Introduction

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Abstract
This section introduces drug–drug interactions involving local anesthetics.

Interestingly, the dental community has been very proactive in raising awareness of drug–drug interactions (DDIs) including those involving the local anesthetics. Reports, summaries, and clinical guidelines were published as early as the early 1990s and have continued to this day.[1–4] And this makes sense in a certain way. The dentists and their allied practitioners have a compelling need for anesthetics that are both reliable and safe. The dental extraction or repair doesn't go forward if the block doesn't set up or the patient is bleeding profusely and, the recent development of "sedation dentistry" aside, the dentists don't have what we have to get them through—the intravenous lines, the propofol, the ketamine, etc. Similarly, they are not equipped, on a routine basis, to handle clinically significant local anesthetic toxicity.

And this is the issue with local anesthetic DDIs that we would like to highlight for the reader. It is generally not a question of a little dizziness—these DDIs either result in blocks that don't work, blocks that last too long and distress the patient and provider both, or toxicity, all of which are clinical events to be avoided. Local anesthetic toxicity due to DDIs is an especially important consideration. One is taught of the thresholds between bupivacaine neurological toxicity and cardiovascular toxicity, but as every experienced anesthesia practitioner can tell you, this threshold can and is broached more quickly than you think while you are still trying to diagnose and manage the initial presentation.

DDIs involving local anesthetics are a particular interest of the editors and, in 2006, we published a case report on a patient who suffered cardiac arrest and needed cardiac pacing for an extended period of time after an apparently uncomplicated

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axillary block.[5] Elements of the complicated DDI we believe this patient suffered are presented in this book in the cases "Smoking Guns I and II." There was a little bit of pushback, if memory serves correct, in the form of letters to the editor from readers who didn't buy the DDI story and felt certain that frank overdose or intravascular injection was the cause. Because we ourselves had not done the block and did not have bupivacaine blood levels, we could not prove that the DDI had happened, but were confident in our reasoning and pharmacology. And, slowly but surely, the anesthesia community seems to have become more aware of this potentially serious, but often unrecognized clinical situation. Recently, we read a report on convulsions after normal dosing of lidocaine which the authors felt were caused by a probable drug interaction.[6]

As you go through these chapters, keep in mind that the local anesthetics are substrates of cytochromes (CYP) 1A2 and 3A4—and a lot of other drugs and substrates also interact with these particular isoenzymes. Bupivacaine is the outlier, as it is a substrate of cytochromes 3A4, 2D6, and 2C19. Of course, as these drugs also have potent effects on the sympathetic nervous system, as such they are involved in their share of pharmacodynamic DDIs as well.

A careful perusal of local anesthetic DDIs will make you both a safer and more precise practitioner of regional anesthesia as well as give you something to chat about the next time you are at a reception over at the dental school.

References

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