mythbusters
opioids and hydration in palliative care

Daniella Osaghae explores the evidence

You've heard of evidence based medicine – practising medicine backed up by reliable, *critically appraised* research. Let me introduce you to evidence based ethics! Christian medical ethics shouldn't shy away from engaging with scientific evidence. Here I hope to show you through logic and critical appraisal, how some myths around palliative care can be dispelled by peer-reviewed research.

introduction to logical fallacies

Examples of fallacies used to support myths include:

- **'When I sit down to eat my breakfast, the postman comes. My post must be arriving because I am eating breakfast!'**
  'We know that morphine kills because a patient often dies after a morphine injection.'
  - This is *post hoc fallacy* as the two events running chronologically are presented as causally related.

- **'My essay is due in a week – I must choose between sleeping OR writing my essay. I can't possibly do both!'**
  'We have to choose between treating the pain and distress knowing it will shorten life OR leaving the patient suffering unnecessarily.'
  - This is a *false dilemma* – giving the false impression that the choice is only between the essay and sleep in the first example (one can in fact write a great essay without sleep deprivation). Similarly, suffering can be relieved without shortening life.

- **'I haven't been a student at any other university and I don't look at official rankings, but it is a fact that my university is the best. I've had the best time, so it is the best in the world.'**
  Doctors believe that morphine kills and 'experience proves' that those on morphine die.
  - This is circular reasoning, where the original premise (that my university is best or that morphine kills) assumes the conclusion.

Critical appraisal is 'the process of carefully and systematically examining research to judge its trustworthiness and its value and relevance in a particular context'[1]

With these fallacies in mind, let's now look at the evidence for two common myths...

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MYTH 1

Doctors regularly kill their patients with morphine as a 'double-effect'

It is still a widely held belief by the general public that death is hastened by opioid overdose in palliative patients. At work, I have come across relatives of patients who voice concerns about opioid prescribing based on this misconception. Death in such cases is often attributed to respiratory depression, even though it takes a significant amount of morphine to cause this.

When the risk of a potential, unintended consequence (side effect) of a treatment is deemed justified due to the high chance of benefit from giving the treatment, this is known as the doctrine of double effect.[2] In fact, most treatments prescribed by doctors have side effects (as we see listed at length on drug packaging) but the decision on whether to give a drug is a balance of risks and benefits. It is thus widely assumed that death is a side effect of opioid use, justified when trying to relieve suffering at the end of life.

Estfan *et al* [3] explore this premise by seeking to determine if there is an association between opioid titration and hypoventilation for cancer pain in the palliative setting. It is an observational study in the US. Patients were selected based on strict inclusion criteria such as: age over 18 and cancer pain necessitating continuous opioid infusion via syringe driver; exclusion criteria included inability to consent and previous parenteral (intravenous or subcutaneous) opioid use.

method

Baseline data was collected including pain characteristics, vital signs and end-tidal carbon dioxide. End-tidal carbon dioxide, oxygen saturation and respiratory rate were then monitored at the same time each day as measures of respiratory function. End-tidal carbon dioxide was used as the primary variable as it is directly influenced by alveolar gas exchange, so a good marker of respiratory depression.

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results & discussion

The mean increase in end-tidal carbon dioxide following opioid titration was not statistically significant, with all subjects maintaining oxygen saturations greater than 92%.This finding was in spite of equianalgesic opioid dosage (ie high enough dose to be effective in pain relief) being given to the patients. The discussion notes that pain is a known antagonist to respiratory depression, making it very difficult to induce respiratory depression if opioid is only given when the patient is in pain.

limitations

So were there any limitations? This was a small cohort study at one centre, and was not blinded. Many participants were withdrawn due to changes in clinical condition including delirium (not carbon dioxide-induced, as the study checks), withdrawal of consent and out-of-hours admission; of the 129 recruited, only 30 completed the study reflecting the inherent difficulties in recruiting palliative patients.

conclusion

Opioids for relief of moderate cancer pain are not associated with respiratory depression and thus they do not hasten death in end of life patients. As few studies of this nature had been done previously, further studies need to be done in different centres – although, notably there was a randomised controlled trial from Switzerland showing similar results to those presented here.[4]

MYTH 2

Doctors regularly allow their patients to die by withholding fluids at the end of life

Another widely held belief is that end of-life patients become clinically dehydrated, with corresponding biochemical changes seen in blood tests, when parenteral fluids are withheld.

