

# Medication overuse as a cause of chronic headache in shunted hydrocephalus patients

L Willer,<sup>1,2</sup> R H Jensen,<sup>1</sup> M Juhler<sup>2</sup>

<sup>1</sup>Danish Headache Centre, Department of Neurology, Glostrup Hospital, University of Copenhagen, Denmark  
<sup>2</sup>Department of Neurosurgery, Rigshospitalet, University of Copenhagen, Denmark

## Correspondence to

Professor M Juhler, Department of Neurosurgery, Rigshospitalet, University of Copenhagen, Blegdamsvej 9, DK-2100 Copenhagen 2092, Denmark; [mjuhler@webspeed.dk](mailto:mjuhler@webspeed.dk)

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## ABSTRACT

**Purpose** To highlight the group of hydrocephalus patients known to have a long history of shunt revisions and refractory chronic headache. When a shunt in perfect working order has no effect on headache, other causes of headache should be investigated. In this paper, patients with medication overuse headache are identified and the positive effect of medication withdrawal are described.

**Materials and method** Patients with hydrocephalus and shunt referred from the neurosurgical department to the Danish Headache Centre were identified. In all cases, over- and underdrainage was ruled out prior to referral. Six patients with medication overuse headache were documented and their charts were reviewed retrospectively with specific attention to: shunt revisions, inpatient and outpatient contacts, headache data and medication use before and after withdrawal of analgesic medication overuse.

**Results** A marked reduction in shunt revisions and inpatient contacts in five out of six patients was found and a reduction in outpatient contacts in four out of six patients. Furthermore, an improvement in headache intensity was found in three out of six patients and a reduction in duration was found in two out of six patients.

**Conclusion** This study indicates that it is important to identify shunt patients with persistent chronic headache from causes other than shunt malfunction. By reducing their analgesic intake, it is possible to reduce headaches, the number of surgical interventions and hospital contacts. Hopefully this will raise awareness and lead to further research on the subject.

## INTRODUCTION

Hydrocephalus is often treated with a ventriculo-peritoneal shunt. Headache is a common complaint of shunt malfunction, caused by either shunt blockage or overdrainage. This can be overcome by surgical revision of the shunt or by reprogramming the valve.<sup>1 2</sup> However, some shunt patients suffer from chronic headache, even with an appropriately controlled intracranial pressure (ICP) and without mechanical failure of the shunt. Typically, their history contains several admissions or outpatient contacts as well as surgical revisions in the absence of certain mechanical shunt failure. This group of shunt patients is one of the most difficult to manage. They continue to complain of chronic refractory headache despite intense medical effort and a shunt in perfect working order. Although a relatively small group, they use a disproportionately large amount of resources in the health system and their quality of life is seriously affected.

Our hypothesis is that other causes of headache unrelated to the shunt can be defined and treated. The purpose of this paper is to define and describe one such cause.

Headache in general is the most frequently reported type of pain and can represent anything from symptoms of life threatening disease to a mild insignificant primary tension-type headache.<sup>3 4</sup> A precise diagnosis is therefore of the utmost importance. According to the International Classification of Headache Disorders-II, more than 100 different primary and secondary headache diagnoses are now defined.<sup>5</sup> The most frequent types of primary headaches are migraine and tension-type headache. Secondary headache is related to an underlying specific cause—for example, abnormal intracranial pressure caused by shunt dysfunction. Distinguishing deterioration in a chronic primary headache from new onset secondary headache may be very difficult.<sup>5 6</sup>

Chronic overuse of substances normally used to alleviate headaches such as migraine and tension-type headache has long been known to contribute to the development of chronic headache.<sup>7</sup> This is now classified as medication overuse headache (MOH) and is estimated to cause chronic headache refractory to treatment in approximately 2% of the general population.<sup>8 9</sup>

MOH was mainly thought to be closely related to primary headaches, such as migraine or tension-type headache, but in recent years it has also been recognised in secondary headaches, such as post-traumatic headache and postcraniotomy headaches, and is also likely to exist in relation to other secondary headaches.<sup>9 10</sup> The prognosis after detoxification is usually favourable and MOH should therefore be considered in all patients complaining of chronic headache.<sup>11</sup>

These observations led to the hypothesis that medication overuse might be the cause of unnecessary hospital contacts and even surgery in a number of shunt patients with chronic headache.

