EUROPEAN RESPIRATORY *journal*

FLAGSHIP SCIENTIFIC JOURNAL OF ERS

Early View

Research letter

Attitudes of patients with chronic breathlessness towards treatment with opioids

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Please cite this article as: Verberkt CA, van den Beuken-van Everdingen MHJ, Wouters EFM, *et al*. Attitudes of patients with chronic breathlessness towards treatment with opioids. *Eur Respir J* 2019; in press (https://doi.org/10.1183/13993003.01752-2019).

This manuscript has recently been accepted for publication in the *European Respiratory Journal*. It is published here in its accepted form prior to copyediting and typesetting by our production team. After these production processes are complete and the authors have approved the resulting proofs, the article will move to the latest issue of the ERJ online.

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Attitudes of patients with chronic breathlessness towards treatment with opioids

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Take home message

Attitudes of patients towards opioid treatment for chronic breathlessness are mixed, with 37% of patients willing to use opioids, 25% unwilling, and 38% of patients indecisive. Physicians are an important source of information for these patients.

To the editor:

Breathlessness is the most common symptom in advanced chronic lung disease or chronic heart failure (CHF) [1]. Opioids are recommended for palliative treatment of breathlessness persisting despite optimal pharmacological and non-pharmacological treatment *[2, 3]*. However, physicians don't always consider opioids for chronic breathlessness [4, 5] and experience barriers when considering opioids, like resistance of patients [6]. This can limit effective palliative treatment. Qualitative studies in patients with COPD and CHF revealed fear of dependence and fear of imminent death as most important barriers to opioid use. Reason to start treatment was to do as much as possible [7-9]. These qualitative studies were only conducted in small patient populations. Therefore, our aims were 1) to assess the willingness of patients with chronic lung disease or CHF to use opioids for breathlessness, irrespective of a current indication for opioid treatment, and 2) to assess their barriers towards opioid use and reasons to use opioids. Finally, we aimed to compare willingness between sexes, age, educational level, diagnosis and breathlessness severity.

An exploratory convenience sample of 175 patients referred for a baseline assessment prior to pulmonary or heart failure rehabilitation was recruited, independent of their level of breathlessness. Patients were excluded when they could not read or write, did not master Dutch, were <18 years or were unable to give informed consent. The Maastricht University Medical Centre (MUMC+) medical ethical committee, Maastricht, the Netherlands, reviewed the study protocol and concluded that the study didn't fall under the Medical Research Involving Human Subjects Act (METC 2018-0790). Patients completed a survey including: demographic characteristics, educational level, previous and current opioid use (which opioid, dosage and reason for prescription) and willingness to use opioids for breathlessness. Patients willing to use opioids and patients who had experience with opioids were asked to indicate their reasons to use opioids; patients unwilling to use opioids were asked to indicate their barriers. Patients who were indecisive were asked to indicate their barriers against and the reasons to use opioids. Patients were also invited to report other than the predefined reasons using a free text field. The predefined reasons were selected based on previous research [7-9], expert opinion of the project group and experience from patient inclusion for an opioid trial (MORDYC) [10]. Disease characteristics (diagnosis, disease history, lung function, six minute walk distance (6MWD) [11]) and breathlessness severity (modified Medical Research Council (mMRC) Scale) [12] were recorded using chart review.

Data were described using mean (SD) or median (interquartile range [IQR]) for continuous variables and number (percentage) for categorical variables. We compared the willingness to use opioids between sexes, age (< or ≥65 years), educational level (lower education, defined as having finished secondary vocational education vs. high education, defined as having finished at least Higher

General Secondary Education) [13], diagnosis and mMRC score (< or ≥2 points) using Chi-squared test or Fisher-Freeman-Halton test, as appropriate.

