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SHORT COMMENTARY

Eighty years of Medication-Overuse Headache: what about Medication-Overuse Backpain?

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Abstract

Introduction Although chronic low back pain (CLBP) is one of the most common pain syndromes, up to now, clear pathophysiological causes or specific treatment options are missing. Medication-overuse has been associated with chronic headache, but never with CLBP.

Hypothesis Based on several similarities between CLBP and Medication-Overuse Headache (MOH), we hypothesized that medication-overuse might contribute to CLBP as well, maybe even as an own entity. Might there be something like Medication-Overuse Backpain (MOB)?

Methods We substantiate our hypothesis with a preliminary case-series analyzing five patients suffering from CLBP with a marked medication-overuse. In these patients, a stepwise analgesic withdrawal was recommended.

Results Within 6 months of recruitment, five patients fulfilled the inclusion criteria and successfully completed discontinuation of their medication. All patients reported noticeable pain relief, despite the discontinuation of their analgesics. Withdrawal was well tolerated in all cases.

Conclusions Considering our results, the described withdrawal method seems to be a simple and safe method to achieve pain reduction while simultaneously preventing organ damage. Despite the preliminary character of our results, our hypothesis might stimulate a new understanding of CLBP's pathophysiology.

Keywords Pain · Headache · Medication-Overuse Headache · Back pain

Introduction

In 1936, Lennox and his colleagues were the first to describe Medication-Overuse Headache (MOH). Since then, MOH has become a worldwide-accepted phenomenon [1]. Graham, Friedman, and Lippman independently reported the first ergotamine withdrawal protocols in 1955 [1]. In the third Edition of the International Classification of Headache Disorders, MOH is recognized as a separate secondary entity in patients with a pre-existing primary headache disorder, caused by medication-overuse [3]. Although MOH is currently a controversial topic among headache specialists and the best way to clinically manage this is not clear [2], medication withdrawal is still recommended as the first step in the treatment of patients with frequent headaches [3]. The prevalence of MOH is around 1–2% in the general population [4], making it one of the most common chronic pain conditions.

Even more common than MOH is chronic low back pain (CLBP) which affects people of all ages and is a leading contributor to disease burden worldwide [5, 6]. Low back pain has a lifetime prevalence of nearly 84%, the prevalence of CLBP is assumed with about 23% and almost 12% of the afflicted patients are severely disabled [7]. As non-specific CLBP does not have a clear pathophysiological or pathoanatomical cause, specific treatment options are missing. Primary treatment recommendations include a biopsychosocial framework including education, exercise, and psychological programs with prudent use of medication, imaging, and surgery [5, 8]. Nevertheless, an adequate treatment is challenging and often ineffective [5]. Regarding risk factors

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for the development of MOH and CLBP, several similarities can be found: there seems to be a congruent relationship between lifestyle factors (physical inactivity, smoking, obesity) [9], stress [10, 11], and limited coping resources [12]. Furthermore, comparable comorbidities exist, like depression, anxiety, as well as dependence-type behavior, such as loss of control over pain medication use [3, 5, 13, 14]. Up to now, pathophysiology in both pain states is not completely understood, but numerous pathophysiological similarities have been described, e.g., central sensitization, upregulation of pro-inflammatory mediators, and changes in the neuromodulatory system [15]. Like in MOH, an analgesic overuse constitutes a widespread problem in CLBP.

Hypothesis

Interestingly, despite the above-mentioned similarities between MOH and CLBP, up to now, no attention has been paid to medication-overuse as a potential cause of CLBP. We hypothesized that medication-overuse could be partly contributed to CLBP, maybe even as an own entity. Might there be something like Medication-Overuse Backpain (MOB)?

