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Tapering of iatrogenic opioid use in patients with chronic non-malignant pain

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ABSTRACT

Introduction. Iatrogenic opioid use by patients with chronic malignant pain remains an important focus point. The positive effects of opioids seem to decline over time, whereas tapering will have positive effects in many patients. The purpose of the project was to optimise the process for patients with a wish or a need to taper opioids.

Methods. Patients were referred to a multidisciplinary pain treatment centre with the aim of tapering their opioid use. The use of opioids before and after the intervention at the pain treatment centre was registered. Questionnaires about quality of life, sleep quality and level of depression were completed before and after the study, participants were allowed to add comments to the questionnaires and interviews were conducted.

Results. A total of 22 patients participated. They had complex pain issues and had received opioids for a median period of nine years. The participants achieved a significant reduction of opioids (median 23 mg). Four patients completely stopped using opioids in the project period, four did not benefit from the project and two achieved reductions to the lowest dose possible allowing them to maintain an acceptable level of function. The remaining patients had a tapering plan to be continued in cooperation with their general practitioner. Most patients experienced the process as very satisfactory or satisfactory but achieved no measurable improvements in quality of life, sleep quality or level of depression.

Conclusion. Even though the tapering of opioids had appeared difficult beforehand, a significant reduction in opioid consumption was achieved.

Funding. The project was funded by the Danish Health Authority.

Trial registration. not relevant.

In 2019, approximately 441,000 persons among the Danish population of 5.8 million were treated with opioids. A total of 146,000 of those persons had prescriptions exceeding six months. From 2015 to 2019, the number of Danish users consuming opioids above the recommended levels had declined by 5%, and the number of users with an inappropriately high use was reduced by 20%. Even so, Denmark maintained a higher consumption of opioids than the other Nordic countries [1].

Signs indicating the need to taper opioids are numerous. Opioids may produce anxiety, sleep disorders, sexual problems, constipation and a poor quality of life [2]. Opioids, high doses in particular, may produce an aggravation of the pain experience (opioid-induced hyperalgesia), which can be hard for patients and doctors to understand [3]. The positive effects of opioids seem to decline over time, and in many patients tapering will reduce pain levels and improve their health-related quality of life [2-4].

However, some patients with chronic non-malignant pain need opioids to maintain sufficient pain reduction and uphold an acceptable level of activity [5]. Many patients can taper opioids gradually without encountering serious problems, but 15-20% experience significant withdrawal symptoms; and some require help, specialised support and medical treatment beyond general practice in order to succeed. Tapering of opioids is more complicated for patients with a complex chronic pain condition. It is essential to motivate the patient to engage in tapering, and the process must be based on mutual trust [3].

Addictive behaviour is not uncommon among patients with chronic pain. The prevalence of addictive behavior is 14.4-19.3% depending on the criteria applied [6, 7]. An important distinction to make is whether the addictive behaviour is due to undertreatment of pain ("pseudo-addiction behaviour") [8].

The purpose of the present project was to help patients reduce their intake of opioids by providing a facility to assist the GPs and the patients in the most difficult of cases with previous failed attempts.

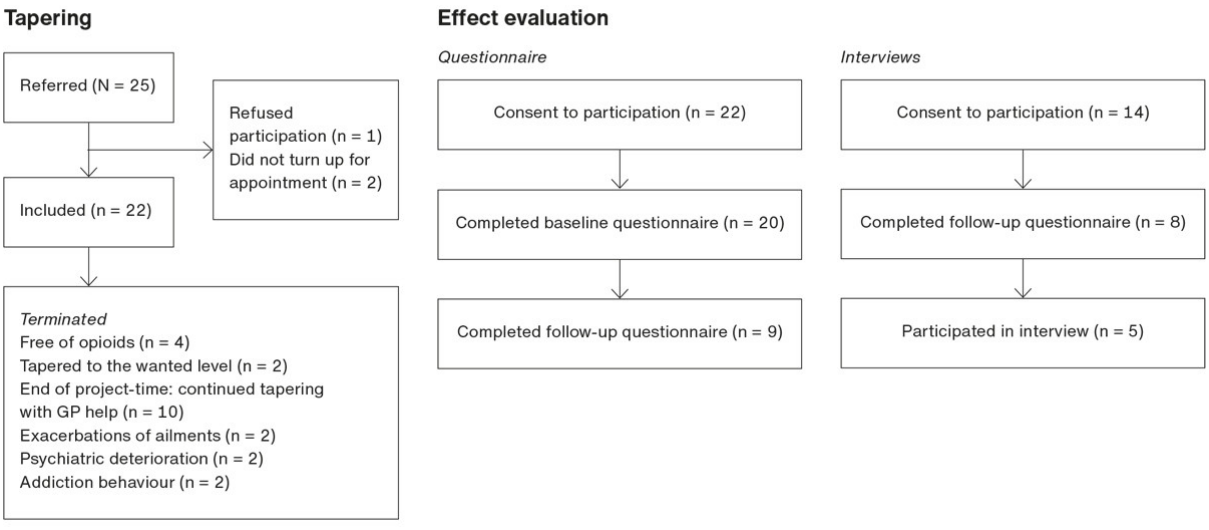
Prior to the present project, no possibility existed of obtaining assistance in the region of the study site.

