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Considering that the temporomandibular joint requires the activity of masticatory muscles for its development and homeostasis, it is highly relevant to understand the effect of the BoNTA intervention in the masticatory apparatus. Künn-Darbois et al. reported trabecular bone loss in alveolar (-20%) and condylar (-35%) areas in adult rats 4 weeks after a unilateral injection of 1U of Botulinum toxin type A (BoNTA) in both the masseter and temporalis muscles. The same intervention in masseter muscles of growing mice (5 weeks-old) resulted in a significant decrease in condylar width of the treated side after 4 weeks. Moreover, decreased cell proliferation and increased cell death by apoptosis was observed in subchondral bone of the mandibular condyle. Recently, our group assessed the effect of unilateral injection of Botulinum toxin type A (BoNTA) in masseter muscle (0.2U/10µl) of adult BALB/c mice (8 weeks-old) at molecular and microstructural levels. Our results demonstrated a significant increase in the mRNA expression of Rankl in the mandibular condyle of the treated side 2 days after intervention. Also, there was a significant increase in the mRNA expression of both atrophy (atrogin-1/MAFbx and MURF-1) and muscle regeneration markers (myogenin) in the treated masseter muscles after 7 days. These findings, together with the significant reduction in the masseter mass and muscle fibers diameter at the BoNTA-injected side observed after 14 days, support the hypothesis that molecular events precede the onset of BoNTA-induced masseter muscle atrophy. In addition, the bone histomorphometry performed on the mandibular condyles at 14 days post-intervention showed a significant reduction of the trabecular bone (-30%) and trabecular thickness (-55%). Taken as a whole, these results demonstrate that masseter muscle atrophy induced by BoNTA single injections leads to significant microanatomical changes in the masseter muscle and the mandibular condyle of the same side after 14 days, preceded by molecular changes as early as 2 days in bone and 7 days in muscle.

In humans, the bone effects derived from IM injection of BoNTA in masticatory muscles have been much less studied and are more difficult to address. In a pilot qualitative study, cone-beam computed tomography (CBCT) images of mandibular condyles from 7 adult female patients with temporomandibular joint dysfunction (TMJD), receiving two or more BoNTA IM injections for facial pain, were compared with those from 9 demographically matched control patients. Two independent oral and maxillofacial radiologists, blinded to BoNTA exposure conditions, rated bone density patterns in the trabecular region of mandibular heads.

Both radiologists noted a reduction in bone density in all the patients exposed to BoNTA, and in none of the 9 control subjects. In a recent Letter to the Editor, Aziz et al. introduced the clinical case of a patient (female, 55 years-old) with a 13-year history of TMJD and a Meige Syndrome diagnosis. Comparing magnetic resonance imaging and computed tomography data within a time span of 15 months, in which the patient admitted she had privately had Botulinum toxin type A injections every three months (140U) into her left masseter, a severe mandibular condyle resorption of the treated side was observed.

Authors are cautious to point out that is difficult to tell if Botulinum toxin type A was the cause of bone resorption, because this is an isolated cause and iatrogenic injury cannot be excluded. However, they highlight the idea that the condylar degeneration may be associated with BoNTA injections. These reports, reinforced by results from experimental studies in animal models, makes it highly recommended for both clinicians and patients to consider the putative bone loss evoked by BoNTA-induced masseter muscle atrophy as a relevant factor prior to a treatment. Therefore, the presented evidence suggests the importance of considering the need to develop follow-up protocols to permanently monitor the associated bone structure by proper imaging techniques after BoNTA intervention in the masseter muscle. This is especially relevant in patients who require multiple successive applications of toxin to maintain the desired effect. Finally, there is not enough evidence to know if BoNTA intervention in the masseter muscle (or other masticatory muscles) predisposes, initiates or perpetuates the TMJD.

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