Death from COVID-19: management of breathlessness: a retrospective multicentre study

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ABSTRACT

Objectives Breathlessness is the most significant symptom in those dying of COVID-19. Historically, though, it has often been palliated poorly at end of life. The aim of this work was to assess whether breathlessness in patients dying from COVID-19 was being managed appropriately.

Methods A multicentre, retrospective analysis of clinical data was undertaken. Patients who had died of COVID-19 across three acute hospitals over a 2-month period were included. Those already prescribed background opioids and those who died in intensive care were excluded. Data were collected from clinical notes, where available.

Results 71 patients from 18 wards (3 hospitals) were included. The median total dose of opioid and midazolam given in the last 24 hours of life (continuous subcutaneous infusion ± 'as required' medication) was 33 mg (14–55) and 15 mg (6–26), respectively. 37 patients (52%) were prescribed continuous subcutaneous infusions. There were 426 recorded respiratory rates of at least 25 breaths per minute, for which an opioid or benzodiazepine was given in 113 (27%) of instances.

Conclusions Less than a third of episodes of breathlessness, as measured by respiratory rate, were palliated with anticipatory medicines. Specific palliative care guidelines for COVID-19 are necessary but may not always be followed.

Key messages

What was already known?
⇒ Breathlessness is the most significant symptom in those dying of COVID-19.
⇒ COVID-19-specific guidelines advocate the use of opioids and/or benzodiazepines to manage severe breathlessness at end of life.

What are the new findings?
⇒ The majority of patients dying of COVID-19 are tachypnoeic during their last days of life, but only a minority of these respiratory events are palliated with 'as required' medication.

What is their significance?
⇒ Specific palliative care guidelines for COVID-19 are necessary but should be accompanied by education on symptom management to support healthcare professionals to manage breathlessness and associated distress effectively.

INTRODUCTION

Breathlessness, the subjective experience of breathing discomfort, is a highly prevalent and distressing symptom in patients with COVID-19 and particularly in those at the end of life, with tachypnoea (an elevated respiratory rate) being a common clinical sign and acute respiratory distress syndrome (an acute inflammatory lung injury resulting in hypoxaemic respiratory failure) being the most common mode of dying.[1–3]

Recognising this, in the early months of the pandemic, COVID-19-specific guidelines, including those published by the National Institute for Health and Care Excellence, made clear that severe breathlessness was expected and should be managed using 'as required' doses of opioids and/or benzodiazepine.[4] Some centres also recommended starting a continuous subcutaneous infusion (CSCI) of opioid to ensure that patients did not die before their symptoms could be controlled.[5]

The importance of palliating breathlessness effectively at the end of life has long been recognised, and yet it remains a frequently overlooked symptom that is often palliated poorly, if at all.[6]

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The aim of this work was to assess whether breathlessness in patients dying from COVID-19 was being managed appropriately, in a real-world (as opposed to a research) setting.

METHODS

We undertook a retrospective analysis of clinical data from patients who had died from COVID-19 within a secondary care setting serving a geographically defined region with a population of approximately one million (NHS Lothian, UK, three acute hospitals). A convenience sampling approach of patients admitted between 19 February 2020 and 24 April 20 was used.

Eligible patients met the following criteria: death during the admission under review; COVID-19 (or equivalent term) recorded as the primary cause of death (1a, 1b or 1c); end-of-life care had been provided on a general hospital ward as opposed to an intensive care unit; the patient had not been taking regular opioid medication on admission; and necessary data were available to complete key parameters needed for analysis.

The following data were recorded: age, sex, usual place of care, comorbidities, diagnosis of the dying phase of illness and referral to the hospital palliative care team. Data on medications prescribed to alleviate symptoms near the end of life (termed anticipatory medications) were collected, including type (eg, opioid, benzodiazepines (midazolam)), doses, use of a CSCI and use of 'as required' medication. All opioid doses were calculated in terms of morphine equivalence (morphine equivalent daily dose (MEDD)) to allow comparison.

Data on respiratory rate and corresponding use of opioid, benzodiazepine or both to treat a respiratory rate ≥25 breaths per minute were recorded. This cut-off corresponded to a 'severe respiratory event' under the National Early Warning Score (NEWS).[7] Only respiratory events occurring after the prescription of anticipatory medications were recorded. For each event, it was noted whether an 'as required' opioid or benzodiazepine had been administered in the 30 min prior to or following the event.

As this was a retrospective analysis and not designed to test any hypothesis, the sample size was based on the number of patients eligible during the defined period. These data are presented descriptively using proportions and, where appropriate, median and IQR. All analyses were performed in SPSS V.21.

As this was an observational study, it was done in accordance with Strengthening the Reporting of Observational studies in Epidemiology guidelines.

RESULTS

Data on 71 patients were assessed from 18 wards across three hospitals. Most patients were male (65%) and over 75 years (70%), with a median age of 81 years (73–86). The majority of the patients (89%) had been admitted from their own home, with cardiovascular disease (80%), diabetes mellitus (22%) and respiratory disease (15%) being the most common comorbidities. The median length of admission was 7 (4–10) days. The median time before death that a diagnosis of dying was made was 1 (1–2) day.