METHODS

The study was conducted at a multidisciplinary pain treatment centre for treatment of patients with chronic complex non-malignant pain. Aside from educating the staff and a study visit at another multidisciplinary pain treatment centre with knowledge about opioid tapering, an external consultant doctor with extensive experience in treating addiction and psychiatry and an associate professor were affiliated with the project.

The inclusion criteria were: failed attempts of tapering in general practice or a hospital ward in chronic pain patients who provided informed consent to undertake another attempt at our clinic. Patients were included consecutively (**Figure 1**). The exclusion criteria were: a previously recognized heavy addiction to opioids.

FIGURE 1 Inclusion of patients in tapering and effect evaluation.



This was a pilot-intervention study. The primary outcome was consumption of opioids. The secondary outcomes were: quality of life, level of pain, signs of depression, quality of sleep and patient experiences.

A dedicated outpatient clinic consisting of a doctor, two nurses and a secretary was established from January to November 2020. Initially, all patients had a consultation with the doctor and a nurse. As a starting point, tapering was attempted with the support of person-to-person calls without the additional medicinal support, unless tangible problems had been encountered in earlier tapering attempts.

Individual opioid doses were converted to morphine using the online calculator at [9].

The prescriptions of opioids and supportive medicine (if needed) were handled by the tapering team during the project period, whereas the rest of the patients' prescriptions continued to be handled by their GPs. Short-acting opioids used on demand were converted to sustained-release opioids. Those already on sustained-release opioids had their doses adjusted or their opioids converted into morphine if deemed necessary [2-4]. The method of tapering was individualised and gradual and the tapering process was decided upon in collaboration with the patient [3, 4].

Participants were terminated from the project for the following reasons: the patient did not want to continue or was completely free of opioids; the patient exhibited "addictive behaviour" [7, 8] or failed to attend appointments; the project period expired. Unresolved patients with a chronic complex pain condition were referred to a multidisciplinary pain centre instead.

Evaluation

Questionnaires

The participants completed a questionnaire on an iPad before the first consultation. The questionnaire comprised questions about gender, age, the original reason for the prescription, the number of years with opioids, the type of opioids prescribed and three relevant validated questionnaires from "PainData" [10].

The questionnaire included ten questions about quality of life (PROMIS GLOBAL-10 Score) [11], five about sleep quality (from the Karolinska Sleep Questionnaire) [12] and finally nine questions about degree of depression (from the Patient Health Questionnaire (PHQ)) [13]. The patients were also given the opportunity to describe their expectations. Three weeks after the end of their tapering period, patients who had provided their consent received a follow-up questionnaire sent to their national electronic mailbox (E-boks). The follow-up contained a question about their overall evaluation and provided an opportunity to describe their experiences and suggest ideas for improvement. The questions from the baseline questionnaire were repeated (PROMIS CLOBAL-10 Score, KSQ and PHQ-9). A reminder was sent two weeks later to those not completing the follow-up.

Interviews

Consenting patients were contacted by e-mail after completing the follow-up questionnaire. If they were still willing to participate, a time was scheduled for a phone interview. All interviews were digitally recorded.

Data analysis

Quantitative data were analysed with descriptive and comparative statistics using the statistical program Stata 16. PHQ-9 produces a depression score ranging from 0 to 27 where higher scores are associated with increased symptom-related challenges. Scores ≤ 4 signify minimal depression. From the PROMIS Global-10, two sum scores are calculated: the Global Physical Health Score and the Global Mental Health. These scores are then standardised to a T-score where the norm is 50 points, with a standard deviation of ± 10. Higher scores mean a higher quality of life. A two-sided p-value below 0.05 was considered significant. Qualitative data were analysed using content analyses [14].

