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Patients with Covid-19 at the End of Life

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Abstract

Introduction

Management of Covid-19 has been among the biggest challenges in our medical careers. Unfortunately, it has led to a rapid end of life for some. Our aim was to describe symptomatology and medication requirements at the End of Life for patients with COVID-19 and explore the value of education, with Specialist Palliative Medical availability around the clock for all medical staff.

Case 1

A male patient with End Stage Kidney Disease (ESKD) and COVID-19 deteriorated rapidly on day 8 of his illness. The main symptoms were dyspnea and agitation.

Case 2

A male patient with ESKD and COVID-19 had progressive dyspnea over the first 5 days of his illness and his symptoms later escalated rapidly over a period of hours.

Case 3

A female patient with multiple co-morbidities who developed COVID-19 and initially appeared to be recovering well later deteriorated rapidly, over hours, on day 16 of her illness. Her main symptoms were dyspnea and agitation.

Outcome

Patients with Covid-19 experienced rapidly escalating dyspnoea and agitation in the End of Life phase, with respiratory secretions being less prominent in this cohort. Medication requirements to achieve symptom control varied considerably.

Discussion

Major obstacles encountered were the need for strict isolation with Personal Protective Equipment (PPE) for staff and family, and restricted visiting to reduce external exposure to Covid-19. Prior End of Life care education delivered to medical staff focusing on symptom management and medications, may have positively influenced early symptom assessment, proactive initiation of appropriate medications and methods of medication delivery. The availability of around the clock Specialist Palliative Medical advice may have helped other Medical staff cope with this new illness for patients in the dying phase.

Introduction

Similar to cohorts described in recent literature,[1-3] patients dying from Covid-19 infection can deteriorate rapidly, within hours, with escalating oxygen (O_2) requirements and symptoms. We describe the clinical course of the dying phase of three patients referred to a Hospital Specialist Palliative Care Service (HSPCS) within a tertiary referral centre, outlining the heterogeneity within the cohort and the importance of vigilant monitoring for escalating symptoms at End of Life. Patient assessment and advice regarding symptom management occurred via phone consultation by the Covid-19 medical team with the Hospital Specialist Palliative Care Service, around-the-clock.

We performed a retrospective observational analysis of clinical notes of three patients with Covid-19 referred to Hospital Specialist Palliative Care Service for End of Life care. Data was collected using a proforma, extracting information regarding symptoms and associated medications prescribed for symptom management in the last forty-eight hours of life. Verbal consent for inclusion was obtained from the patients' next-of-kin. A waiver was granted from the Clinical Research Ethics Committee.

Patient characteristics are outlined in Table 1. All patients were opioid naive.

Table 1: Patient Characteristics.

	Patient 1	**Patient 2**	**Patient 3**
Age	79	69	86
Sex	Male	Male	Female
Comorbidities	8	6	4
Rockwood Frailty Score	7	6	4
Days from initial illness[a] to referral to HSPCS	9	5	22
Time of Referral to death (hours)	24	27	72

a Initial onset of COVID-19 symptoms (e.g. cough, dyspnea, fever) or initial positive swab if symptom onset unknown

Case 1

A male in his seventies with End Stage Kidney Disease (ESKD) and multiple co-morbidities was admitted to hospital 5 days after a positive Covid-19 swab. He acutely deteriorated on day 8 of his illness with acute dyspnoea, associated anxiety and agitation. The previous day he had been relatively well and mobilising around his isolation room. Symptoms rapidly escalated over short hours with increased work of breathing, use of accessory muscles and pursed lip breathing/tripod positioning. A stat dose of morphine sulphate 5mg subcutaneously (SC) was administered for dyspnoea management. A trial of intravenous (IV) steroids, antibiotics and diuretics were also initiated. Despite this, imaging confirmed worsening pulmonary infiltrates secondary to Covid-19. The patient required morphine sulphate 20mg as required (PRN) SC for dyspnoea and midazolam 15mg PRN SC for agitation in the 24 hours prior to referral to the Hospital Specialist Palliative Care Service.

On Day 9, he was referred to the Hospital Specialist Palliative Care Service and a 24-hour continuous subcutaneous infusion with alfentanil 1000mcg and midazolam 10mg was commenced (Table 2).

He required a further midazolam 10mg PRN SC for agitation and morphine sulphate 12.5mg PRN SC for dyspnoea and died peacefully on day 10, well symptom controlled with his wife at his bedside in full Personal Protective Equipment (PPE). Respiratory secretions had minimal contribution to symptom burden observed. (Table 3).

