EFFECT OF OPIOIDS ON THE PHAGOCYTOSIS OF NEUTROPHILS AND MONOCYTES: A SYSTEMATIC IN VITRO ANALYSIS

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Background Bacterial infection is a common complication in patients with advanced disease, including cancer. Ingestion (phagocytosis) and subsequent killing of bacteria by neutrophils and monocytes are critical in the control of infection. Using a range of different methodologies, previous in vitro and in vivo studies have generally reported that some commonly prescribed opioids are immunosuppressive (ie, morphine), whereas others have been shown to be immunoneutral (ie, fentanyl), and even immunostimulatory (ie, tramadol). However, direct, comparative, systematic studies aimed at analysing their relative impact remain lacking.

Aims To systematically assess the in vitro effects of clinically-relevant concentrations of commonly used opioids on the phagocytosis of *E coli* by peripheral blood neutrophils and monocytes.

Methods Peripheral blood was collected from healthy volunteers and incubated with clinically-relevant concentrations of morphine, fentanyl, tramadol, buprenorphine, oxycodone, diamorphine, methadone or codeine for 60 min. Samples were then incubated with FITC-conjugated *E. coli* for 10 min at 37°C, at which time the proportion of neutrophils and monocytes that had phagocytosed *E. coli*, and the intensity of the phagocytic response was determined using whole blood flow cytometry (PHAGOTEST, Orpegen Pharma GmbH, Germany). Control samples were incubated at 4°C.

Results Although morphine, fentanyl, tramadol and buprenorphine inhibited the phagocytic responses of neutrophils and monocytes by up to 75% in some individuals, due to inter-individual variability this did not reach statistical significance. Codeine, oxycodone, diamorphine and methadone had no detectable effect on neutrophil or monocyte phagocytosis.

Conclusion Although the true impact of opioid treatment on the susceptibility of patients to bacterial infection in vivo has yet to be defined, these systematically observed in vitro findings indicate that opioid choice might impact on the clinical status of some patients who are at an increased risk of bacterial infection. Future work needs to elucidate the population prevalence to the susceptibility from these potentially immunosuppressive opioids.