

Franco Marinangeli, MD
 Cristiana Guetti, MD
 Chiara Angeletti, MD
 Cristina Bonetti, MD
 Antonella Paladini, MD
 Alba Piroli, MD
 Giustino Varrassi, MD
 Department of Anesthesiology
 and Pain Medicine
 University of L'Aquila
 L'Aquila, Italy

doi:10.1016/j.jpainsymman.2009.05.008

References

1. Tarcatu D, Tamasdan C, Moryl N, Obbens E. Are we still scratching the surface? A case of intractable pruritus following systemic opioid analgesia. *J Opioid Manag* 2007;3:167–170.
2. Chang Y, Golkar L. The use of naltrexone in the management of severe generalized pruritus in biliary atresia: report of a case. *Pediatr Dermatol* 2008;25:403–404.
3. Juby LD, Wong VS, Losowsky MS. Buprenorphine and hepatic pruritus [abstract]. *Br J Clin Pract* 1994;48:331.
4. Kiefel JM, Cooper ML, Bodnar RJ. Serotonin receptor subtype antagonists in the medial ventral medulla inhibit mesencephalic opiate analgesia. *Brain Res* 1992;597:331–338.
5. Larijani GE, Goldberg ME, Rogers KH. Treatment of opioid-induced pruritus with ondansetron: report of four patients. *Pharmacotherapy* 1996;16:958–960.
6. Jones EA, Bergasa NV. The pruritus of cholestasis and the opioid system. *JAMA* 1992;268:3359–3362.
7. Raderer M, Muller CH, Scheithauer W. Ondansetron for pruritus due to cholestasis [letter]. *N Engl J Med* 1994;330:1540.
8. Schworer H, Hartmann H, Ramadori G. Relief of cholestatic pruritus by a novel class of drugs: 5-hydroxytryptamine type 3 (5-HT₃) receptor antagonists; effectiveness of ondansetron. *Pain* 1995;61:33–37.
9. Jones EA, Bergasa NV. The pruritus of cholestasis. From bile acids to opiate agonists. *Hepatology* 1990;11:884–887.
10. Bergasa NV, Jones EA. The pruritus of cholestasis: potential pathogenic and therapeutic implications of opioids. *Gastroenterology* 1995;108:1582–1588.
11. Choi JH, Lee J, Bishop MJ. Epidural naloxone reduces pruritus and nausea without affecting analgesia by epidural morphine in bupivacaine. *Can J Anaesth* 2000;47:33–37.
12. Andersen LW, Friedberg M, Lokkegaard N. Naloxone in the treatment of uremic pruritus: a case history. *Clin Nephrol* 1984;21:355–356.
13. Tejwani GA, Rattan AK. The role of spinal opioid receptors in antinociceptive effects produced by intrathecal administration of hydromorphone and buprenorphine in the rat. *Anesth Analg* 2002;94:1542–1546.
14. Greenwald MK, Johanson CE, Moody DE, et al. Effects of buprenorphine maintenance dose on m-opioid receptor availability, plasma concentrations, and antagonist blockade in heroin-dependent volunteers. *Neuropsychopharmacology* 2003;28:2000–2009.
15. Bergasa NV, Talbot TL, Alling DW, et al. A controlled trial of naloxone infusions for the pruritus of chronic cholestasis. *Gastroenterology* 1992;102:544–549.
16. Knape JTA. Early respiratory depression resistant to naloxone following epidural buprenorphine. *Anesth* 1986;64:382–384.
17. Bickel WK, Amass L. Buprenorphine treatment in opioid dependence: a review. *Exp Clin Psychopharmacol* 1995;3:477–489.
18. Friedman JD, Dello Buono FA. Opioid antagonists in the treatment of opioid-induced constipation and pruritus. *Ann Pharmacother* 2001;35:85–91.

