Botox injections may reduce anxiety

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Botox, or Botulinum toxin, a medication derived from a bacterial toxin, is commonly injected to ease wrinkles, migraines, muscle spasms, excessive sweating and incontinence. Researchers at Skaggs School of Pharmacy and Pharmaceutical Sciences at University of California San Diego, in collaboration with two physicians from Germany, may have

found a new use thanks to the U.S. Food and Drug Administration (FDA)'s Adverse Effect Reporting System (FAERS) database, in which nearly 40,000 people reported what happened to them after Botox treatment for a variety of reasons.

The study, publishing Dec. 21, 2021 in the journal *Scientific Reports*, found that people receiving Botox injections at four different sites—not just in the forehead—reported anxiety significantly less often than patients undergoing different treatments for the same conditions.

"A large number of diverse adverse effects are being reported to the FDA and the main objective usually is to find those harmful side effects that had not been identified during clinical trials," said Ruben Abagyan, Ph.D., professor of pharmacy. "However, our idea was different. Why don't we do the opposite? Why don't we find beneficial effects?"

Abagyan and his team scoured the database for the absence or reduced frequency of anxiety and anxiety-related disorders as a health complaint, compared to a control group, when taking Botox. Then the team applied a mathematical algorithm to look for statistically significant differences between Botox users and patients who received different treatments for the same conditions.

What they found was that the reported anxiety risk was 22 to 72 percent lower in Botox-treated patients for four of eight conditions and injection sites: facial muscles for cosmetic use; facial and head muscles for migraine; upper and lower limbs for spasm and spasticity; and neck muscles for torticollis. (For the other four injection sites, there was not enough data for statistically significant confidence intervals, according to Abagyan.)

Anxiety disorders are the most common class of psychiatric disorders, according to the National Comorbidity Survey Replication, a survey of

the prevalence and correlates of mental disorders in the U.S. carried out between 2001 and 2003. According to the survey, 32 percent of the U.S. population are negatively affected by anxiety at some point in their lives, and treatments are ineffective for nearly one-third of them. That's why clinicians and researchers seek other therapeutic options.

To be clear, the data used in this study was not collected for the purpose of exploring the association between Botox use and anxiety exclusively. In addition, the FAERS data represents only the subset of Botox users who experienced negative side effects. While the team excluded reports in which a person was also taking antidepressants (often used in treating anxiety) or anxiolytic medications, the use of other prescription and over-the-counter medications could have been underreported in some cases.

Abagyan and his team published a similar study—in Scientific Reports in July 2020—in which, using the same database, they found that people who received Botox injections reported depression significantly less often than patients undergoing different treatments for the same conditions. Both studies found a decrease in reported symptoms regardless of injection site, thereby casting doubt on speculation that patients may have felt happier because they had fewer wrinkles, or because Botox prevents frowning. But the researchers believe the specific molecular mechanisms by which Botox reduces depression and anxiety—while not known—may be different.

"They may be related, but there are different pathways responsible for anxiety attacks versus depression," he said.

Abagyan and collaborators hypothesize a few possible mechanisms worth investigating: Botulinum toxins could be transported to the regions of the central nervous systems involved in mood and emotions. Alternatively, the Botox-affected neuromuscular junctions may directly communicate with the brain. Finally, since Botox is commonly used to

treat chronic conditions that may contribute to anxiety, its success in relieving the underlying problem may indirectly also relieve anxiety.

More research is needed to determine the mechanism by which Botox reduces anxiety, Abagyan said, and clinical trials will be necessary to work out the best site and dose to administer the medication specifically for anxiety.

Abagyan led the study with Tigran Makunts, PharmD, a former research fellow at the FDA who has joined UC San Diego as a research scientist, and German psychiatrists Marc Axel Wollmer and Tillman Kruger.

More information: Ruben Abagyan is co-founder of Molsoft, LLC and has equity. M. Axel Wollmer has consulted for Allergan pharmaceuticals, *Scientific Reports* (2021).

Provided by University of California - San Diego

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