Ethics

The project was registered with the Danish Data Protection Agency (20/12317). All patients received oral and written information and provided written consent for the use of data from their medical records and to participate in the evaluation. Consenting patients completed the baseline questionnaire. The participants could also provide separate consent to receive the follow-up questionnaire and/or be contacted for an interview.

Trial registration: not relevant.

RESULTS

See Figure 1 for an overview of inclusion and effect evaluation. A total of 68% of the patients were referred from their general practitioner, three internally from the pain centre and four from other hospital departments.

Disease was the most common reason for the start-up of opioids (**Table 1**), and back pain was a substantial component in 14/22 patients (64%). The majority of the patients used long-acting opioids (Table 1). The forms of opioid included oxycodone (eight participants), morphine (five participants), mixed opiods (three participants), tramadol (two participants), methadone (two participants), hydromorphone (one participant) and fentanyl patches (one participant). A total of 13 participants used supplemental medicines: clonidine (seven participants) and gabapentin (six participants).

TABLE 1 Demographic data for all participants and for those who participated in the follow-up evaluation.

	Baseline (N_b = 20)		Follow-up (N_f = 9)	
	mean (range)	n (%)	mean (range)	n (%)
Age, yrs	59 (29-87)		56 (29-74)	
Female		11 (55)		6 (67)
Reason for start-up of opioids				
Trauma		3 (15)		1 (11)
Operation		2 (10)		
Disease		9 (45)		6 (67)
Other[a]		6 (30)		2 (22)
Type of opioid				
Rapid-acting		5 (25)		1 (11)
Long-acting		18 (90)		8 (89)

a) Headaches, pain in neck or back, work-related injuries, chronic diseases.

Tapering

Two patients were unable to taper due to exacerbations of their ailments, two dropped out due to psychiatric deterioration and two dropped out due to addictive behaviour.

Patients had 1-3 visits with the doctor (median: two) and 0–44 contacts with a nurse (median: 12). The patients achieved a significant decrease in the use of opioids (**Table 2**).

TABLE 2 Use of opioids and level of tapering (n = 22).

	Median (IQR) [range]	p-value[a]
Time with opioids, years	9 (4-12) [1-26]	
Opioid use, mg		< 0.001
Before	86 (60-150) [25-720]	
After[b]	60 (20-100) [0-435]	
Tapering, mg	23 (8-50) [–15[c]-420]	

IQR = interquartile range.
a) Wilcoxon signed rank test.
b) At the time of termination of the patient's participation in project.
c) 2 patients increased their opioid use: from 25 to 40 mg and from 82.5 to 90 mg, respectively.

Evaluation

Questionnaires

Compared with the whole population, more women participated in the follow-up (Table 2). At baseline, the participants' main expectations were to improve their quality of life and to receive the right help to taper their use of opioids without compromising their pain levels. One wrote: *"To feel better and to get [my] life back*".

The participants had lower quality of life scores than the general population, both physically and mentally. The level of pain was high, most had symptoms of depression and their sleep was affected by their pain (**Table 3**). For those who completed the follow-up questionnaire, scores were, by and large, unchanged after the course of tapering (Table 3). Even so, 56% experienced the course of tapering as very satisfactory, 11% as satisfactory, and 33% as both satisfactory and unsatisfactory. Noted as good elements were ongoing conversations, tapering at the patient's rate, being trusted by the staff and interaction with very friendly and accommodating staff. Among the negative elements noted were that tapering entailed physical unrest, and some patients would have preferred to remain in the project for a longer period of time.

TABLE 3 Quality of life, pain, depression and sleep scores for all participants and for those who participated in the follow-up evaluation.

	All, baseline	2 responses	
	n = 20[a]	baseline (n = 9)	follow-up (n = 9)
Quality of life			
GPH, T-score[b] ± SD	34.9 ± 4.1	34.9 ± 4.1	34.9 ± 4.1
GMH, T-score[b] ± SD	41.1 ± 3.6	38.8 ± 3.6	41.1 ± 3.6
Pain[c], median (IQR)	7 (5-8)	8 (7-8)	7 (4-9)
Depression[d], median (IQR)	12 (8-14)	10.5 (8-13)	7 (5-14)
Sleep, n (%)			
Disturbed/restless sleep (n = 19):			
Every night or almost every night	12 (63)	5 (56)	5 (56)
Various times every week	3 (16)	3 (33)	2 (22)
Less	4 (21)	1 (13)	2 (22)
Difficulties falling asleep (n = 20):			
Every night or almost every night	6 (30)	2 (22)	2 (22)
Various times every week	6 (30)	3 (33)	4 (44)
Less	8 (40)	4 (45)	3 (33)
Waking up too early (n = 20):			
Every night or almost every night	10 (50)	3 (33)	4 (44)
Various times every week	6 (30)	3 (33)	2 (22)
Less	4 (20)	3 (33)	3 (33)
Wakes up several times, difficulties falling asleep again (n = 19):			
Every night or almost every night	9 (47)	4 (50)	1 (11)
Various times every week	6 (32)	3 (38)	5 (56)
Less	4 (21)	1 (12)	3 (33)
Pain affects sleep (n = 19)	16 (84)	7 (88)	6 (67)

