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Ice pack test for myasthenia gravis

A simple, noninvasive and safe diagnostic method

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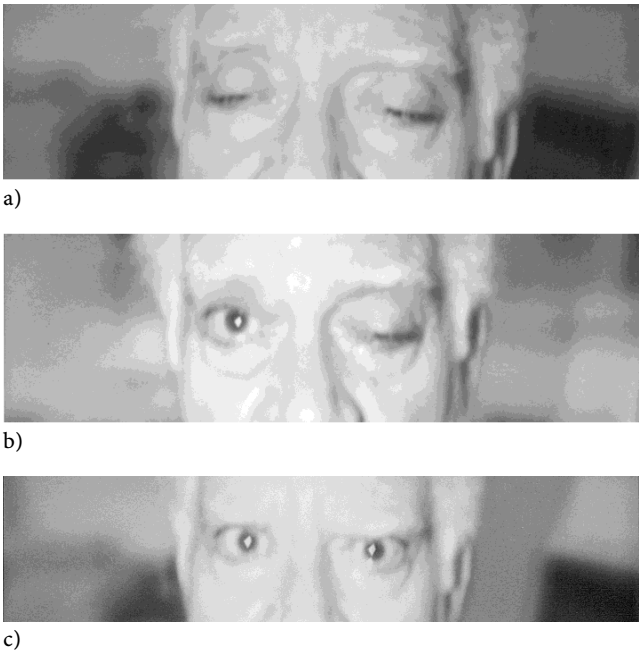
Sirs: Intravenous injection of the acetylcholinesterase inhibitor edrophonium (tensilon) is commonly used in the diagnosis of myasthenia gravis (MG), because of rapid onset and short duration of its effects. The estimated sensitivity of tensilon testing in myasthenia gravis is high; however, false-negative responses have been reported. Tensilon, however, may produce serious side effects, including significant bradycardia, loss of consciousness and death [4]. Consequently its use has been restricted in Switzerland and in other European countries. According to previous publications local cooling improves neuromuscular transmission, whereas warming has the opposite effect [1]. However, the precise mechanism of this effect is unclear. Reduction or inhibition of the activity of acetylcholinesterase by lowering temperature is a possible mechanism [8]. The purpose of the present article is to be a reminder of an alternate method to tensilon testing that is simple and safe but seems to have fallen into oblivion in the neurological literature.

Design/Methods: Five patients with ptosis from previously undiagnosed myasthenia gravis and five with non-myasthenic ptosis were studied with the use of tensilon testing, orbital cooling, and other tests for MG such as repetitive nerve stimulation and determination of antiacetylcholine receptor antibody (AchR-ab) levels. Each patient was photographed before ice or tensilon testing. In the ice test, the patient was asked to hold an ice pack (ice cube wrapped in a surgical glove) over the closed eye with ptosis. If ptosis was bilateral, we cooled the more affected eye. The ice pack was then removed after 2 minutes. After 10 minutes, three i. v. injections, one containing 10 mg edrophonium and two placebo, were administered in a double blinded fashion by a nurse. Photographs were taken immediately after cooling or 1 minute after injection. All pictures were reviewed by a blinded observer. Outcome measure was the effect of ice or edrophonium on ptosis.

Results: Five subjects improved with the ice test; however, in one of them the edrophonium test was negative. All subjects with positive response to orbital cooling were subsequently shown to have myasthenia gravis by other tests (elevated titers of anti-acetylcholine receptor antibody and compound muscle action potential (CMAP) amplitude decrement to repetitive stimulation greater than 20 %). Patients with non-myasthenic ptosis (negative anti-acetylcholine receptor antibody titer and no decremental response in repetitive nerve stimulation tests) did not improve in either ice or edrophonium test.



a)

b)

c)

Fig. 1 (**A**) before testing; (**B**) after ice-test (ice application to the right eyelid); (**C**) after edrophonium test

No patient had a false-positive or paradoxical response to the ice test. No side effects, except for moderate local discomfort in the ice test, were observed.

Discussion: According to our limited data, the ice test seems to be relatively sensitive for the diagnosis of myasthenia gravis in patients with ocular symptoms: in our group all patients subsequently shown to have myasthenia gravis by other tests improved in ice test. These results are in agreement with the previously published studies. Golnik et al. observed improvement in myasthenic ptosis after the ice test in 16 of 20 patients with myasthenia gravis [3], Sethi et al. in 8 of 10 patients [8] and Lertchavanakul in 19 of 20 patients [6]. Although the sensitivity of the ice test was not 100 %, as has been also reported [2, 5] these results support the validity of the ice test in the diagnosis of MG. Moreover, the specificity of the ice test appears to be very high. Patients with non-myasthenic ptosis do not improve in the ice test [2, 3, 5, 6, 8]. The ice test may also be useful in the diagnosis of myasthenia gravis, even in patients in whom edrophonium testing is negative. Patients with a positive response in the ice test but with negative edrophonium test were found in our study and also in the studies of Sethi et al. and Golnik et al. However, both ice and edrophonium tests yield also false negative responses. According to previous studies improvement in eyelid elevation after the ice test is in part caused by rest [7]. A comparison of both ice and sleep test in a group of 10 subjects with myasthenic ptosis and 15 with non-myasthenic ptosis in a randomised trial was performed by Kubis et al. [5]. Whereas there was no improvement in ptosis in non-myasthenic subjects, in myasthenic patients the median improvement of ptosis with the rest test was 2 mm and with the ice test was 4,5 mm. This difference between the rest (sleep) test and ice tests was significant ($p < 0.001$). Both our results and review of the literature confirm that the ice test seems to be a reliable, safe, simple, sensitive and specific diagnostic method for the diagnosis of myasthenia gravis in patients with ocular ptosis. However, the most important disadvantage of this method in comparison with the tensilon test is the inability to conduct this test in a double-blind fashion.

References

1. Borenstein S, Desmedt JE (1975) Local cooling in myasthenia. Improvement of neuromuscular failure. Arch Neurol 32: 152–157
2. Ellis FD, Hoyt CS, Ellis FJ, Jeffery AR, Sondhi N (2000) Extraocular muscle responses to orbital cooling (ice test) for ocular myasthenia gravis diagnosis. J AAPOS 4:271–281
3. Golnik KC, Pena R, Lee AG, Eggenberger ER (1999) An ice test for the diagnosis of myasthenia gravis. Ophthalmology 106:1282–1286
4. Ing EB, Ing SY, Ramocki JA (2000) The complication rate of edrophonium testing for suspected myasthenia gravis. Can J Ophthalmol 35:141–144
5. Kubis KC, Danesh-Meyer HV, Savino PJ, Sergott RC (2000) The ice test versus rest test in myasthenia gravis. Ophthalmology 107:1195–1198
6. Lerchavanakul A, Gamnerdsiri P, Hirunwiwatkul P (2001) Ice test for ocular myasthenia gravis. J Med Assoc Thai 84 (Suppl 1):S31–S36
7. Movaghar M, Slavin ML (2000) Effect of local heat versus ice on blepharoptosis resulting from ocular myasthenia. Ophthalmology 107:2209–2214
8. Sethi KD, Rivner MH, Swift TR (1987) Ice pack test for myasthenia gravis. Neurology 37:1383–1385

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