There are few data on the relationship between abnormal ICP and headache. Friedman *et al* describes patients with treated idiopathic intracranial hypertension developing subsequent headaches, different from their idiopathic intracranial hypertension headache.<sup>12</sup> Furthermore, a reduction in headache in hydrocephalic children has been achieved with prophylactic migraine medication. Other primary headaches have also been reported to play a role in chronic headache in hydrocephalic children.<sup>13 14</sup>

We could find no data directly related to the causes of chronic headache in shunted patients.

**CASE REPORT**

A 32-year-old woman was the first to be referred from the Department of Neurosurgery to the Danish Headache Centre. Her symptoms and medical history were later found to be characteristic of the association between shunt treatment and MOH. At the age of 22 years she was diagnosed with idiopathic intracranial hypertension and a ventriculoperitoneal shunt was inserted. Her symptoms subsided immediately thereafter. For the next 7 years the shunt was revised five times due to intraperitoneal inflammation and was then changed to a ventriculoatrial shunt.

Thereafter she complained of a severe constant chronic headache often associated with nausea. This was interpreted as shunt dysfunction and several surgical shunt revisions were performed, always with good immediate effect followed by recurrence of the severe headache days after. Overdrainage was now suspected and neuroimaging showed very narrow ventricles. This led to several attempts to adjust the valve, repeated revisions and an open surgical ventriculostomy in 2002. After 1.5 years, 14 hospital admissions and 29 shunt revisions, she used increasingly larger doses of pain medication with little effect on the chronic headache. Several times the shunt was found to be in perfect working order and hence other causes of headache were looked for. She was then referred to the Danish Headache Centre. She had a daily intake of tramadol, acetaminophen and morphine. She underwent detoxification for all three analgesics. She was then almost headache free for 1.5 years with no contact with the neurosurgical department during this period. The diagnosis was MOH and migraine related to medication withdrawal. Subsequently, the shunt has been revised five times for verified mechanical obstruction with no post-surgical recurrence of the headache.

Her current situation is described by herself as a marked improvement in quality of life and mild infrequent headache episodes. She has resumed normal social activities and a normal working life.

**METHODS**

We used the International Classification of Headache Disorders-II definition of chronic headache, which specifies a daily occurrence lasting more than 4 h a day for more than 15 days a month.<sup>5</sup>

MOH is further defined by intake of simple analgesics for >15 days/month for at least 3 months, or opioids, specific migraine compounds or combination analgesics for >10 days/month (table 1).<sup>5</sup>

The burden of headache can be monitored in several ways. We used the number of headache days per month as the primary

**Table 1** Revised diagnostic criteria for medication overuse headache (modified from new appendix criteria)<sup>6</sup>

A. Headache duration	≥15 days/month
B. Regular medication overuse for >3 months	<ul style="list-style-type: none"> <li>▶ One or more acute/symptomatic treatment drugs</li> <li>▶ ≥10 days/month</li> <li>–Ergotamine, triptans, opioids</li> <li>–Combination analgesic medications</li> <li>▶ Simple analgesics <i>or</i></li> <li>▶ Any combination of ergotamine, triptans, analgesics opioids</li> <li>▶ ≥15 days/month</li> <li>▶ Without overuse of any single class alone</li> </ul>
C. Headache development	Developed or markedly worsened during medication overuse

outcome parameter. Other parameters that can be used are pain intensity on a 4 point (0–3) Likert scale<sup>5</sup> and duration of pain in hours per day.

Following the ‘proband case’ presented above, we have systematically referred shunt patients with persistent headache despite optimised shunt function for secondary headache diagnosis to a specialist headache clinic. Prior to referral, shunt function and/or normal ICP has to be verified and documented so that no patient with a headache related to overdrainage or shunt blockage is referred.

