

Phenobarbitone and feeding in dogs

Thurman and co-workers (JSAVA 59: 86-89) reported an apparent effect of food on the systemic availability of phenobarbitone administered by mouth in dogs. Their data showed that feeding dogs immediately after dosing resulted in an AUC_{0-24} (area under the serum drug concentration - time curve from 0 to 24 h after dosing) which was 10% less than that obtained after dosage on an empty stomach. The peak mean serum drug concentration also appeared to be reduced by feeding while times to peak concentrations were unaffected.

The authors suggested that these findings indicated that ingesta reduced phenobarbitone absorption. However, comparison of AUC_{0-24} values might be inadequate for assessing changes in the extent of absorption, given the long half-

time of elimination of the drug (mean 29,3 h). The flatter slope of the terminal portion of the curve shown for fed dogs suggests absorption might have been delayed, even though peak times were unchanged. In rats, food intake delayed phenobarbitone absorption by slowing gastric emptying, thus increasing the time for the drug to reach its main absorption site in the small intestine¹. By contrast, no consistent effect of food was evident in a clinical study involving human infants².

As the authors noted, even a 10% reduction in phenobarbitone absorption might have no effect on control of epilepsy. However, if higher doses are given with food in compensation, and if absorption is delayed rather than reduced, phenobarbitone might accumulate to toxic concentrations. If such adjustments are

made, it would be advisable to monitor serum or plasma drug concentrations to ensure they remain in the safe and effective range.

There appears to be an error on page 88, as the factor 0,232 should convert μmol to mg, not mmol to mg as shown (i.e. $1 \mu\text{mol} = 0,232 \text{ mg}$ phenobarbital).

1. Kajima S, Smith R B, Doluisio J T 1971 Drug absorption V Influence of food on oral absorption of phenobarbital in rats. *Journal of Pharmaceutical Sciences* 60: 1639-1641
2. Jalling B 1974 Plasma and cerebrospinal fluid concentrations of phenobarbital in infants given single doses. *Developmental Medicine and Child Neurology* 16: 781-793

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