GMH = Global Mental Health; GPH = Global Physical Health; IQR = interquartile range; SD = standard deviation.
a) Different n due to missing data for single items, 2 of the total number of 22 participants failed to complete the baseline questionnaire.
b) Normal population 50, higher scores mean a higher quality of life.
c) Numeric rating scale 0-10.
d) The Patient Health Questionnaire-9 depression score 0-27, higher scores are associated with increased symptom-related challenges, scores ≤ 4 equal minimal depression.

One patient wrote: "Thank you so much for the opportunity to be part of this project, so that I and my general practitioner have got help to learn how my tapering should be conducted, so it is not too quick and will then backfire".

Interviews

Of the patients who consented to participate in an interview, eight also completed the follow-up questionnaire. They were all contacted for an interview, and five (three women and two men) accepted. The interviews had a mean duration of 17 minutes. All interviewees stressed that the ongoing conversations had been very valuable. It

was a good back-up and it afforded them peace of mind to know that contacts would be continuous. The necessary time was allocated for the conversation, and the participants experienced being part of managing the speed of tapering, depending on how they felt. Some of them had tried to taper with help from their general practitioner, but had failed because tapering had been too rapid and thus resulted in serious side effects. The participants experienced a good introductory consultation and felt that the staff believed what they said and had considerable knowledge in the area. This made them trust the recommendations given. Several of the participants had reached their goal of partial or complete tapering, whereas others were satisfied with the plan for further tapering. However, some wished that they could have stayed in the project until they had reached their goal, and one was not prepared for the termination of project participation and felt abandoned.

DISCUSSION

The 22 patients constituted a complicated group of patients with a complex chronic non-malignant pain condition. About 40% had previously had treatment at a pain clinic, and most had been treated with opioids for many years. Four patients did not benefit from treatment in the project, but another four patients completely stopped their use of opioids. The remaining patients achieved reductions to a smaller or larger extent, and the majority were disposed towards continuing the tapering process in cooperation with their GP. For two of the patients, we agreed upon the achieved dose of opioids as the lowest dose allowing for an acceptable level of functioning.

For the nurses in the project in particular, the process of tapering required patience and persistence as most patients exhibited a large degree of psychological dependence. Only one patient was referred back to his GP at the initial consultation to continue his tapering process there; the others had a median of 12 contacts with their contact nurse. The two patients most in need of nurse support (44 and 32 contacts) included one patient with "addictive behaviour" in need of coordination with the district nurses, and one especially frail patient with many years of disability due to rheumatoid arthritis. Even so, for the majority of patients, the task was manageable. In comparison, only one or two contacts with the doctor were needed, typically at the beginning and the end of the patient's participation in the project.

In comparison, a prospective multicentre study concerning pain clinic patients engaging in the process of tapering out of opioids also showed only minor improvements in cognitive function but produced unaltered health-related quality of life, depression and anxiety scores [15].

A proposal for a future organisation may be referral of complex patients from a GP to a primary consultation (or a video consultation) by a doctor at the multidisciplinary pain centre with a view to preparing an opiods tapering plan in cooperation with the patient. The support process provided by the nurses may be handled in primary care with the possibility of acquiring assistance from a specialised pain centre nurse. Additional consultations would be necessary only in response to problems in the tapering process.

The strength of this project was the use of specialised knowledge about pain treatment and the tapering of opioids in a group of patients with complex non-malignant pain conditions based on a multidisciplinary approach. The weaknesses of the project include the relatively small number of participants and the low number of patients participating in the subsequent evaluation.

CONCLUSION

Even though the patients constituted a group in which the tapering of opioids had seemed very difficult beforehand, the patients achieved a statistically significant reduction in their consumption of opioids, and four

stopped using opioids altogether. Most patients experienced the process as very satisfactory or satisfactory, but no measurable improvements were recorded in their quality of life, pain or depression or sleep scores.

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Conflicts of interest Potential conflicts of interest have been declared. Disclosure forms provided by the authors are available with the article at ugeskriftet.dk/dmj

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