The electronic patient management system (Green System) was retrospectively searched for all patients with a hydrocephalus or shunt diagnosis *and* a referral to the Danish Headache Centre so that all cases could be identified. All patients completed a diagnostic headache diary 1–2 months before the first visit to the Danish Headache Centre. They were interviewed thoroughly by a senior neurologist at the headache clinic.

An abrupt withdrawal from the drug(s) causing MOH was applied. Our standard is a detailed outpatient programme.<sup>11</sup> If barbiturates, opioids, combinations with codeine or tranquilisers were overused and an outpatient programme has failed, we use an inpatient programme.

**RESULTS**

Six patients (table 2) were identified following the proband case, up until 1 January 2009. In the corresponding period (May 2005–May 2009), a total of 136 patients >18 years were treated for shunt dysfunction. The total number of shunt revisions during that period was 203. The revision statistics were thus 203/136/4=0.4 shunt revisions per patient per year for the entire group.

The length of clinical ‘shunt history’ before referral for chronic headache ranged from seven to 27 years. The follow-up period after referral was a mean of 3.8 years (range 2–5 years). Data on admissions, shunt revisions and outpatient contacts is presented in table 2. Because most of the patients had a long neurosurgical history before referral, we looked at neurosurgical contacts during the last 3 years before medication withdrawal (table 2). The number of shunt revisions was reduced from a mean of 2.3/year to 0.6/year. ICP measurements were reduced from 1.2/year to 0.07/year. On average, patients were admitted 3.6 times/year before withdrawal and this rate was reduced to 0.6 admissions/year after detoxification. Likewise, the number of days admitted was reduced from a mean of 20.5 days/year to 4.7 days/year. Finally, the number of outpatient contacts was reduced from 2.8/year before to 0.9/year after.

Headache data are presented in table 3. Three out of six patients had reported a prior headache history, one with episodic migraine and two with episodic tension-type headache. Two patients had a reduction in headache frequency after withdrawal. Three patients had a reduction in headache intensity and two patients had a reduction in headache duration after withdrawal. All patients had a significant and lasting reduction in their intake of analgesics.

All results were analysed using Wilcoxon’s test, as each patient served as their own comparison before compared with after medication withdrawal. Statistical significance was accepted at  $p < 0.05$ .

**DISCUSSION**

The most interesting finding in the present pilot study is the reduction of shunt revisions from a mean of 2.3 before to 0.6 after withdrawal, and the reduction in inpatient as well as

**Table 2** Hospital admissions and shunt revisions before and after medication withdrawal

Patient	Age at withdrawal (years)	Annual No of operations before vs after withdrawal		No of ICP measurements before vs after withdrawal		No of hospital admissions before vs after withdrawal		No of days admitted to hospital before vs after withdrawal		No of outpatient contacts before vs after withdrawal	
M	24	2	0	1	0	2.7	0	16.3	0	1.3	0
F	33	6	1	2	0.4	9.3	1.2	43	9.2	3	0.8
F	60	2	0	1.3	0	3.3	0	18.3	0	2.7	0.5
M	19	1	1.5	1.3	0	2	1.1	15.7	11.3	3.7	1.6
M	28	1.7	1	1	0	3.3	1	20.7	7.5	5	1.3
F	39	1	0	0.3	0	0.7	0.2	9	0.2	1.3	0.9
Mean values	33.8	2.3	0.6*	1.2	0.07*	3.6	0.6*	20.5	4.7*	2.8	0.9*

Values averaged per year over the last 3 years before withdrawal and as an average per follow-up year after withdrawal.

\* $p < 0.05$  using the Wilcoxon test.

ICP, intracranial pressure.

outpatient contacts to the neurosurgical department. Combined with headache data on the same patients, it is tempting to draw the conclusion that the hospital contact reduction is due to medication withdrawal and that the previous chronic headache was caused by MOH. The condition of MOH is characterised as a slowly progressing headache leading to an increase in medication use, which further increases the headache, thus resulting in a vicious circle. Shunt dysfunction on the other hand usually has a more acute/subacute onset of symptoms. Patients and professionals should become more aware of these differences in symptoms, and of MOH as a potential differential diagnosis.

The follow-up period after medication withdrawal varied from 2 to 5 years, and the medication free period for one of the patients is therefore shorter than the 3 year period chosen before withdrawal.