(Note, this does not include enteral fluids/feeding.) Morita *et al*[5] explore these associations in terminally ill patients in their last three weeks of life, looking at:

- The link between hydration volume and laboratory findings.
- The link between calculated fluid balance and changes in clinical signs of dehydration and fluid retention.

method

This observational study recruited patients from a variety of hospital and community palliative and oncology settings in Japan. Inclusion criteria included life expectancy of three months or less, age over 20 and incurable malignancy of lung or abdominal origin. Patients with conditions predisposing to fluid overload, such as liver cirrhosis and renal failure, and those using artificial enteral nutrition were excluded. Patients were examined for clinical signs of dehydration and fluid retention. Fluid balance was monitored with recording of fluid input (parenteral fluids) and output (urine, fluid draining, vomiting and insensible body loss). For this part of the study, only patients whose oral fluid intake happened to be less than 500ml/day in the previous three weeks were chosen for simplicity and ethical reasons. Therefore, oral fluid intake was not strictly monitored and oral fluids were not withheld from patients at any time. Sodium, potassium, urea, creatinine and albumin levels on blood tests that happened to be done in the previous week were analysed and patients divided into hydration (so given supplemental parenteral fluids) and non-hydration groups. All of this data was gathered prospectively.

results & discussion

The study had several interesting findings. Mean albumin levels were significantly lower (hypoalbuminaemia) in the hydration group compared to the non-hydration group. This demonstrates that giving parenteral fluids can cause measurable harm as hypoalbuminaemia is linked with fluid retention. On the other hand, there was no significant difference between the hydration and non-hydration groups in their sodium, potassium, urea and creatinine levels (these markers would be expected to go up with dehydration).

The calculated fluid balance was not significantly different between those who had clinical signs of dehydration and fluid retention and those who did not. This may be because terminally ill patients have different physiology, where there is fluid shift from intravascular to interstitial spaces rather than total body dehydration, as shown by the same study group in another paper.[6]

limitations

Being an observational study leaves it open to treatment bias. It also focused on abdominal and lung malignancies. Insensible body loss was estimated at 500ml per day per patient, as this is very hard to measure in practice. Patients withdrew for various reasons, but the study helpfully performs analysis to show that there was no significant difference in demographics and cancer type between those excluded and included in the fluid balance part of the study.

conclusion

Active artificial hydration is associated with hypoalbuminaemia. There are no clear benefits in giving artificial hydration to normalise urea, creatinine, sodium and potassium. Calculated fluid balance does not correlate with clinical signs of fluid retention or dehydration. So, when withholding parenteral fluids, doctors are not dehydrating patients. This begs the question of whether there is any need for performing blood tests and monitoring fluid balance when patients are in their final days.

In summary, we've dispelled two myths of death causation in palliative care. Doctors do not expedite death by prescribing opioids nor do they cause dehydration by withholding parenteral fluids in dying patients. The more studies that are done in this area, the greater the evidence base will become to support the findings here.

you can also empower patients and their families to make informed decisions about their care, based on evidence

I hope this encourages you to explore how research can be directly applied to the way you engage with ethics in your future clinical practice. Evidence based ethics can help as you approach discussions around end of life issues, including sensitively clarifying what is fact or myth. As well as demonstrating integrity as a healthcare professional by dispelling myths, you can also empower patients and their families to make informed decisions about their care, based on evidence. ■

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