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Reduction in Post-Botulinum Toxin Flu-like Symptoms After Injection with Incobotulinum Toxin

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ABSTRACT

OBJECTIVE: To determine if patients reporting flu-like symptoms (FLS) after botulinum toxin (BoNT) injections are less susceptible to this reaction after incobotulinum toxin.

BACKGROUND: Approximately 10% of patients injected with BoNT in our clinic complain of FLS, primarily malaise, myalgias and rhinorrhea, beginning a few days to one week after injection and lasting one week or less. A review by Baizabal-Carvallo et al. (Toxicon, 2011, 58:1-7) found rates of FLS between 1.7 and 20% in patients after various preparations of botulinum toxin A, and a subsequent study showed increased cytokines in patients with FLS (Neurotoxicity Research, 2013, 24:298-306). Besides the neurotoxin itself, most BoNT preparations contain associated complexing proteins (NAPs), most of which are hemagglutinins. It is thought that NAPs induce the release of inflammatory cytokines, which may cause the FLS. Incobotulinum toxin is a botulinum toxin A preparation where the active peptide is separated from the NAPs (hemagglutinins and non-hemagglutinins) through a series of steps yielding the active neurotoxin with removal of the NAPs, without accessory proteins.

METHODS: Consecutive patients who reported FLS consistently occurring after previous BoNT injections (≥ 2 prior treatment sessions, average 21 sessions, patients reporting FLS after “most sessions”) were offered further injections with incobotulinum toxin at similar doses.

RESULTS: Six patients were identified as having had FLS and given injections with incobotulinum toxin. Three were cervical dystonia patients, and one each with blepharospasm, hemi-facial spasm and tics secondary to Tourette’s. All reported a satisfactory clinical response similar to their prior injections. One patient had only rhinorrhea, the others had malaise and myalgias. None of the patients experienced flu-like symptoms after the prior injections we decided to offer incobotulinum toxin A injections to patients who had previously reported any of the flu-like symptoms after botulinum toxin injections. Three were cervical dystonia patients, and one each with blepharospasm, hemi-facial spasm and tics secondary to Tourette’s. All reported a satisfactory clinical response similar to their prior injections. One patient had only rhinorrhea, the others had malaise and myalgias. None of the patients experienced flu-like symptoms after the prior injections.

CONCLUSIONS: Initial results from this open-label, unblinded series suggests patients who have consistently experienced FLS after botulinum toxin injections (16 treatment sessions). Incobotulinum toxin is a botulinum toxin A preparation where the active peptide is separated from the neurotoxin associated proteins (hemagglutinins and non-hemagglutinins) through a series of steps yielding the active neurotoxin with removal of the NAPs, without accessory proteins. Since it is thought the neurotoxin associated proteins may be responsible for the flu-like symptoms associated with botulinum toxin injections, we decided to offer incobotulinum toxin A injections to patients who had previously reported any of the flu-like symptoms after botulinum toxin injections. Six patients were identified as having had flu-like symptoms and given injections with incobotulinum toxin (3 male, 3 female, mean age 59 years, range 26-80 years). Three were cervical dystonia patients, and one each with blepharospasm, hemi-facial spasm and tics secondary to Tourette’s. All reported a satisfactory clinical response similar to our clinical experience suggests they are real.

DISCUSSION

This was an open-label, unblinded clinical series with a very small number of patients, so the interpretation is limited. None of the patients identified had been on abobotulinum toxin A (Dysport®). The package insert for Xeomin® (incobotulinum toxin A) indicates that nasopharyngitis and respiratory tract infection were reported in clinical trials at rates greater than for placebo (5% vs. 3%), and although myalgias and malaise were not listed as adverse effects seen in clinical trials, myalgia is mentioned as occurring in post-marketing reports. Nonetheless, rates of flu-like symptoms reported for the other botulinum toxin preparations are higher, similar to our own experience of approximately 10% (Toxicon, 2011, 58:1-7). These differences are of uncertain significance, but the cross-over nature of our clinical experience suggests they are real.

CONCLUSIONS

Six patients were identified as having had flu-like symptoms and given injections with incobotulinum toxin (3 male, 3 female, mean age 59 years, range 26-80 years). Three were cervical dystonia patients, and one each with blepharospasm, hemi-facial spasm and tics secondary to Tourette’s. All reported a satisfactory clinical response similar to our own experience of approximately 10% (Toxicon, 2011, 58:1-7). These differences are of uncertain significance, but the cross-over nature of our clinical experience suggests they are real.