Between November 2018 and May 2019, 237 patients were eligible and 175 patients (50% male), aged median 65 years (IQR 57-70), completed the survey (response rate 74%). Patients were diagnosed with COPD (124; 71%), CHF (18; 10%), asthma (17; 10%), interstitial lung disease (8; 5%), COPD-asthma Overlap Syndrome (3; 2%), pulmonary hypertension (3; 2%) and other (2; 1%). Median mMRC score was 2.5 points (IQR 2-3), 6MWD was 393m (107m) and 141 patients (81%) only completed lower education. Non-responders were 45% male and aged median 66 years (IQR 59-71; both p>0.05 compared to responders).

Seventy-two out of 175 patients (41%) previously used ≥1 different opioids (49 (68%) for pain, ten (14%) for breathlessness, eight (11%) for both pain and breathlessness, five (7%) for drug dependence), in six patients (8%) previous opioid use was unknown. Used opioids were morphine (45; 63%), oxycodone (30; 42%), fentanyl (7; 10%), methadone (6; 8%) and buprenorphine (3; 4%). At the time of the survey, 14/175 patients (8%) used an opioid (seven (50%) for pain, five (36%) for breathlessness, one (7%) for both pain and breathlessness and one (7%) for drug dependence). Six patients (43%) used morphine, four patients (29%) used fentanyl, four patients (29%) used oxycodone and one patient (7%) used methadone. Median daily morphine equivalent dose was 27.5mg (IQR 16.25-30) with an outlier of 480mg (dependence).

In total, 64 patients (37%) were willing to use opioids for breathlessness, 44 patients (25%) were unwilling and 67 patients (38%) were indecisive. Patients unwilling to use opioids were older compared to patients willing to use opioids and indecisive patients (66 vs. 63 and 62 years, p<0.01). Gender, educational level, diagnosis, mMRC score and previous opioid use were comparable between groups (p=0.79, p=0.06, p=0.42, p=0.06 and p=0.07 respectively).

Main reasons to use opioids were on physician's recommendation (89/131; 68%) and doing as much as possible to feel better (79/131; 60%). Main reasons not to use opioids were concerns of adverse effects (49/111; 44%) and fear of dependence (47/111; 42%). Differences existed between decisive patients and indecisive patients (Table 1). Free text considerations were not being familiar with opioids, fear of getting high and fear for weight increase.

	Willing to use opioids; n (%)			Not willing to use opioids; n (%)			Indecisive; n (%)		
	Total	Used opioid before	Never used opioid	Total	Used opioid before	Never used opioid	Total	Used opioid before	Never used opioid
	n=64	n=25#	n=36#	n=44	n=24#	n=18#	n=67	n=23#	n=43#
Reasons to use opioids									
If recommended by physician	40 (63)	18 (72)	20 (56)	NA			49 (73)	16 (70)	33 (77)
Doing as much as possible to feel better	47 (73)	18 (72)	27 (75)				29 (43)	11 (48)	18 (42)
If it doesn't help, it doesn't harm	18 (28)	8 (32)	8 (22)				7 (10)	2 (9)	5 (12)
Heard of positive effects	6 (9)	2 (8)	4 (11)				7 (10)	1 (4)	5 (12)
Read about positive effects	5 (8)	2 (8)	2 (6)				4 (6)	3 (13)	1 (2)
If recommended by other health care professional	6 (9)	0 (0)	6 (17)				1 (1)	1 (4)	0 (0)
Good experiences of loved one(s)	1 (2)	0 (0)	1 (3)				2 (3)	0 (0)	2 (5)
Other	0 (0)	0 (0)	0 (0)				1 (1)	0 (0)	1 (2)
Reasons not to use opioids									
Concerns about adverse effects	NA			28 (64)	15 (63)	11 (61)	21 (31)	10 (43)	11 (26)
Fear of adverse effects				*17 (39)*	*6 (25)*	*9 (50)*	*10 (15)*	*6 (26)*	*4 (9%)*
Used opioids before, experienced adverse effects				*8 (18)*	*8 (33)*	*0 (0)**	*6 (9)*	*6 (26)*	*0 (0%)**
Read about negative effects				*7 (16)*	*3 (13)*	*3 (17)*	*3 (4)*	*3 (13)*	*0 (0%)*
Heard of negative effects				*4 (9)*	*0 (0)*	*3 (17)*	*5 (7)*	*0 (0)*	*5 (12%)*
Negative experiences of loved one(s)				*4 (9)*	*2 (8)*	*2 (11)*	*3 (4)*	*0 (0)*	*3 (7%)*
Fear of dependence				26 (59)	11 (46)	14 (78)	21 (31)	7 (30)	14 (33)
Against physicians advice				1 (2)	1 (4)	0 (0)	35 (52)	10 (43)	25 (58)
Not being able to drive a car				14 (32)	7 (29)	6 (33)	16 (24)	4 (17)	12 (28)
Use enough medication, don't want more				13 (30)	7 (29)	5 (28)	16 (24)	6 (26)	10 (23)
Breathlessness is not that bad yet				9 (20)	3 (13)	6 (33)	6 (9)	1 (4)	5 (12)
Against advice of loved one(s)				6 (14)	2 (8)	3 (17)	2 (3)	0 (0)	2 (5)
Fear of increase of breathlessness				4 (9)	2 (8)	2 (11)	2 (3)	2 (9)	0 (0)
Used opioids before, didn't help				4 (9)	4 (17)	0 (0)	0 (0)	0 (0)	0 (0)
Fear of imminent death				3 (7)	0 (0)	3 (17)	0 (0)	0 (0)	0 (0)
My religion doesn't allow using opioids				1 (2)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)
Other				3 (7)	3 (13)	0 (0)	1 (1)	0 (0)	1 (2)

