Botox Backed by Nearly 20 Years of Safety Data

BY DOUG BRUNK

LAS VEGAS — Although Botox has enjoyed a top-notch safety and efficacy record for nearly 2 decades, a mouse study published in the Journal of Neuroscience piqued the interest of Dr. Jean D.A. Carruthers, who, with her husband, Dr. Alastair Carruthers, pioneered the cosmetic use of botulinum toxin type A.

For the study, Italian investigators injected a research neurotoxin into the rat whiskers and found that it cleaved SNAP-25 (synaptosomal-associated protein, 25 kDa) in the seventh cranial nerve nucleus (J. Neurosci. 2008;28:3689-96).

In two other experiments, hippocampal injection of the neurotoxin crossed to the opposite hippocampus, whereas tectal injection led to cleaved SNAP-25 in the opposite retina.

"This is fascinating, because it's never been shown before that neurotoxin can migrate toward the brain or away from the brain," Dr. Carruthers said at the annual meeting of the American Society of Cosmetic Dermatology and Aesthetic Surgery. "However, they were using enormous doses compared with our human dosing; it's like a fire hose compared to a drip. [There haven't been] any human data to support this."

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She did, however, note some published studies that demonstrated that a glabellar injection of Botox improves mood and helps people cope with their depression and anxiety, "so maybe there is something happening there. Maybe this opens up a new area for research. But in 25 years of clinical use, there haven't been studies that show there are intracranial abnormalities. There is something going on here that requires different analysis and more study."

In 2005 Dr. Carruthers, a Vancouver-based ophthalmologist and oculoplastic surgeon, and her husband, a dermatologist and dermatologic surgeon, performed a long-term safety study of 50 subjects after a minimum of 5 years since their initial Botox treatment. "They'd had at least 10 treatment sessions; these weren't novices," she said.

The mean age of the patients was 42 years, and 92% were female.

Of 851 treatment sessions, there were three cases of brow ptosis in two subjects, one case of eyelid ptosis, and one case of dysphagia. "All of the side effects were mild and transient," said Dr. Carruthers, also of the department of ophthalmology at the University of British Columbia, Vancouver, where she specializes in facial cosmetic surgery. "None of the patients were particularly concerned about the adverse events because they all settled down."

A systematic review and meta-analysis of 36 studies of 2,309 subjects yielded similar results (J. Curr. Med. Res. Opin. 2004;20:981-90). Mild to moderate adverse events occurred in 25% of the Botox-treated group, compared with 15% for placebo. Focal weakness was the only adverse event with significantly higher incidence in the Botox-treated group. No serious adverse events were reported.

Transient, local complications "are what we want to continue seeing from the use of Botox," she said. "Immunogenicity is an overstated problem. Use only [Food and Drug Administration]–approved toxins, even for off-label indications."

She concluded that Botox is "a great drug that we should have great respect for. So when we see reports of serious adverse events, let's find out if it is Botox or if it's something else that's being used in a nonapproved way. Remember that there is nearly 20 years of Botox safety in worldwide publications."

Dr. Carruthers disclosed that she has relevant relationships with a number of pharmaceutical and medical device companies, including Allergan Inc. and Bioform Medical Inc. ■