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Levobupivacaine

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In the century since cocaine was introduced into clinical practice, a large number of local anaesthetic agents have been tested; although many have been used clinically, most have been discarded.

When the bupivacaine family was first reported, the butyl homologue bupivacaine was essentially discarded because it was found to be about 4 times more toxic than the methyl homologue mepivacaine.[1] However, it was realised during the early 1960s that even when the dose of bupivacaine was scaled to one-quarter that of mepivacaine, the duration of neural blockade was still much longer. Nevertheless, a disproportionate number of deaths has subsequently been reported with longer-acting agents such as bupivacaine compared with shorter-acting agents such as lidocaine and mepivacaine.[2,3]

Increased molecular lipophilicity of local anaesthetic agents produces parallel increases in potency, duration of action and systemic toxicity.[4] However, the real toxicity problem of bupivacaine fatalities derives not from CNS stimulation nor from myocardial contractility depression which are common to all of the agents but from unexpected cardiac arrhythmias. Hence there have been continued attempts to make the molecules safer.

Except for lidocaine, the amide-caines are racemic mixtures of *R*- and *S*-enantiomers which have quantitatively different pharmacology. The 'chiral caines', ropivacaine and levobupivacaine, have been introduced in attempts to reduce toxicity through deletion of the more toxic *R*-enantiomer. Ropivacaine was designed *de novo* as a single enantiomer and launched in 1996; *S*(–)-bupivacaine (with the nonproprietary name of levobupivacaine) has now entered trials. Being enantiopure homologues, the 2 agents should be pharmacologically similar, perhaps with a slightly greater molar potency of the more lipophilic levobupivacaine. Thus, both provide a long-acting agent with greater safety than the current standard bupivacaine, but this should not lead the anaesthetist into thinking that now we have a 'safe' long-acting agent; they are 'safer', not 'safe'. ▲

References

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