 1.25 , $p < 0.000$) respectively. Stress 43 (24.9%), irregular sleep 36 (20.8%), and much reading 32 (18.5%) were the most common triggering factors.

Conclusion: There is a high prevalence of migraine among medical students in Kuwait University. The frequency and severity of headache increase with years of educations.

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A randomized doubled blinded trial of treatment with diamino-oxidase (DAO) in patients with migraine and deficit of enzyme's activity

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Background: Histamine has been considered as a chemical mediator of migraine. The degradation is done in two different pathways. One of the enzymes that allow this process is the diamino-oxidase (DAO).

Objective: The aim of this study is to identify the prevalence of the deficit in the activity of DAO in patients with migraine, and test the supplementation of this enzyme in a randomized controlled double-blind trial.

Material and methods: This was a randomized parallel-group controlled study. After a 1-month run-in, patients with migraine attacks/month between 4 and 14 were randomized 1:1 to placebo or DAO three times a day during one month. Primary outcome measures were diminution of hours of pain, and the use of antimigraine drugs.

Results: We studied 137 patients with migraine, and find the deficit of DAO activity (< 80 HDU/ml) in 119 (87%).

One hundred patients were randomized and included in the intention-to-treat analysis. Between run-in and first month of treatment, the mean number of hours of pain decreases in both groups but with significant difference in the final control in the group treated with DAO compared with placebo (6,3 vs 5,1: $p < 0.03$).

The use of the acute antimigraine drug was significantly reduced in the DAO but not in placebo group ($p > 0.022$).

There were no adverse events in either group.

Conclusions: Deficit in the activity of DAO is very prevalent in population with migraine.

The supplementation with the enzyme is effective and safe as a preventive therapy for migraine.

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Subdural haematoma as a late complication of spontaneous cerebrospinal fluid hypovolemia (SCH) syndrome:

Two case reports

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Background: SCH syndrome is relatively common, and a CSF leakage can be occasionally demonstrated. Subdural haematoma (SDH) has been reported in patients with SCH, mainly in older men, or these displaying longer time to diagnosis of SCH.

Objectives: We report two cases that developed SDH after apparent resolution of SCH.

Material and methods: A 41 year old man developed severe orthostatic headache and neck stiffness after repeated sneezing. Lumbar puncture showed an opening pressure of 0 mm H₂O. Cisternography demonstrated cervicothoracic CSF leak. A 43 year old man presented sudden headache after sport activity, highly suggestive of SCH, developing unilateral abducens palsy after several days. Cranial tomography (CT) was normal in both cases, with resolution of symptoms after 3 months of conservative therapy.

Results: Three months after the onset, when patients were almost asymptomatic, a control MRI showed subacute bilateral SDH. In both, resolution of the haematomas was verified after some weeks without need of drainage.

Conclusion: SCH is characterized by orthostatic headache, low CSF pressure, and sometimes typical MRI image. The development of SDH, although rare, has been reported. In our cases the late development of SDH is remarkable, perhaps related to the persistence of SCH for a long time. We emphasize the importance of monitoring patients with SCH, and consider conservative measures only in cases with a brief course. Epidural patching or surgical repair may prevent potentially serious complications such as SDH. Moreover, SCH should be excluded as a cause of SDH in young patients without risk factors.

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Analysis of MAP0004 subjects with menstrually related migraine vs. non-menstrually related migraine

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Background: Menstrually related migraine (MRM), as defined by The International Classification of Headache Disorders, 2nd edition, occurs from days –2 to +3 of menstruation in ³2 of 3 menstrual cycles and at other times of the cycle. MRM generally lasts longer and is more severe and difficult to treat than non-MRM. MAP0004 is an investigational product that delivers dihydroergotamine through the lungs via a breath-synchronized metered-dose inhaler.

Objective: This post hoc analysis of phase 3 data evaluated the efficacy and tolerability of MAP0004 in MRM vs non-MRM.

Patients and methods: This analysis included 149 women from a modified intent-to-treat population who treated MRM (n = 45) and non-MRM (n = 104) with MAP0004. The study used the following clinical end points: pain relief and pain free at 2 h and sustained pain relief and sustained pain free at 2–24 h and 2–48 h.

Results: The efficacy of MAP0004 did not differ significantly in MRM vs non-MRM at 2 h (pain relief 62% vs 64%; pain free 36% vs 29%), at 2–24 h (pain relief 53% vs 49%; pain free 31% vs 23%), and at 2–48 h (pain relief 38% vs 38%; pain free 24% vs 15%). No significant differences were found in frequency of adverse events, and no drug-related serious adverse events were reported.

Conclusion: In this post hoc analysis of phase 3 data, MAP0004 was similarly effective and well tolerated in treating both MRM and non-MRM.

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Topic: 8 – Headache

Analysis of the development of allodynia: Correlation between migraine duration and severity

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Background: Allodynia, the perception of pain from non-nociceptive stimuli, is a clinical presentation of central sensitization. Allodynia is reportedly common during migraine attacks. Although factors leading to development of allodynia are not well understood, duration and severity of migraine have been implicated.

Objective: This retrospective analysis evaluated the relationship between allodynia and the duration and severity of migraine to better understand the mechanisms related to migraine-induced central sensitization.

Patients and methods: This analysis included 792 patients from the double-blind period of a phase 3, placebo-controlled, randomized clinical trial of an investigational acute treatment for migraine (MAP0004). Baseline pain levels were recorded by patients using an electronic diary, and baseline allodynia data were obtained using a standard questionnaire. Correlations between percentage of patients reporting allodynia, severity of migraine, and duration of migraine were analyzed by Fisher's exact test or Chi-square test, as indicated.

Results: At baseline, 53% of patients reported allodynia. The presence of allodynia did not change in relation to the duration of the migraine (Chi-square $P = 0.2182$), regardless of migraine severity (moderate pain, Chi-square $P = 0.1807$; severe pain, Chi-square $P = 0.5830$). Patients reporting severe pain experienced significantly more allodynia (58.4%) than patients with moderate pain (48.2%; Fisher's exact test $P = 0.0053$).