Methods

In our preliminary clinical case-series, all patients appearing in our outpatient Interdisciplinary Pain Center suffering from non-specific CLBP with a marked medication-overuse were assessed. After informing patients about the questionable effectiveness of their current medication, potential side effects, risk factors, and contraindications, we recommended a stepwise analgesic withdrawal. At the same time, patients were instructed to write a pain diary. In MOH, there is consensus that the abrupt withdrawal is the treatment of choice, since headache medications (non-opioids, NSAIDs, triptans, and ergotamines) do not cause severe withdrawal symptoms [15, 16]. Since CLBP patients may exhibit manifest fear-avoidance beliefs, we established a modified, stepwise outpatient withdrawal protocol: in the first week, patients took analgesics only every second day to reduce catastrophizing thoughts and to avoid an increase in fear-avoidance behavior. Beginning in the second week, no analgesics were taken for a minimum of 2 weeks (Fig. 1). To avoid the potential bias of doctor/patient relationship, we kept the contact time between doctor and patient at a minimum. In addition, no further recommendations or treatments such as injections, physiotherapy or psychological intervention were offered during that time.

Results

Within 6 months of recruitment, five patients fulfilled the inclusion criteria and were enrolled. All patients had a history of overuse of non-opioid-analgesics and displayed contraindications or first signs of renal dysfunction (overuse criteria analogous to those defined for MOH: analgesics $\geq$ 15 days/month). None of the patients exhibit exaggerated fear-avoidance behavior. Regardless of our hypothesis, it was decided that all five patients needed to discontinue their current medication to avoid future organ damage. Characteristics of the participating patients, history of pain, and analgesic use are shown in Table 1.

Outcome of withdrawal

Within a period of 2 months, all patients successfully completed discontinuation of their medication. None of the patients reported withdrawal symptoms. One patient needed two withdrawal attempts.

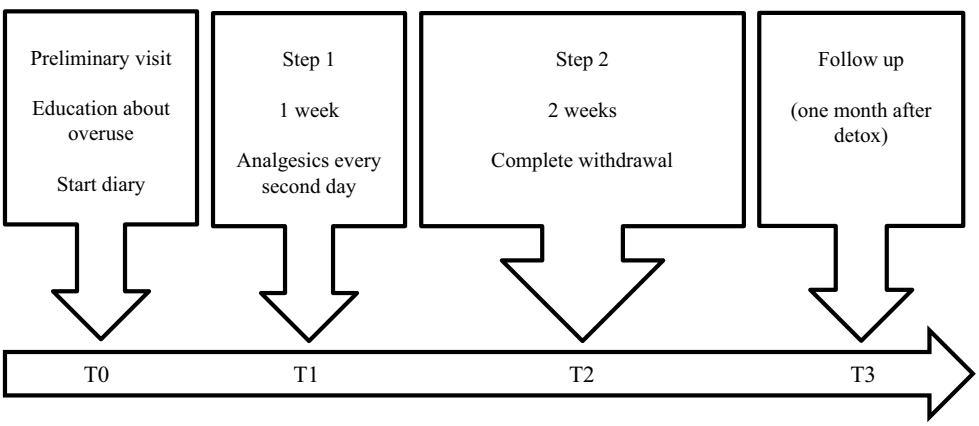

Fig. 1 Author's analgesic withdrawal scheme

Table 1 Demographic and clinical characteristics of the patients

Patient	Age (years)	Sex (m/f)	Pain syndrome	Drug	Dosage (mg)	Duration of overuse (years)	Frequency of medication (d/m)
1	48	f	CLBP (+MOH)	Ibuprofen	1800	2	30
2	50	m	CLBP	Ibuprofen	300–1800	2	30
3	67	f	CLBP	Ibuprofen/ etoricoxib	1200/90	20	30
4	54	f	CLBP	Ibuprofen	2400	1.5	30
5	78	f	CLBP (+Groin pain)	Dipyrone (metamizole)	2000	15	30

