

Botox May Improve Blood Flow in Raynaud's

BY BETSY BATES

Los Angeles Bureau

BEVERLY HILLS, CALIF. — Sympathectomy may become rare as a treatment for Raynaud's phenomenon, even in severe cases, if early success with botulinum toxin type A injections proves lasting and replicable, Dr. Michael Neumeister said at the annual meeting of the American Association for Hand Surgery.

"These days, fewer and fewer people are candidates for surgery," remarked Dr. Neumeister, professor and chair of the division of plastic surgery at Southern Illinois University, Springfield.

Sympathectomy produces benefit in approximately half of people who undergo the complex procedure, he noted, and many Raynaud's symptoms recur, requiring reoperation.

Botox (botulinum toxin type A), meanwhile, has sharply reduced pain, improved blood flow, and fostered healing of ischemic fingertip ulcerations in every patient he has treated—16 to date—said Dr. Neumeister.

Ranging in age from 23 to 64 years, all patients treated by Dr. Neumeister had failed medical therapy; three had undergone prior sympathectomies.

The first patient he injected was a 53-year-old man who was desperate for relief from painful ulcerations, which persisted despite surgery and hospitalization for administration of intravenous morphine.

"Cut my fingers off," Dr. Neumeister recalled the patient saying.

Instead, within minutes of palmar injections, the patient's pain had disappeared and has not recurred in more than 3 years.

Color sometimes returns to the fingertips of some patients quite soon after injections into the neurovascular bundles and web space of the palms.

Laser Doppler scans show that blood flow improves by 300% in some patients within 30 minutes after injection.

Within 24 hours, patients report full pain relief.

Dr. Neumeister said he has begun administering a wrist block prior to the procedure, because the injections can be painful.

Grip strength is affected for several months; however, intrinsic function returns after 2-3 months.

In most patients, Raynaud's pain and other symptoms do not recur; however, five patients required repeat injections 4, 6, 12, 13, and 24 months following initial palmar injections of 30-200 U of Botox. In four cases, revision amputations were required for preexisting, bone-exposing ulcers.

Dr. Neumeister is studying possible mechanisms of action that would explain the near-instantaneous pain relief achieved by Botox injections, a contrast to the 2- to 4-day time of onset of the agent's paralytic impact on muscles.

"Botox works right away [in Raynaud's phenomenon patients]," he said. "It's got to be a different mechanism."

Thus far, he has determined that the effect on Raynaud's phenomenon is not at the vascular level, but in the sympathetic nervous system. It may be that patients

with the vasospastic disease develop ectopic sodium channels not seen in normal nerves and that Botox is acting directly on those.

It is known that Botox is taken up by nerve terminals and then by vesicles containing acetylcholine. These vesicles are surrounded by SNAP-25 proteins, which Botox blocks.

"The vesicle can't migrate to the end of the nerve terminal and can't release acetylcholine that causes contraction of the muscle," Dr. Neumeister said at the meeting.

Botox also may block stimulation of C fibers, the agents of secondary pain experienced a few seconds after one's hands are pulled out of very hot water.

"I think Botox is working against those C fibers and also working on sympathetic directly and on the cross talk between nerves in chronic pain," he said.

Allergan Inc., the company that makes Botox, is funding Dr. Neumeister's research on the agent's mechanisms of action in Raynaud's disease and phenomenon.

However, the company does not underwrite patient treatments, and many insurance companies have refused to pay.

"There's no problem with reimbursement; you just don't get paid," he quipped.

He has been able to convince several insurance companies that the cost of Botox injections, which run less than \$1,000, are much preferable—"if they work"—to the \$25,000 price tag of a sympathectomy.

Dr. Neumeister did not report any disclosures related to his presentation. ■

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