

Brief Skin Cooling Prior to Intramuscular Botulinum Toxin Injections

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We propose that brief skin cooling prior to intramuscular botulinum toxin (BoNT) injections is unlikely to adversely affect toxin binding and uptake. The temporary analgesic effects of skin cooling are well known in the area of cosmetic procedures and focal spasticity management¹ with BoNT injections. Skin cooling is thought to desensitize skin receptors resulting in temporary analgesia. BoNT injections can elicit needle insertional pain and discomfort when used to manage limb spasticity or limb dystonia; however, this pain can be significantly decreased by skin cooling using a brief application of a small commercially available icepack for 60 s.¹ Although the analgesic effect of icepack applications is uncontested, it has been suggested that skin cooling prior to BoNT injections for spasticity can decrease toxin uptake.² As a result, Hallett² argues that skin cooling should be avoided prior to BoNT injections for spasticity.²

The alternative to skin cooling as a local anesthetic is an application of a Eutectic Mixture of Local Anesthetics (EMLA) cream to allay the pain and patient anxieties associated with multiple needle insertions that are typically associated with BoNT injections. Although the use of EMLA cream is an effective way of reducing needle insertional pain, it is not as feasible as skin cooling because of the duration of application time which can be close to an hour and the effect can unnecessarily last for a few hours.¹ In contrast, skin cooling is brief in duration (~60 s) and the effect wears off in a short period of time usually in minutes. Having established the efficacy and need for skin cooling prior to BoNT injections, the duration and effect of skin cooling on BoNT efficacy need to be considered carefully. We propose that a brief period of skin cooling prior to BoNT injections poses no effect on toxin uptake and we present some arguments to support this position.

First, a significant skin and muscle temperature drop are required to elicit changes in BoNT uptake. Hallett's² argument cautioning the use of skin cooling is based on an *in vitro* study using nerve-muscle preparation that showed that BoNT uptake (but not transmission) was prevented at 10°C preparation temperature compared with 22°C.³ Even at 22°C muscle temperature, it was reported that both the uptake and to a lesser degree

binding of toxin can be affected.⁴ The normal intramuscular temperature is usually around 35°C, which is significantly warmer than the tested temperature in the *in vitro* studies.⁴ One can imagine that in a patient being treated, inducing an intramuscular temperature drop from 35°C to 22°C will require a much longer period of icepack application compared to the 60 s application used prior to BoNT injections. It should be noted that the *in vitro* studies required cooling at 22°C for 20 min prior to testing toxin uptake,⁴ which is degrees longer than the 60 s application time used for BoNT injections.

Second, the depth at which the intramuscular injection is delivered in relation to the cooled skin is a factor that will influence the intramuscular temperature drop. A recent study found that icepack application decreased intramuscular temperature (at 1 and 2 cm depths) by 2°C after 5 min of application.⁵ So even in the muscle fibers closest to the skin, it takes five times longer for an icepack application to reduce muscle temperature compared with the 1 min application used prior to BoNT application.¹ Thus, the duration and depth of cooling will be also affected by the size of the muscle. It will likely need longer skin cooling in the large muscles compared with the smaller hand or facial muscles to induce a comparable temperature drop large enough to affect toxin movement. In addition to the effects of skin cooling on BoNT binding and uptake, decreased transmission in the peripheral nerves will also likely impact the effectiveness of the toxin.

Finally, electrical muscle stimulation after BoNT has been associated with greater effectiveness of BoNT.⁶ Thus, decreased nerve transmission is likely to affect the effectiveness of BoNT as well. The amount of cooling required to decrease nerve transmission is also much longer than the duration of 60 s icepack application prior to BoNT. A large drop in temperature is needed to cause overt neuronal changes – intramuscular temperature drop (cooling) of up to 12°C resulted in a decrease in the compound motor action potential of the soleus.⁷ A similar study showed that 30 min of cooling using a 7°C bath (intramuscular temperature not reported) resulted in a decrease in nerve conduction velocity and increase spasticity.⁸ Considering the above studies, it is highly improbable that a 60 s skin cooling prior to BoNT

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injection will adversely affect BoNT binding or uptake. To conclude, we feel that clinicians have no strong evidence nor physiological and anatomical considerations and thus, should not hesitate in providing skin cooling options (including icepacks for up to a minute) to their patients to minimize the needle insertion pain prior to intramuscular BoNT injections for spasticity or dystonia in the limbs and cosmetic applications.

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CONFLICT OF INTEREST

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STATEMENT OF AUTHORSHIP

All authors (CB, FI, CP) provided equal contribution in manuscript conception, drafting, writing, and review.

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