Nocturnal Hypoxemia in Patients with Cancer

To the Editor:

In a survey of 100 palliative care inpatients with a variety of cancers, we found that 35 experienced nocturnal hypoxemia, as defined by an oxygen saturation (SaO₂) <90% for ≥2% of the monitored nighttime, together with higher levels of mental fatigue.¹ When considering possible etiologic factors, we had excluded patients with a daytime SaO₂ <90% or known obstructive sleep apnea. Those with nocturnal hypoxemia were more likely to have pulmonary disease and lower values of percent predicted forced expiratory volume in 1 second and day SaO₂. There was no difference in performance status, body mass index, sniff nasal inspiratory pressure, and opioid or other sedative drug use between those with and without nocturnal hypoxemia.¹ However, sleep per se can reduce ventilation.² This does not normally lead to a significant change in the oxygen content of blood because of the horizontal portion of the oxygen dissociation curve. Nonetheless, patients with a lower day SaO₂ will lie closer to the steep part of the oxygen dissociation curve and a reduction in

ventilation with sleep could then lead to significant hypoxemia. To explore this, we have further examined our data.

A wrist oximeter (Pulsox 3i, Minolta, NJ) recorded daytime SaO₂ after 20 minutes resting in both a sitting and a lying position, and the lower value used in the analysis. Mean nocturnal SaO₂ was assessed over a single night, using a minimum period of five hours of sleep as judged by an absence of movement artefact. For those patients exhibiting a fall between day and mean night SaO₂, the difference was plotted against day SaO₂. SaO₂ values were also converted to an estimated partial pressure of oxygen in arterial blood (PaO₂) using an equation that assumes a standard oxygen dissociation

curve.³ Spearman's rank correlation coefficient was used to examine relationships.

There was a fall between day and mean night SaO₂ in 47 patients, representing 24 (69%) and 23 (35%) of those categorized with and without nocturnal hypoxemia, respectively. The mean (standard deviation) day SaO₂ was lower in those with nocturnal hypoxemia compared with those without (94 [2] vs. 96 [1], $P < 0.001$). There was no significant correlation between fall at night and day SaO₂ ($R^2 = 0.001$, $P = 0.84$) (Fig. 1a). This most likely reflects the narrow range we studied; others finding a relationship included patients with day SaO₂ levels as low as 70% and night falls as high as 20%.² Nonetheless, the

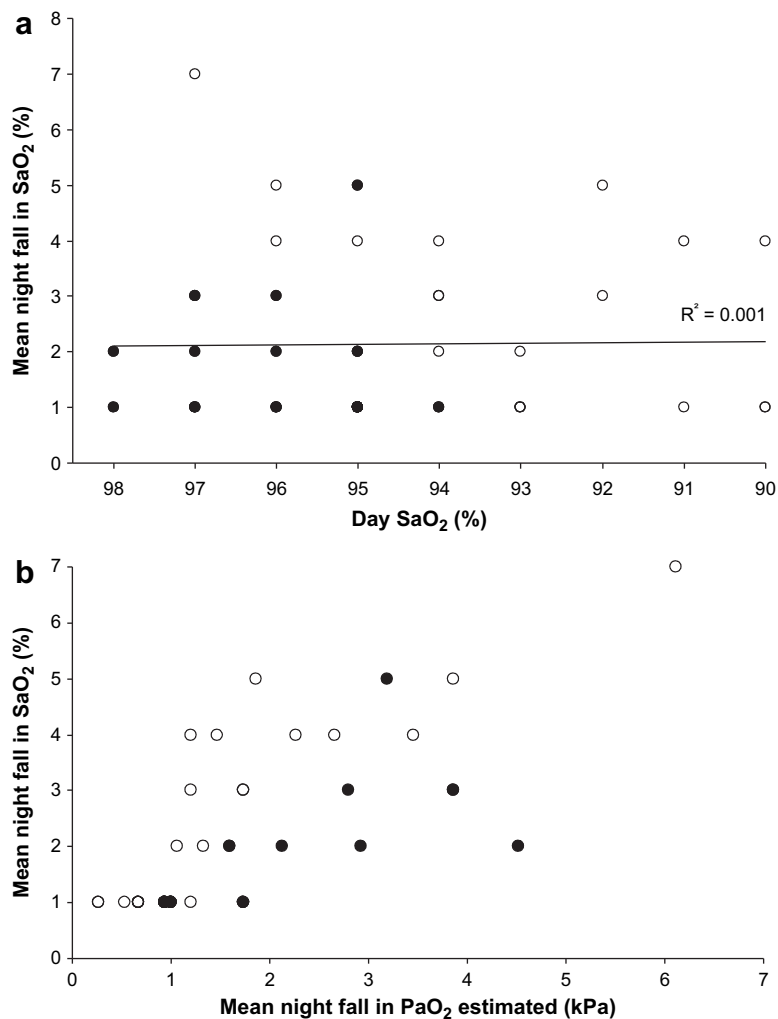


Fig. 1. Mean night fall in SaO₂ vs. a) day SaO₂ and b) fall in night PaO₂ (estimated) for patients with (open circles) and without (closed circles) nocturnal hypoxemia.