Table 2: *CSCI medications/24hours at time of death.*

	Patient 1	**Patient 2**	**Patient 3**
Alfentanil	1000mcg	1000mcg	
Morphine Sulphate	-	-	40mg
Midazolam	10mg	15mg	40mg
Levomepromazine	-	-	50mg
Hyoscine Butylbromide	-	-	120mg

Table 3: *Medication requirements in the last 48 hours of life.*

	Morphine Sulphate*	**Midazolam**	**Levomepromazine**	**Hyoscine Butylbromide**	**Glycopyrronium Bromide**	**Hyoscine Hydrobromide**
Patient 1						
PRN[b]	25mg	12.5mg	-	-	400mcg	-
Total[c]	40mg	22.5mg	-	-	400mcg	-
Patient 2						
PRN	12.5mg	17.5mg	-	-	-	-
Total	35mg	40mg	-	-	-	-
Patient 3						
PRN	42.5mg	55mg	43.75mg	20mg	-	600mcg
Total	102.5mg	120mg	93.75mg	260mg	-	600mcg
Mean	59.16mg (35mg - 102.5mg)	60.83mg (22.5mg - 120mg)				

b PRN - total PRN dose in last 48 hours

c Total - total dose requirement in last 48 hours including PRN and CSCI delivered medication

** Morphine sulphate or equivalent morphine sulphate dose if alternative opioid used*

Case 2

A male in his sixties with dialysis-dependent ESKD secondary to scleroderma and significant ischaemic heart disease (IHD) was hospitalised with a cough and pyrexia. The admission Covid-19 swab was positive. He was initially treated with IV antibiotics and oral (PO) steroids. Immunosuppressant agents for the management of his scleroderma were held during this infective episode. He became progressively tachypnoeic (respiratory rate rising from 22 to 28 per minute), restless and anxious over the first 5 days of his illness. He developed a delirium and was noted to have a lobar consolidation on chest x-ray.

Antibiotics regime was escalated, and the primary hospital team consulted the Hospital Specialist Palliative Care Service by phone and were advised to prescribe PRN medications for management of dyspnoea, agitation and secretions. The patient deteriorated rapidly overnight, with escalating respiratory distress, requiring morphine sulphate 5mg PRN SC for dyspnoea and pain, midazolam 7.5mg PRN SC for agitation with effect. Following Hospital Specialist Palliative Care Service phone consultation, a 24-hour continuous subcutaneous infusion was commenced for symptom control on day 6 with alfentanil 500mcg and midazolam 7.5mg.

It was then considered inappropriate to continue further dialysis and a comfort care approach was instituted. The following day the 24-hour continuous subcutaneous infusion was titrated, accounting for PRN medication administered with benefit for symptom control (Table 2 and 3). Alfentanil was increased to 1000mcg and midazolam to 15mg SC over 24-hours. He died on day 7 with symptoms well controlled. His wife had visited on day 4 and his family were allowed to visit after death.

Case 3

A female in her eighties living independently despite multiple co-morbidities was admitted to hospital with progressive dyspnoea. She had been unwell for 7 days prior to admission. Her admission COVID-19 swab was positive. Initially, her condition improved and there was a plan for discharge home with increased community supports. However, on day 16 of her illness she deteriorated acutely with dyspnoea, respiratory distress and anxiety. Over 12 hours her condition deteriorated rapidly, developing a Non-ST Elevation Myocardial Infarction (NSTEMI). This resulted in chest pain and a rapidly increasing O_2 requirement. Over the next 4 days the ischaemic chest pain was treated with transdermal nitrate. However, this treatment provided ineffective pain control. Therefore, PRN SC opioids were administered with good effect. Intermittent agitation and anxiety were observed, with increasing O_2 requirements and fluctuating consciousness. On day 21 of her illness, a 24-hour continuous subcutaneous infusion was commenced by the on-call medical team. Morphine sulphate 10mg, midazolam 10mg and hyoscine butylbromide 60mg were prescribed for management of severe dyspnoea and agitation and mild respiratory secretions. The NCHDS had received education around anticipatory prescribing and symptom management at the End of Life in the weeks prior as part of "surge preparations". Two family members were granted a short visit in full PPE on compassionate grounds.

