Blepharospasm: ORAL MEDICATIONS

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The most effective treatment for blepharospasm is botulinum toxin injections. Oral medications have not been adequately evaluated in clinical trials for safety and efficacy in blepharospasm, and are not frequently used as a primary treatment. Anticholinergic drugs, including trihexyphenidyl, benztropine, biperiden, atropine, procyclidine, orphenadrine, scopolamine, and ethopropazine have been used for the treatment of dystonia, and are most frequently administered to children with generalized dystonia. These agents have limited benefit in patients with blepharospasm because of side effects which frequently limit the dose, and lack of proven efficacy. The most frequent side effects associated with anticholinergic agents include blurred vision, dry mouth, sedation, confusion, and memory problems. Additional side effects can include urinary retention, agitation, and anxiety. Anticholinergic agents should not be used in patients with glaucoma.

If anticholinergic drugs are used, it is important to initiate treatment at the lowest possible dose of a given agent and to escalate the dose slowly over a period of weeks to months. Anticholinergic dosing should be divided into 3 or 4 daily doses. Improvement is often delayed thus dose adjustments should be made slowly, allowing a week or two at a dose level. Adults are usually unable to tolerate high doses because of side effects. Ethopropazine appears to have fewer peripheral side effects than most other anticholinergic agents, but it is not available in the United States. If side effects occur in the absence of benefit, anticholinergic treatment should be discontinued. Discontinuation of anticholinergic agents should be done gradually, as withdrawal effects may occur.

Dopaminergic drugs are most frequently used for the treatment of Parkinson's disease. Although dystonia is clearly different from Parkinson's disease, carbidopa/levodopa and other dopamine agonist drugs are sometimes administered to patients with focal dystonia, including blepharospasm. There are insufficient studies to understand whether there is a beneficial effect. Some patients may improve, especially those with a dystonic disorder called dopa responsive dystonia (DRD), a dystonic syndrome arising from mutations in GTP cyclohyrolase 1 gene that shows a marked, sustained response to low doses of levodopa and usually presents in children. Although adult onset focal dystonia would be a rare manifestation of DRD, given the expanding clinical features described, an empiric trial of levodopa could be considered.

Dopamine receptor antagonists (antipsychotic agents, some antiemetic agents) have been suggested as a treatment for dystonia, although not adequately evaluated. The side effects of these types of medications include reversible drug induced parkinsonism and potentially permanent tardive dyskinesia. Because of the nature of these side effects, these agents are not suggested for use in blepharospasm. Although the atypical antipsychotics, including clozapine and quetiapine, may have a lower frequency of tardive dyskinesia, both agents have important side effects, including sedation, orthostatic hypotension, lowered seizure threshold, and metabolic syndrome (diabetes, dyslipidemia, and hypertension, with associated obesity).

Tetrabenazine is a medication that depletes monoamines, including dopamine, and has

dopamine blocking properties. Tetrabenazine is FDA approved for treatment of chorea associated with Huntington's disease. It is not approved for dystonia. Although controlled studies have not been done, open label studies suggest improvement in dystonia in up to 25% to 60% of patients. Side effects from tetrabenazine are common and include sedation, depression, parkinsonism, akathisia, nervousness and insomnia. In the United States, the cost of tetrabenazine treatment may be prohibitive.

Clonazepam is a benzodiazepine that is used frequently for dystonia but has not been evaluated in controlled studies. Small case series have described benefit in blepharospasm patients, especially those patients in whom anxiety is a major exacerbating factor. Clonazepam is gradually escalated to avoid side effects. The adverse effects include sedation, depression, confusion and dependence. Patients should not suddenly stop clonazepam, but should be slowly tapered from the medication under a physician's guidance.

Baclofen is a GABA receptor agonist that has been reported to be of some benefit in dystonia, although controlled studies are lacking. Baclofen may be particularly useful for generalized dystonia in children, but adults seldom tolerate the drug at doses sufficient to provide benefit. Baclofen is started at low doses and slowly increased until benefit or side effects occur. The most common side effects from baclofen are dizziness, sedation, nausea, and urinary symptoms. Confusion, hallucinations and paranoia have been reported, but are rare. Patients should not suddenly stop baclofen as this may cause psychosis, seizures or dramatic increase in dystonia.

There are many other oral medications that have been suggested as treatment for dystonia. At this time, however, for the treatment of blepharospasm, botulinum toxin remains the first line.