Clinical Pharmacokinetics of Epidural and Spinal Anaesthesia

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Summary

Epidural and spinal anaesthesia results from the interaction of local anaesthetics with nerve structures, primarily those located within the subarachnoid space. Local anaesthetics can reach the sites of action along various distribution pathways. Uptake into extraneural tissues (in particular epidural fat) and systemic absorption compete with neural tissue distribution and thereby affect the clinical potency and duration of action. Consequently, epidural doses must be much higher than spinal doses.

The systemic absorption of lignocaine (lidocaine), bupivacaine and etidocaine following lumbar epidural administration has been shown to be biphasic, with a rapid initial absorption phase followed by a much slower absorption phase. Initial absorption rates of lignocaine and bupivacaine following subarachnoid injection are much slower, but the late absorption rates are similar to those after epidural administration.
The tissue distribution characteristics of various amide-type agents are similar, because more extensive plasma binding offsets the greater tissue affinity of the more lipophilic compounds bupivacaine and etidocaine. The amide-type agents are predominantly eliminated by hepatic metabolism, except prilocaine, which is also metabolised elsewhere in the body. Ester-type agents are rapidly hydrolysed in blood and liver and are eliminated much faster than amide-type agents.

The blood concentrations attained depend primarily upon the dose administered. The addition of adrenaline (epinephrine) reduces the peak plasma drug concentrations; similarly, the age of the patient, disease states and drug interactions may alter the pharmacokinetics to various extents.

Because of the low dose requirements, systemic toxicity is not a problem during spinal anaesthesia. During epidural anaesthesia, however, the safety margin is relatively small, and systemic toxicity is very likely to occur after inadvertent intravascular injection of an epidural dose.

Epidural and spinal anaesthesia are commonly used anaesthetic techniques, finding application in the areas of surgery, obstetrics, and diagnosis and management of acute and chronic pain. Both techniques involve injection of a local anaesthetic solution close to the target nerve structures, primarily located within the subarachnoid space. Therefore, unlike general and intravenous anaesthetics, local anaesthetics are not dependent upon the general circulation for transport to their sites of action. However, they do enter the general circulation and systemic uptake is largely responsible for terminating their action. In addition, because local anaesthetics can produce systemic toxicity, uptake into the general circulation is of concern to those practising regional anaesthesia. Toxic effects are likely to occur after inadvertent intravascular injection of epidural doses, so that knowledge of the pharmacokinetics of local anaesthetic agents following local and intravascular injection is essential for the safe application of major regional blockades.

This article summarises the pharmacokinetic characteristics of the local anaesthetics currently used for epidural and spinal anaesthesia, and the implications for the time course of the neural blockade and systemic toxicity. For more detailed considerations, data and additional references on the pharmacokinetics following epidural and subarachnoid administration, as well as other routes, the reader is referred to a recent text by Tucker and Mather (1988). The pharmacokinetics in obstetric patients and neonates have been reviewed in a recent article in the Journal (Kanto 1986), and are therefore not considered in detail.

1. Local Anaesthetic Agents and their Physicochemical Properties

The local anaesthetics used in clinical practice are either amino-esters or amino-amides (table I; fig. 1). Of the amino-esters, procaine is more of historical interest, although it is still used for diagnostic differential spinal blocks. Chloroprocaine achieved great popularity in epidural anaesthesia for short procedures in outpatients and in obstetrics in some countries, but the safety of this agent has been questioned after reports of several cases of persistent neurological damage and prolonged sensory or motor deficits following epidural or accidental subarachnoid injection of large volumes (doses between 360 and 840mg) of chloroprocaine solutions (Moore et al. 1982; Ravindran et al. 1980; Reisner et al. 1980). Recent investigations suggest that these effects may have been due to the low pH and high sodium bisulphite concentrations in the solutions rather than to a neurotoxic action of chloroprocaine (Ford & Raj 1987; Gissen et al. 1984). Amethocaine (tetracaine) is still widely used for spinal anaesthesia.

Of the amino-amides lignocaine (lidocaine), mepivacaine and bupivacaine are used for both