

Peak plasma concentrations after oral morphine

Clinical bottom line

The type of formulation profoundly affects the plasma concentration of morphine after oral administration. Peak morphine concentrations are about 6 nmol/L/mg after immediate release morphine, 3 nmol/L/mg for controlled release morphine and 0.5 nmol/L/mg for once-daily morphine. The time to peak concentration was 1 hour, 2.7 hours and 8.5 hours respectively.

There are many reports of plasma morphine concentrations after oral administration. Almost none are randomised trials, and the studies are complicated by different formulations, different types of patients (healthy volunteers and patients) and different measurement methods. The result has been something of a minefield for interpretation. A systematic review brings some light to the darkness.

Reference

SL Collins et al. Peak plasma concentrations after oral morphine: a systematic review. Journal of Pain and Symptom Management 1998 16: 388-402.

Methods

The review sought studies investigating the plasma

concentrations after oral morphine in adult human subjects, and included searching according to 39 brand names in at least four electronic databases. The date of the last search was July 1997. Reports had to have enough pharmacokinetic information to reliably estimate a maximum plasma concentration and the time to maximum concentration. Information on the maximum plasma concentration and the time to maximum plasma concentration, together with the dose of morphine, together with the formulation. These were divided into immediate release (four to six times a day), controlled release (twice a day), and once daily formulations. For maximum concentration, values were corrected by dividing the concentration by the dose administered (in mg).

Results

There were 129 reports in total, of which 69 met inclusion criteria, and with information on 2146 subjects (454 patients and 1692 healthy volunteers). Healthy volunteers and patient data were similar, but were less variable, perhaps reflecting the sometimes inadequate descriptions of patient condition. There was considerable variability between studies, though method of assay was not an issue, and there was no difference in the range of results between single and multiple dosing.

Peak morphine concentration

The maximum concentration, corrected for dose, was higher for immediate release (5.8 nmol/L/mg) than for controlled release (3.2 nmol/L/mg) and once-daily morphine (0.5 nmol/L/mg).



Time to peak concentration

The time to maximum was <u>1.1 hours</u> for immediate release, 2.7 hours for controlled release, and 8.5 hours for once-daily morphine.



Comment

This is a useful study because it confirms the different release properties of formulations often used for pain treatment in cancer. It also serves to de mystify much of the confusion around morphine measurements - for instance demonstrating that measurement methods make little difference to the results. There was comment on the wayward standards of reporting, with authors failing to state what they were measuring, and the phrase morphine concentration hides much confusion that itself contributes to the variability.