On day 22 she was referred to the Hospital Specialist Palliative Care Service for End of Life care. On review of the PRN medications required since commencement of the 24-hour continuous subcutaneous infusion which were deemed to be pharmacologically effective, the 24-hour continuous subcutaneous infusion was adjusted and a single dose of levomepromazine 25mg s/c was administered for management of severe agitation. Over the following 24 hours agitation continued to be problematic, requiring a further 24-hour continuous subcutaneous infusion adjustment (Table 2 and 3). The patient died symptom controlled on day 24.

Discussion

Dyspnoea and agitation were key symptoms encountered by the Hospital Specialist Palliative Care Service in this Covid-19 cohort at End of Life. Symptoms appeared to escalate rapidly, over the course of hours, and required careful around-the-clock monitoring to ensure adequate administration of PRN medication to maintain symptom control. Case 2 had progressive dyspnea which subsequently escalated rapidly over a period of hours. In contrast, Case 1 and 3 appeared to be improving or were relatively stable prior to their acute deterioration.

Within the last 48 hours of life these patients required a mean dose of morphine sulphate 59.16mg SC for management of dyspnoea and a mean of midazolam 60.83mg SC PRN for agitation and respiratory distress. All patients were opioid naive. Compared to End of Life care for other patient cohorts,[4] there was a noticeable absence of troublesome respiratory secretions. Very few PRN SC doses of anti-secretory medications were required.

As this was in the first wave of Covid-19, obstacles to End of Life care included the need for strict isolation with full PPE and requirement for staff to minimise contact. In all three cases, family members wearing full PPE, were allowed to visit for a short period during the End of Life phase. To overcome this essential and unfortunately inevitable difficulty for families, reassurance that their loved one is maintained comfortable became a vital focus of care. Regular communication with family members on the condition of their dying relative was given priority. To reassure families in this very difficult situation, fulfilling a promise of a comfortable dying for their relative was paramount.

It has been shown that Irish Junior Doctors are regularly carrying out tasks related to End of Life care, resulting in high levels of psychological stress.[5] Linnane et al,[5] suggests that *"Junior Doctors are potentially vulnerable to psychological distress due to lack of skills and knowledge around End of Life care, lack of support from colleagues and a lack of timely decision-making regarding goals of care."* Therefore, local preparations for the first predicted "surge" of Covid-19 cases included Non-Consultant Hospital Doctors (NCHDs) receiving education regarding the principles of End of Life care and associated medications for symptom management at End of Life. Local and national guidelines for anticipatory prescribing and provisional 24-hour continuous subcutaneous infusions for use at the End of Life were disseminated to medical and surgical hospital teams.[6] It is likely that this contributed to early prescription of PRN medications for symptom control and in some cases a 24-hour continuous subcutaneous infusion commencement prior to referral to the Hospital Specialist Palliative Care Service. As noted in recent literature,[7] Covid-19 has placed a renewed emphasis on advanced care planning (ACP). The local Covid-19 admission pro-forma included a prompt for ACP discussion and all patients in this cohort had a resuscitation status documented on admission to hospital.

Specialist Palliative Care aims to provide good Quality of Life for patients living with terminal conditions and good Quality of Dying at End of Life.[8] Introducing undergraduate medical students to *'the person, not the patient'* through education on Subjective Quality of Life was shown to be a positive experience.[9] Knowledge of patients individual Quality of Life and symptom issues by the Primary team in Oncology in a controlled clinical trial was shown to improve these same outcomes significantly.[10,11] The illness trajectory of this patient cohort with Covid-19 is such that patients are at End of Life at the time of referral to the Hospital Specialist Palliative Care Service, resulting in a short duration of the team's involvement. Therefore, the priority is effective, rapid symptom control, awareness of each individual's Quality of Dying with the capacity to respond around-the-clock to rapidly escalating symptomatology while being mindful to minimise the transmission of the virus to other vulnerable patients and staff.

Observation of the End of Life symptom clustering and its management is vital to further enhance our knowledge and preparation for the care of individual patients.[10,11] This requires on-going training of NCHDs and access to senior medical personnel in the Hospital Specialist Palliative Care Service around-the-clock. Our service has around-the-clock availability to a consultant-delivered advisory service that covers nine services. This availability did help to ensure a seamless integration of Hospital Specialist Palliative Care Service for patients in need and ameliorate staff concerns.

Declaration of Conflicts of Interest:
The authors have no conflicts of interest to declare.

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