Botulinum toxin A creates muscle weakness and atrophy following long term use, study suggests

Date: December 2, 2010
Source: University of Calgary
Summary:
A new study found animals injected with Botulinum toxin A experienced muscle weakness and atrophy far from the site of injection. The research raises some important questions about the long-term therapeutic use of Botox.
A new study by researchers at the Faculty of Kinesiology, University of Calgary, is raising questions about the therapeutic use of botulinum toxin A.

The study found that animals injected with Clostridium Botulinum type A neurotoxin complex (BOTOX, Allergan, Inc., Toronto, Ontario, Canada) experienced muscle weakness in muscles throughout the body, even though they were far removed from the injection site. The study also found that repeated injection induced muscle atrophy and loss of contractile tissue in the limb that was not injected with the Toxin.

"We were surprised by the degree of muscle loss and atrophy in the limb that was not injected with the Botulinum toxin," says Rafael Fortuna the lead author of the paper will soon be published in The Journal of Biomechanics, "I think it's fair to say that the paper raises some important questions about the long-term therapeutic use of Botox, especially with children and adolescents."

The study used dosages that approximated therapeutic doses used to treat conditions like cerebral palsy where muscle contraction can't be controlled resulting in muscle dystonia and spasticity. The study follows previous research in Dr. Walter Herzog's lab, which found that Botulinum toxin A, easily crosses the muscle membrane barrier, resulting in muscles weakness in the surrounding (non-injected) muscles.

This study shows, for the first time, that over time Botulinum toxin A use also results in muscle weakness, atrophy and loss of contractile tissue in non-injected muscles far-removed from the injection site."It may be that the benefits of using Botox for these kinds of therapeutic, medical uses, outweighs these potential long-term consequences," says Dr. Herzog, "however I think this study raises some important issues that need to be followed to ensure the best possible outcomes for patients, in the long term."

Botulinum Toxin A is also used as a cosmetic treatment, where the drug paralyzes small muscles in the face to reduce the appearance of wrinkles.

Herzog notes that while this study was looking at larger doses, the results should be valid for any application of the drug.

University of Calgary. "Botulinum toxin A creates muscle weakness and atrophy following long term use, study suggests." ScienceDaily. ScienceDaily, 2 December 2010. <www.sciencedaily.com/releases/2010/12/101202124248.htm>.

SAFETY OF PHENOXYBENZAMINE CHEMODENERVATION WITH REPEATED INJECTIONS

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Phenoxybenzamine From Wikipedia

Phenoxybenzamine (marketed under the trade name Dibenzyline) is a non-selective, irreversible alpha blocker. It is used in the treatment of hypertension, and specifically that caused by pheochromocytoma. It has a slower onset and a longer-lasting effect compared with other alpha blockers. It was also the first alpha blocker to be used for treatment of benign prostatic hyperplasia, although it is currently seldom used for that indication due to unfavourable side effects. It has been used in the treatment of hypoplastic left heart syndrome. It is also used in complex regional pain syndrome (CRPS) type 1 due to its anti-adrenergic affects. It has shown to be beneficial if used in the first 3 months of the CRPS diagnosis.

Investigational

Phenoxybenzamine has long been known to block ejaculation without affecting semen quality or ability to achieve orgasm, which could make it an effective male contraceptive. This effect is completely reversible, and is believed to be the result of alpha-1 adrenoceptor blockade in the longitudinal muscles of the vas deferens. As of 2008, research was underway to identify possible drug candidates that share this effect but act specifically on the reproductive tract, unlike phenoxybenzamine.

Pharmacology

Phenoxybenzamine is used as an anti-hypertensive due to its efficacy in reducing the vasoconstriction caused by epinephrine (adrenaline) and norepinephrine. Phenoxybenzamine forms a permanent covalent bond with adrenergic receptors. Based on known information about the structures of these receptors, it likely involves attack by the cysteine at position 3.36 in transmembrane helix 3 to form a stable linkage. Thus, it remains permanently bound to the receptor, preventing adrenaline and noradrenaline from binding. This causes vasodilatation in blood vessels, due to its antagonistic effect at the alpha-1 adrenoceptor found in the walls of blood vessels, resulting in a drop in blood pressure. A side effect of phenoxybenzamine is reflex tachycardia.

As a non-selective alpha receptor antagonist, it will also affect both the postsynaptic alpha 1 and presynaptic alpha 2 receptors in the nervous system, and so reduce sympathetic activity. This results in further vasodilation, pupil constriction, an increase in GI tract motility and secretions, and glycogen synthesis.

Clinically, non-selective alpha antagonists block alpha receptors (but do not differentiate between alpha-1 and alpha-2). They are used as antihypertensives because they block alpha-receptor-mediated vasoconstriction. The block on alpha-2 receptors further potentiates beta-effects, increasing cardiac output.

Phenoxybenzamine has a long-lasting action, binding covalently to the alpha receptors. Its only current clinical use is in preparing patients with pheochromocytoma for surgery; its irreversible antagonism and the resultant depression in the maximum of the agonist dose-response curve are desirable in a situation where surgical manipulation of the tumour may release a large bolus of pressor amine into the circulation. Typically, phenoxybenzamine is not used in the long term, as new receptors are made to upregulate alpha stimulation. The main limiting side-effects of alpha antagonists is that the baroreceptor reflex is disrupted and thus this can cause postural hypotension.

Phenoxybenzamine also has irreversible antagonist/weak partial agonist properties at the serotonin 5-HT2A receptor. Due to its 5-HT2A receptor antagonism, phenoxybenzamine is useful in the treatment of carcinoid tumor, a neoplasm that secretes large amounts of serotonin and causes diarrhea, bronchoconstriction, and flushing.

"POST-LAMINECTOMY SYNDROME" -- WHAT NOW?

01/14/2015 – 7:03 PM in Back Surgery and Neck Surgery

I'm coming up on 6 months post op from a left side L5-S1 laminectomy and have been in increasing pain ever since. Two post op MRIs show the surgery to be a success but the pain is absurd -- I haven't worked since I've had the surgery and each new day is continuing to get worse. I don't really leave my bed very often any more.

I've seen every major ortho or neuro that my insurance covers. No one really knows what is wrong. I had some blood tests done and the like but nothing outrageous. I have no idea where to go next -- I've tried injections, PT, chiros, painkillers/muscle relaxers, TENS machines, heat/ice, etc. and nothing has stopped my pain from continuing to get worse each day. I recently turned 28 and I'm scared shitless at this point -- I'm afraid my life is over and I have no idea what to try next. My muscles just continue to spasm in my back as the day goes on and I don't think I can take the pain much longer.