

ABSTRACTS

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All authors have certified that, where appropriate, studies have been conducted with the approval of the relevant Human Ethics Committee or Animal Experimental Review Committee. Presenting Author is in BOLD. Edited by DG Lambert.

Perioperative analgesia for colorectal cancer patients

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Persistent postoperative pain is estimated to account for at least a quarter of consultations at UK pain clinics and is well-documented in survivors of cancer surgery¹. Opioids are often prescribed for the management of postoperative pain despite the development of tolerance, dependence and hyperalgesia as a result of chronic use². The chronic usage of opioids worldwide contributes to significant death and disability. Deaths due to chronic opioid usage in North America have been described as an epidemic and becoming a new chronic opioid user has been reported as being the most common complication following elective surgery³. Attention to pain management in the perioperative period through the use of multi-modal opioid-sparing techniques facilitates recovery and may reduce chronic use of opioids. We sought to examine current practice in intraoperative approaches to opioid usage for colorectal cancer patients at our Trust.

Utilising data collected for the Perioperative Quality Improvement Programme (PQIP) from September 2018–March 2020, we conducted a local retrospective observational study. It included all patients recruited who underwent complex-major operations for colorectal cancer.

Data from 120 patients were analysed. Intraoperatively, 74(61.7%) received an opioid-sparing adjunct. Neuraxial techniques and local anaesthetic infiltration were the most commonly used, in 64(53%) and 24(20%) patients respectively. Other adjuncts used in 1-to-3 cases each (0.8–2.5%) included regional techniques, IV paracetamol, gabapentinoids, ketamine, NSAIDs and lignocaine. 48(40.6%) of 118 patients were discharged from hospital on new opioid prescriptions. 36(48.6%) of those who received an opioid-sparing adjunct intraoperatively were discharged with an opioid prescription. 15(32.6%) patients who did not receive an opioid-sparing adjunct intraoperatively were discharged with an opioid prescription.

Over 40% of patients undergoing surgery for colorectal cancer were discharged with a new opioid prescription. In over a third of cases, opioid-sparing adjuncts were not administered intraoperatively. The provision of intraoperative opioid-sparing adjuncts does not appear to have reduced the incidence of opioid prescription at discharge. Further understanding of the attitudes to opioid-sparing techniques amongst anaesthetists and reasons for variation in practice would be beneficial locally as well as research to investigate the longer-term effects of intraoperative practice on chronic opioid usage.

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References

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Effects of 6-hydroxymelatonin in human macrophage model of inflammasome activation in conditions mimicking sepsis

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Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated inflammatory host response to infection, characterised by cytokine release and oxidative stress. Caspase-1 activation and interleukin (IL-1 β) release are classical indicators of inflammasome activation. 6-hydroxymelatonin (6OHM) is the main metabolite of melatonin and has potent antioxidant and anti-inflammatory activity. However little is known about its mode of action. The aim of this study was to investigate the effects of 6OHM in a human macrophage model of inflammasome activation under conditions mimicking sepsis.

Macrophages were cultured with vehicle control (VC) or 2 µg/ml lipopolysaccharide (LPS) plus 20 µg/ml peptidoglycan G (PepG), to mimic sepsis, and 0.1/10/100 µM 6OHM for 4h. Acid phosphatase activity was used as an indication of cell metabolic activity (viability). Caspase-1 activation was assessed using flow cytometry and supernatant levels of IL-1β were measured using enzyme immunoassay. Quantification of the NLRP3 inflammasome and sirtuin-1 was performed with flow cytometry, while pyroptosis was quantified using a luminescence assay. Nuclear factor κB (NFκB) translocation was assessed using imaging flow cytometry. Statistical analysis was performed using Kruskal-Wallis and Mann-Whitney U tests.

6OHM prevented the decrease in acid phosphatase activity ($p=0.0002$) and reduced caspase-1 activation under conditions mimicking sepsis ($p=0.0008$). Additionally, pyroptosis was higher in macrophages treated with LPS/PepG/6OHM than with LPS/PepG alone ($p=0.0001$) (Fig. 1). 6OHM also reduced NFκB translocation in macrophages incubated with LPS/PepG ($p=0.005$).

