Blepharospasm is a focal dystonia. Dystonia is defined as an involuntary pattern of muscle contraction.

How do we decide if a medication is helpful or not? Comparing a drug to a placebo, or sugar pill, is the "gold standard" and considered important because 1) Some patients will improve with just a sugar pill (called the "placebo effect"), and 2) There is variation in the course of the natural disease (some patients get better with no treatment and symptoms often wax and wane in severity). Unfortunately, most of the studies done on blepharospasm are "open-label trials" where a medication is given and rates of improvement reported but no comparison is done with a placebo. This means that high quality scientific data is lacking.

The following classes of medications have been used to treat blepharospasm:

**Anticholinergics**

This is the class of medications that has historically and arguably been considered the most effective. These drugs work by blocking the chemical transmission from the nerve to the muscle (similar to botulinum toxin). However, botulinum toxin has a localized effect, while the effects of these medications are throughout the body. This causes some unwanted side-effects. The most common are sedation, slowing, dry mouth and constipation. These medications are not new and have been around at least 15 years. This class includes the following medications given IV (intravenously): scopolamine, atropine, and benzhexol and the following oral medications: benztropine (Cogentin), trihexyphenidyl (Artane), orphenadrine (Norflex), and ethopropazine (Parsidol).

**Dopamine Agonists**

This class of medications is used in Parkinson's disease and restless leg syndrome. Agonists mimic or increase dopamine levels in the body. This class includes levodopa, bromocriptine, lisuride, apomorphine, amantadine, and methylphenidate. Side-effects include nausea, sedation, and decreased blood pressure. In dystonias, these medications do NOT cause "wiggly" movements (as they can in Parkinson's). Dr. Ondo stated that he personally does not use these medications very often.

**Dopamine Inhibitors**

These drugs either block the effect of dopamine OR prevent its release. They were initially developed as psychiatric medications and used in schizophrenia. This class includes haloperidol, pimozide, oxipimozide, tetrabenazine, valbenzamine, reserpine, and alpha-methylldopa. These drugs tend to be very sedating and cause slowing, weight gain, and extrapyramidal side-effects (Parkinson-like slowing of body movements). A more serious side-effect which can occur is "tardive dyskinesia" (PERMANENT, unwanted movements that do not go away with stopping the medication).

**GABAergic medications**

This includes two types: 1) benzodiazepines (examples: clonazepam (Klonopin), alprazolam (Xanax) and lorazepam (Ativan)) and 2) baclofen.

Benzodiazepines have been used primarily to treat anxiety or as sleeping pills, but they are also muscle relaxants. Baclofen is a slightly different type of muscle relaxant.
Side-effects with these drugs include sedation, slowing, and trouble with balance. There is very little controlled data regarding these medications, however, they are used to treat blepharospasm and some patients do get pretty good results.

**Apraclonidine (eyedrop)**

This medication is a little newer and has been studied at Baylor. It mimics some of the effects of adrenaline. It does not prevent closure of the eye, but instead makes the eye open more.

**Miscellaneous drugs or new trials:**

- Two studies of methylphenidate with only 10 patients showed some improvement in symptoms within 2 hours.
- Tizanidine was studied in 10 patients and showed NO improvement.
- There was one study of CBD oil 400 mg in 5 patients who reported improvement; however, there was no placebo group.
- There were a few case reports in the literature of other drugs, but nothing of significance.

Most of the studies of oral medication involving large numbers of patients were done in the 1980's before botulinum toxin and surgery were options. These are all open-label trials, so without a placebo control.

One of the largest open-label studies was done in 1988. 264 patients were studied; however, many patients in this study also had other conditions affecting their eyelid opening (not pure blepharospasm). In this group, anticholinergics were used most frequently (96 patients). Approximately 21% of patients taking anticholinergics, levodopa, and dopamine agonists reported symptom improvement. 6% of tetrabenazine and 8% of benzodiazepine patients improved. Lithium was listed as 16% improvement but there were only 6 patients in this group; so, this means just 1 patient had improvement. In addition, lithium has fairly potent side-effects.

Another study from1988 which included 83 blepharospasm patients showed that there was 55% improvement with anticholinergics, 29% with baclofen and 22% with clonazepam. Best responses were seen if treatment began in the first 5 years of symptoms.

A study by Dr. Joseph Jankovic in 1983 enrolled patients with mixed dystonias (blepharospasm plus other cranial dystonias). These patients showed 37% improvement with trihexyphenidyl, 26% with tetrabenazine and lithium, 16% with levodopa, and 11% with clonazepam.

A study by Dr. Marsden in 1983 of 127 patients had more negative results. Less than 3% of patients in his study improved with ANY of the following medications: anticholinergics, cholinergics, phenothiazine, tetrabenazine, levodopa, amantadine, amphetamine, or lisuride.

"Sensory tricks" such as talking, singing, touching or head position can improve symptoms. Other non-pharmacologic aids include dark glasses, biofeedback, acupuncture, hypnosis, transcranial magnetic stimulation and mechanical devices such as eyelid crutches.

**CONCLUSIONS:**
1) Treatment of blepharospasm often requires a multi-modal approach.
2) Medications meaningfully improve about 25% of patients but there is little strong scientific data.
3) Data regarding combined chemo-denervation (botulinum toxin) and oral medication is minimal.
4) Non-pharmacologic strategies may also help patients.

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