Our findings in the shunt patients are in accordance with the experience on MOH in non-neurosurgical patients with initial primary or secondary headaches in whom discontinuation of medication overuse segregated the patients in to three groups: 45% improved markedly in frequency, 48% were unchanged and 7% deteriorated slightly.<sup>11 15</sup>

In a subsequent study it has been shown that patients without an initial response may later benefit from withdrawal of analgesics as they become responsive to prophylactic treat-

ment.<sup>16</sup> In accordance, four out of the six patients in our study are now on prophylactic medication.

The duration of medication overuse was, due to the retrospective design of this study, not always attainable from the charts. Based on the interview at the Danish Headache Centre before withdrawal, overuse duration was estimated ranging from 2 to 12 years. The duration of analgesic misuse has been identified by the Head-HUNT study as a predictor of chronic pain and development of MOH.<sup>7</sup> It would be valuable to identify the average time and dose of analgesics needed to develop MOH in shunt patients similar to the experience in patients with migraine and tension-type headache.

An unusual feature of MOH in shunt patients is the male/female ratio of 3/3 in this study. A pronounced gender bias with significant female preponderance has been demonstrated in large population studies of MOH.<sup>7-9</sup> A larger study is needed to determine whether the gender distribution for MOH is really different in shunt patients.

It would have been interesting to investigate the results of the last ICP measurements and the indications given for revision of shunts in all cases during the last years before withdrawal. In this way it might be possible to identify redundant surgeries. Unfortunately, the retrospective design of the study prevented this, as charts did not always provide fully accurate information.

**Table 3** Headache data before and after withdrawal

Patient	Age at withdrawal (years)	Headache frequency in days per month, before and after withdrawal		Headache intensity on a scale from 0 to 3, before and after withdrawal		Duration (hours of the day) before and after withdrawal		Daily analgesic medication use, before and after withdrawal	
M	24*	30	Unknown	2	Unknown	24	Unknown	ASA+caffeine 500+50mg. Acetaminophen 1g×2	None
F	33	30	30	2-3	1	24	24	Tramadol 100 mg×4. Acetaminophen 1 g×4. Morphine 10 mg×3	None
F	60	30	0	2	0	24	0	Codeine 50 mg×4. Acetaminophen 1 g×4.	None
M	19	30	30	2	3	24	24	Acetaminophen 1 g×2. Ibuprofen 600 mg×2. Tramadol 50 mg×2	Acetaminophen 1 g
M	28	30	30	2	2	24	10-12	Acetaminophen 2 g. Tolfenamic acid 300 mg (20 days a month). Tramadol 100 mg (20 days a month)	None
F	39	30	1-2	2	1-2	24	Unknown	Ibuprofen 400 mg×4. Acetaminophen 1 g×4	Acetaminophen 1 g (1-2 days a week)
Mean values	33.8	30	-	2.3	-	24	-		

Following withdrawal, prophylactic medication was given to patient Nos 2 (candetersan 16 mg), 5 and 6 (amitriptyline 100 mg), and 7 (topiramate 50 mg).

\*No scale has been used to define the intensity of pain but the patient describes it as less than before medication withdrawal. No reports on frequency, intensity or duration after, only a marked reduction in medication use.

ASA, acetylsalicylic acid.

## Research paper

Patients of the type described in this study have been submitted to numerous operations and all suffer from chronic pain. Chronic pain syndromes after surgery have also been described in other fields of surgery. It has been suggested that preoperative and postoperative initiatives are taken to prevent surgical pain from becoming chronic.<sup>17</sup> Similar initiatives might be attempted with neurosurgical patients in order to ascertain whether chronic pain can be related to and produced by repeated shunt operations.

With this retrospective review of six cases, we hope to raise awareness of a possible explanation and possible solution to the small but very challenging proportion of shunt patients with a frustrating surgical history based on chronic headache and many shunt operations with little or no relief. Prospective studies with a larger sample size, with predefined outcome measurements, are required to further describe this phenomenon in depth.

**Competing interests** None.

**Patient consent** Obtained.

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