These results provide an insight into the mode of action of 6OHM in inflammation and suggest that 6OHM may have a therapeutic role in sepsis. Further work is required to describe the mechanisms behind the effects observed in this study.

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Myocardial inflammation after major non-cardiac thoracic surgery

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Following major non-cardiac surgery, large numbers of patients have biochemical evidence of perioperative myocardial injury (PMI) associated with increased perioperative and long-term morbidity and mortality.¹ Recent work suggests inflammation is a major driver of PMI.² Our research group have previously demonstrated right (but not left) ventricular dysfunction in patients undergoing lung resection and hypothesised that an inflammatory injury to the right ventricle (RV) was implicated in its aetiology.

With informed consent and ethical approval, 15 patients undergoing lobectomy underwent T1-weighted cardiac magnetic resonance imaging (CMR) pre and post contrast; pre-operatively, post-operative day two (POD2) and at 2-months. Imaging correlates of myocardial inflammation, native T1 time and extra-cellular volume (ECV) were measured on CMR in the LV and RV (at the ventricular insertion points) using Circle cvi42 (Calgary, Canada) post-processing software.

As previously reported, RV ejection fraction fell post-operatively from 62.3% (9.2) pre-op to 51.7% (9.6) on POD2 ($p=0.001$) whilst left ventricular ejection fraction was unchanged over time ($p=0.90$). Both native T1 time and ECV were significantly increased in the RV, but not in the LV (T1 changes depicted in Fig. 2); ECV rose from 25.9% (3.2) pre-operatively to 43% (4.4) on POD2 ($p=0.001$), with no change in LV ($p=0.50$).

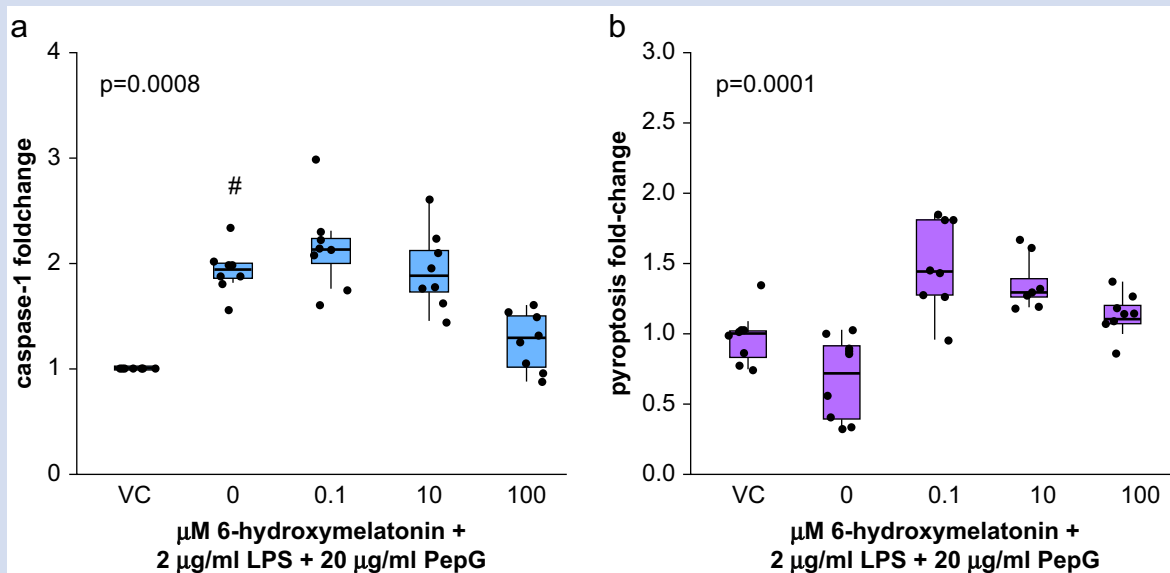


Fig 1. (a) Caspase-1 activation and (b) pyroptosis in THP-1 macrophages incubated with LPS/PepG and 6OHM ($n=8$). Data are shown as data points with box and whisker plots showing median, interquartile range and full range. P value shown is Kruskal-Wallis.