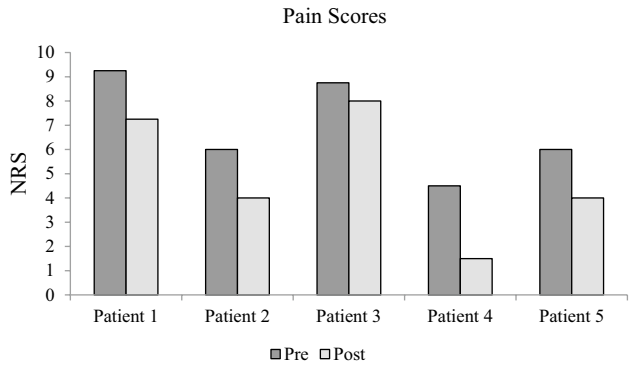

Fig. 2 Self-reported pain scores before (Pre) and 1 month after successful withdrawal from analgesics (Post). The stated pain score represents the mean pain score of the current week

Outcome of pain scores

After an initial slight increase in pain, all patients reported noticeable pain relief at the 1-month follow-up, despite the absence of their analgesics (Fig. 2). Furthermore, patients reported individual days with very low pain levels. Interestingly, after successful withdrawal, the previously overused analgesics appeared to be effective again as a restrictive, on-demand medication.

Conclusions

Since medication-overuse has been accepted as a reason for chronic headache, we wondered whether the phenomenon of medication-induced pain enhancement could also be a contributing cause in CLBP. Therefore, we tested our hypothesis of a potential Medication-Overuse Backpain (MOB) in this preliminary case-series. While nearly all patients showed a notable pain relief, exclusively attributable to withdrawal from analgesics, the reduction in pain was only minimal in patient three. This finding is in line with the findings in patients with MOH [17]. Several risk factors have been identified for non-responders of the medication withdrawal concept. These risk factors include male sex, and problem with and deviations from the discussed withdrawal therapy and taking the causative medication again after withdrawal therapy [17]. In our case, this patient was also male and needed two withdrawal attempts. However, although the pathophysiology of MOH is still not fully understood, there is some evidence that functional and structural changes in the central nervous system, changes in mediators, and genetic variations seem to be involved. These include in detail:

- Genetic polymorphisms: in the dopaminergic system (SLC6A3, DRD2, and DRD4) and in drug-dependent pathways (HDAC3, ACE, BDNF, and WSF1)
- Upregulation of vasoactive and pro-inflammatory mediators (substance P, nitric oxide, and calcitonin gene-related peptide)
- Central sensitization
- Increase of nociceptive sensory fields
- Structural changes in the central nervous system (hippocampus, cerebellum, ventral striatum, periaqueductal grey area, and posterior cingulate cortex)
- Functional changes in the central nervous system (memory processing network, salience network, fronto-parietal network, and mesocorticolimbic network) [18-24]

Since withdrawal seems to work in patients with MOH and MOB, one can speculate that the underlying pathomechanisms might be also comparable. The future will show whether this is the case or different mechanisms are an issue in patients with MOB. However, in our patients, the described stepwise withdrawal method seems to be a simple and safe method to achieve pain reduction while simultaneously preventing organ damage. In addition, discontinuation of medication was well tolerated without any withdrawal symptoms. Despite the preliminary character of these results, our hypothesis might stimulate a new way of elucidating the pathophysiology of CLBP. Since several ongoing research projects currently deal with medication use or overuse in MOH, investigators should also consider analyzing patients with CLBP in the same way. This would help to answer three important questions:

1. Might there be something like Medication-Overuse Backpain (MOB)?
2. Which factors may lead to MOB?
3. Which patients may benefit from withdrawing pain medication?

Author contributions All authors contributed to the case-series conception and design. Hypothesis and data collection were performed by BL. Conceptualization, data analysis, writing, review, and editing were performed by BL and JH. The first draft of the manuscript was written by BL, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Compliance with ethical standards

Conflicts of interest The authors declare that they have no conflict of interest.

Ethical standards The manuscript does not contain a clinical study.

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