relationship between the night fall in PaO₂ and night fall in SaO₂ was such that, across a range of values of PaO₂, the change in SaO₂ was generally greater for the group with nocturnal hypoxemia, which had lower day SaO₂ levels (Fig. 1b).

In conclusion, a sleep-related reduction in ventilation could be sufficient to explain the falls in night PaO₂ and SaO₂ seen in patients with cancer, with those with a lower day SaO₂ level more likely to experience a degree of nocturnal hypoxemia associated with impaired mental functioning. Further work, including more detailed sleep studies, is required to confirm our findings.

Andrew Wilcock, DM, FRCP
Aqdas Kazi, MRCP
Abi Walton, MRCP
Matthew Maddocks, MCSP
Department of Palliative Medicine
Hayward House
Nottingham University Hospitals
NHS Trust
Nottingham, United Kingdom

doi:10.1016/j.jpainsymman.2009.05.009

References

1. Wilcock A, England R, El Khoury B, et al. The prevalence of nocturnal hypoxemia in advanced cancer. *J Pain Symptom Manage* 2008;36:351–357.
2. Stradling JR, Lane DJ. Nocturnal hypoxaemia in chronic obstructive pulmonary disease. *Clin Sci* 1983;64:213–222.
3. Kelman GR. Digital computer subroutine for the conversion of oxygen tension into saturation. *J Appl Physiol* 1966;21:1375–1376.

Acute Opioid Withdrawal Precipitated by Blood Transfusion in a 21-Year-Old Male

To the Editor:

Cancer patients can be among the most challenging groups in which to maintain pain control. At our institution, many cancer patients are managed with patient-controlled analgesia (PCA) opioids, sometimes on an out-patient basis. These patients frequently undergo multiple surgeries as well as courses of chemotherapy and radiotherapy and, as

a result, often require multiple blood product transfusions. According to the American Association of Blood Banks standard,¹ blood transfusions should not be coadministered with any intravenous drugs or fluids apart from 0.9% sodium chloride. For many cancer patients, it is difficult or impractical to establish additional intravenous access solely for blood product administration, and therefore, the practice at our institution has been to disconnect any current intravenous infusion for the duration of blood product transfusion. Here, we describe a case of severe opioid withdrawal after disconnection of intravenous hydromorphone PCA and initiation of a blood transfusion.

Case

The patient was a 21-year-old, 46 kg, white male with a history of osteosarcoma of the right distal femur diagnosed 13 years earlier. He received chemotherapy and limb-sparing surgery. He developed a new focus of osteosarcoma in the left distal femur six years later, for which he underwent limb-sparing surgery and further chemotherapy. Two years later, a third focus of osteosarcoma was diagnosed in the left proximal tibia, for which he underwent left above-knee amputation. One year before the incident described in this case report, he presented with metastasis to the thoracic spine, for which he underwent surgery and radiation therapy.

The patient had experienced phantom pain after his amputation five years earlier, but it became especially troublesome after the spinal surgery. He required increasing doses of PCA hydromorphone for breakthrough pain while an inpatient and was discharged with PCA. At the time of the incident, his pain management regimen included oral modified-release oxycodone, 40 mg in the morning and 60 mg in the evening; hydromorphone intravenous PCA with a bolus of 3 mg every 10 minutes and no basal rate, gabapentin 900 mg three times daily, and amitriptyline 50 mg at bedtime. He considered his pain control to be adequate but continued to experience phantom pain episodes, especially when he became tired.

During the 13 years since diagnosis, the patient had received multiple transfusions of blood products, particularly during chemotherapy treatment. On the day of the incident,