Table 1 details the prescribing data. Anticipatory medications were prescribed for 70 (99%) patients and administered in 66 (94%) cases. Thirty-seven (52%) patients were prescribed a CSCI, but of these six (16%) were started within 4 hours of death. The median time before death that CSCIs were started was 18 (8–32) hours. The median total dose of opioid in the last 24 hours of life (ie, CSCI ± 'as required') was 33 mg (14–55) MEDD. The median total dose of midazolam in the last 24 hours of life was 15 mg (6–26).

In 10 (14%) patients, NEWS were recorded until death, and in 44 (62%) patients monitoring continued to within 24 hours of death (data not shown). A total of 426 separate respiratory events (ie, respiratory rate ≥25) were recorded, with 57 (80%) patients having at least one respiratory event. The median (IQR) number of events per person was 4 (1–9). There were 113 respiratory events treated with opioids and/or midazolam. There were 313 (73%) respiratory events during which neither opioids nor midazolam was used.

DISCUSSION

The findings show that the majority of patients dying of COVID-19 are tachypnoeic during the last days of their life but that only a minority of these respiratory events are palliated with 'as required' medication. This is of interest given COVID-19-specific palliative care guidelines emphasise the need to use more frequent or higher doses of opioid medication, either alone or in combination with benzodiazepines, until comfort is achieved.

We propose three possible reasons for the low proportion of palliated respiratory events. First, many healthcare professionals remain anxious about using opioids in patients with respiratory disease and do not feel confident in administering an opioid, especially in the context of hypoxia, for fear of worsening respiratory compromise. Second, many healthcare professionals tend not to recognise the need to use anticipatory medicines until they have first recognised dying itself. Many feel that symptom-focused care can only commence once active treatment has stopped, rather than it being delivered in parallel. Third, during the COVID-19 pandemic, clinical staff have faced unprecedented challenges, including an increased volume of work and at times redeployment to other departments. Some respiratory events may have been overlooked because staff were unfamiliar with providing end-of-life care or were caring for many acutely unwell patients.

Table 1 Use of medicines to alleviate symptoms prior to death and in relation to respiratory events

	n	%	Median	IQR
Anticipatory medication				
Medication prescribed	70	99		
Days prescribed after diagnosis of dying			0	0–1
Medication administered	66	94		
'As required' medication				
Opioid used in the last 24 hours of life (mg)			16	7–37
Midazolam used in the last 24 hours of life (mg)			7.5	2–20
Continuous subcutaneous infusion (CSCI) of medication				
Prescribed	37	52		
Time started prior to death (hours)			18	8–32
<4 hours	6	9		
4–12 hours	8	11		
12–24 hours	10	14		
>24 hours	13	18		
CSCI opioid, starting dose (mg)			20	20–30
CSCI opioid, dose at death (mg)			30	20–40
CSCI midazolam, starting dose (mg)			10	10–12.5
CSCI midazolam, dose at death (mg)			10	10–20
Total medication use				
Total dose of opioid in the last 24 hours of life (mg)			33	14–55
Total dose of midazolam in the last 24 hours of life (mg)			15	6–26
Respiratory events (respiratory rate ≥25)				
Total	426	100		
Events when opioid and/or midazolam given	113	27		
Events when no opioid or midazolam given	313	73		

In our cohort, the doses of opioid and benzodiazepine used in the last 24 hours of a patient's life were consistent with doses reported in other studies since the beginning of the pandemic.[8–10] Interestingly, in response to their data, Jackson and colleagues[10] concluded that new or adapted guidelines for COVID-19 may not be required because the doses of opioid and benzodiazepine typically used were within existing 'normal' guidelines. Our data suggest that dose total alone may be an unreliable indicator of what is actually required to maintain comfort and may underestimate need.

The present study has a number of limitations. First, as this is a retrospective review, we have examined available data on respiratory rate, but we do not have reliable supporting data on patients' subjective assessment of their symptoms. As breathlessness is a subjective experience, it is therefore possible that some patients may have been tachypnoeic but not felt dyspnoeic or distressed. However, we believe that, for most, a respiratory rate of at least 25 breaths per minute would represent an uncomfortable sensation. Second, monitoring of respiratory rate ceased when observations were discontinued towards end of life. As such, our data do not capture the palliation of any respiratory events arising between this time point and death. However, in 62% of cases, monitoring continued within the last 24 hours of life.

CONCLUSION

Our findings add to the evidence that patients dying of COVID-19 have clinical features of acute respiratory distress. To our knowledge, this is the first study to attempt to measure whether what was given to treat this correlates with what was needed, and by doing so provides some evidence that these doses may not have been sufficient. We believe that specific palliative care guidelines for COVID-19 are necessary but may not always be followed.

Moving forward, it is imperative to deliver education on the management of breathlessness to empower healthcare professionals to palliate it effectively and to ensure that future patients dying from COVID-19 do so with their symptoms controlled.

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