

## CONSENSUS REPORT

# Good clinical practice points on the use of acetylcholinesterase inhibitors in myasthenia gravis: Recommendations from the Special Interest Group in Myasthenia Gravis in Asia

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Acetylcholinesterase inhibitors (AChEI) are an integral part in the pharmacotherapy of myasthenia gravis (MG). However, their use has been based primarily on clinical experience rather than on evidence from randomised, placebo controlled, clinical trials.<sup>1</sup> In April 2009, a group of physicians (consisting of neurologists and a neuro-ophthalmologist) with special interest in MG from various countries in the Asian region met in Kuala Lumpur, Malaysia, to discuss and to come to a consensus on the role of AChEI, especially pyridostigmine, a widely used long-acting AChEI, in the management of MG. Prior to the meeting several aspects on the use of AChEI were identified. During the meeting, several experts in the group presented on these aspects based on their clinical experience and after reviewing the literature. As a result of discussion at the meeting, the panel came up with a consensus on the use of AChEI in MG and formulated good clinical practice points for use by clinicians in the management of MG. The following are the key discussion points:-

### *Diagnosis of myasthenia gravis*

Intravenous edrophonium is used as a diagnostic test for MG. In instances where edrophonium is unavailable, neostigmine, given intravenously (0.5 mg) or intramuscularly (1 mg) preceded by 0.6 mg atropine intravenously, can be used. Alternatively, oral pyridostigmine can be given with a starting

dose of 30 mg increasing to 60 mg two or three times daily for up to two weeks. Diagnosis should be made based on patient's response with clearly defined clinical end-points.

### *Treatment of myasthenia gravis*

Pyridostigmine should be the initial treatment of MG with a recommended starting dose of 60 mg three times a day. A starting dose of 30 mg three times a day may be used in patients with ocular MG. Treatment regimes should be individualized. Dose of pyridostigmine may range from 60 to 120 mg, with a frequency of four to six times per day, based on clinical response and adverse effects. Doses beyond 600 mg per day or exceeding 120 mg per dose are not recommended as the side effects increase with limited additional benefit. When a patient fails to respond adequately, immunosuppressive drugs such as prednisolone should be considered.<sup>1,2</sup>

### *Ocular myasthenia*

Ocular myasthenia patients are usually treated with pyridostigmine only. However, some studies have suggested that steroids have greater efficacy than pyridostigmine and suggested that early immunosuppressive treatment may be partially responsible for patients achieving remission and decreasing their risk of progression to generalized MG.<sup>3,4</sup> An evidence-based review by the Quality Standards Subcommittee of the American

Academy of Neurology pointed out that there is a need for well-designed, randomized, placebo controlled studies of the efficacy of AChEI, corticosteroids and other immunosuppressive agents in ocular myasthenia in terms of their effect on the risk of progression to generalised MG.<sup>5</sup>

#### *Thymectomy*

In patients undergoing thymectomy, their preoperative condition should be optimised with a combination of adequate doses of AChEI as well as immunosuppressive agents. However, for patients who respond well to AChEI, preoperative immunosuppression is not necessary. There was no consensus in stopping the AChEI on the day of surgery. If AChEI is to be continued, parenteral preparations may be used. Some patients may be more responsive to an AChEI following thymectomy and may require careful dose reduction with close monitoring to avoid excessive secretions and risk of cholinergic crisis.

#### *Myasthenic crisis*

Myasthenic crisis is a reversible condition of neuromuscular paralysis and may be present as severe weakness of respiratory muscles, bulbar muscles or both. Diagnosis of myasthenic crisis can be made by history, neurological examination and evaluation of respiratory function. There is no role for the intravenous edrophonium test in patients presenting with symptoms of crisis as there is a risk of worsening muscle weakness due to excessive AChEI. The possibility of cholinergic crisis contributing to the patient's clinical presentation must be considered. Patients may be less responsive to AChEI during myasthenic crisis, while excessive secretions may complicate their management. Therefore, consideration should be given to stopping or reducing AChEI medications temporarily while other measures of control are instituted.

#### *Cholinergic crisis*

Cholinergic crisis is an over-stimulation at a neuromuscular junction due to an excess of acetylcholine. This crisis is seen in patients who have taken an excessive dose of AChEI medication. Signs of cholinergic crisis include muscle weakness and excessive bronchial secretions due to parasympathetic stimulation. It is vital to recognize the signs of cholinergic crisis in patients who are on high doses of AChEI by close follow-up. Caution should be exercised if a dose

of more than 300 mg is used. Once cholinergic crisis is diagnosed, AChEI should be discontinued until the patient has recovered.

#### **DISCLOSURE**

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