Data are presented as number (%). NA=not applicable. *: $p<0.01$ for difference between patients who used opioids before and patients who never used opioids. #: 6 patients didn't know if they used opioids before and are therefore excluded from this stratified analysis.

This study has assessed attitudes towards opioid treatment in patients with chronic breathlessness with or without an indication for palliative treatment with opioids. The results showed that attitudes towards opioids are mixed, with only a quarter of the patients unwilling to use opioids. These results do not correspond with the physicians' assumptions, who indicate not to prescribe opioids among other things because patients are resistant [6]. Three quarters of the indecisive patients indicate to rely on the physician's positive advice and one third indicates to rely on a negative advice. So, the physician is an important source of information and open and honest communication is important [8]. Since physicians state to be insecure in prescribing opioids because of a lack of knowledge [6, 8], more emphasis should be on educating physicians about when and how to treat breathlessness with opioids.

The main barriers against and reasons to use opioids mentioned in this study were consistent with previous studies [7-9]. Concerns related to adverse effects and fear of dependence are the main reasons not to use opioids or to be indecisive. Qualitative studies show that patients experience that small improvements in breathlessness can have a big impact on the quality of life [9], which fits with the attitude of being willing to do as much as possible.

This study's results have also shown that there are as many opinions as people, which also applies to the way patients gather information to form this opinion. Therefore, a proper provision of information for patients using different channels is necessary.

Low dose opioids appear to be effective and safe in patients with severe chronic breathlessness [14-16]. However, adverse effects might occur [15]. Physicians and patients should therefore discuss benefits and possible harms when considering low dose opioids.

Limitation of this study is that the convenience sample consisted of only 175 patients referred to one center. Another limitation is that not all included patients had an indication for opioid treatment. However, there was no difference in attitude between patients with mild (mMRC<2) and severe breathlessness, indicating that forming an opinion about opioids is irrespective of breathlessness severity and therefore information should be suitable and accessable to all patients with chronic breathlessness. Nevertheless, opioids should be reserved for patients with chronic breathlessness, persisting despite optimal pharmacological and non-pharmacological treatment [17, 18].

Acknowledgements

We would like to thank Miranda Coenjaerds from CIRO for contributing to the data collection.

Furthermore, we would like to thank Liesbeth van Hoef and Wendy Engering from the Centre of Expertise for Palliative Care, Maastricht University Medical Centre (MUMC+) for entering the data.

This project was funded by The Netherlands Organisation for Health Research and Development (ZonMW), The Hague, The Netherlands (Grant number 836031012).

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