THE ICE TEST FOR DIAGNOSING MYASTHENIA GRAVIS

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Abstract- There are many tests for diagnosis of myasthenia gravis including Tensilon test and ice test. To compare the ice test with Tensilon test in subjects with myasthenic and nonmyasthenic ptosis a process research study was designed. This study was performed in patients complaining of acquired ptosis in the neuro-ophthalmology center of Farabi Hospital. All 156 patients were tested with ice pack and edrophonium with an interval of 15 minutes. The patient was instructed to hold an ice filled plastic glove on the closed ptotic eyelid. Before and after 2 minutes of ice application on the ptotic eyelid, the distance between the upper and lower margin was measured by the neuro-ophthalmologist. An increase of 2 mm or higher was considered a positive test result. Patients with positive Tensilon test were considered as control. In all 61 patients with positive Tensilon test the ice test was positive, and in none of the 95 patients with negative Tensilon test the ice test was positive. The ice test is a simple, fast, specific and sensitive test for the diagnosis of myasthenic ptosis.

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INTRODUCTION

Myasthenia gravis (MG) is an autoimmune disorder in witch acetylcholine receptor antibodies attack the post synaptic membrane of the neuromuscular junction (1). The levator palpebral superior and extra-ocular muscles are initially affected in about 70% of cases and these muscles are eventually affected in over 90% of patients (2). The hallmarks of MG are fluctuation and fatigue. Weakness varies from day to day and from hour to hour, typically increasing toward evening (2). MG should be considered in every patient with ptosis and/or diplopia (3). Diagnostic tests include serum acetylcholine receptor antibody levels, repetitive nerve stimulation (RNS), Tensilon test, the sleep test, the rest test and the ice test (1). None of these tests, however, are 100% sensitive or specific (2).

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Local cooling was first shown to improve function in ptotic eyelid by Saavedra in 1979 (4). It is rapid, simple and inexpensive.

We conducted a prospective study in subjects with ptosis to evaluate specificity and sensitivity of ice test compared to Tensilon test.

MATERIALS AND METHODS

A process research study was designed. This study was performed in patients complaining of acquired and fluctuating ptosis in neuro-ophthalmology center of Farabi Hospital, Tehran. All patients were tested with ice pack and edrophonium. The diagnostic test for MG was Tensilon test. Since false positive result for Tensilon test is infrequent we accept these positive patients as proven myasthenic. On this way, ice test was compared with positive Tensilon test group and cases of false negative Tensilon test, which could be myasthenic, were ignored. The distance between the upper and lower eyelid margin was measured. The ice test was

performed by placing a surgical glove filled with crushed ice on the more ptotic eyelid for 2 minutes, then the ice pack was removed and the palpebral fissure was remeausured within 10 seconds. An increase of 2 mm or higher was considered as positive. The Tensilon test was performed 15 minutes after the ice test. The Tensilon test was performed in operation room and standard way.

RESULTS

A total of 156 patients entered the study. There were 64 (41%) men and 92(59%) women, ranging in age from 3 to 75 years (mean, 29.32 years).

There were 25 (41%) men and 36 (59%) women with positive Tensilon test ranging in age from 6 to 57 years (means 28.3 years).

There were 38 (40%) men and 57(60%) women with negative Tensilon test ranging in age from 3 to 75 years (means 29.9). All cases with positive Tensilon test had positive ice test whereas none of cases with negative Tensilon test had positive ice test ($P < 0.001$, chi square). In comparison with Tensinlon test, the ice test had sensitivity and specificity of 100%.

DISCUSSION

Patients with MG often have ophthalmologic signs and symptoms including ptosis, diplopia, ophthalmoplegia and orbicularis weakness (2). Although the disease is usually a systemic disorder, half of the affected patients have ocular symptoms and signs at onset (5).

The most common sign of MG is ptosis (5). Ptosis, however, may be caused by a variety of disorders, so the distinction between myasthenic and nonmyasthenic ptosis is critical (1).

Diagnostic tests to establish the diagnosis of MG include serum acetylcholine receptor antibody levels, RNS, the Tensilon test, the sleep test, the rest test and the ice test (3). The sensitivity of the antiacetylcholine receptor antibody test is 34% to 56% in subjects with ocular myasthenia, although it's specificity is high (6). RNS is both invasive and lacks 100% sensitivity. Single fiber EMG testing is positive in 88% to 99% of objects (2). Testing the orbicularis muscle or the superior rectus levator complex greatly increase the specificity (1). The sleep test has the disadvantage of requiring spending 30 minutes in a darkroom and its specificity in MG has not been established (7).

The estimated sensitivity of Tensilon test is 86% in ocular and 95% in systemic MG (8). The Tensilon test may produce false-positive and false-negative results and also carries with it a risk of cardiac and other complications (including significant bradycardia, loss of consciousness and death) (9).

Simpson first described the effects of temperature in MG in 1960 (10). Bronestein and Desmedt later showed that the local cooling improved myasthenic neuromuscular block, whereas warming had the opposite effect (11). The exact mechanism by which cooling improve myasthenic muscle function has not been completely explained. It is believed to affect the neuromuscular junction both by decreasing cholinesterase activity and by prompting efficacy of acetylcholine at eliciting depolarizations at the end plate (2). Saavedra and coworkers in 1979 first described a cold test for MG used in evaluation of ptosis. They reported that myasthenic ptosis improved transiently in six eyes after application of ice to the eye for 5 to 10 minutes. Two patients with nonmyasthenic ptosis did not improve(12).

Sethi *et al.* in 1987 applied ice to a ptotic eyelid of 10 patients with MG and 7 without MG with the use of ice; 8 of the 10 subjects with MG had improvement in their ptosis. None of the subjects in the control group showed any improvement in their ptosis with the ice test (13).

Ertas *et al.* in 1994 evaluated the ice test in 12 subjects with myasthenic ptosis and 15 control subjects. None of the control patients improved, whereas all patients with MG improved (14). Golink and coworkers confirmed previous findings regarding the ice test by showing improvement in ptosis of at least 2 mm in 16 of 20 patients with MG, with less than 0.5 mm of improvement in 20 control subjects, yielding a sensitivity of 80% and specificity of 100% if a positive test was defined as improvement of ptosis greater than or equal to 2 mm (15).

Our study also supports the validity of the ice test

for the diagnosis of myasthenic ptosis. In our study, 156 patients with ptosis were initially studied by ice test and then Tensilon test. Patients with positive Tensilon test were considered as MG. All patients with myasthenic ptosis had positive ice test whereas none of cases with negative Tensilon test had positive ice test. In all patients with positive Tensilon test, ice test was also positive and vice versa, therefore in comparison with Tensilon test, ice test had 100% sensitivity and specificity. In other studies too the ice test have had high specificity and sensitivity.

Clinically, the use of ice test is more advantageous than the Tensilon test because this test is rapid, simple and inexpensive with a high degree of specificity and sensitivity. The ice test is particularly useful in patients in whom the use of anticholinesterase agents is contraindicated by either cardiac status or age.

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