AUGS Practice Advisory
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Possible drug induced retinal maculopathy secondary to long-term use of pentosan polysulfate sodium (Elmiron)

Scope of the problem:
Pentosan polysulfate sodium (PPS) was approved by the Food and Drug Administration (FDA) in 1985 for the relief of bladder pain or discomfort associated with Interstitial Cystitis (IC)/Painful Bladder Syndrome (PBS). Currently, it is the only FDA approved oral agent for the treatment of IC/PBS. Due to the limited availability of alternative treatments for IC/PBS, many patients may rely on long-term continuation of this drug for relief of symptoms.

The most common side effects are hair loss (4%), nausea (4%), diarrhea (4%), headache (3%), rash (3%), abdominal pain (2%), abnormal liver function tests (1%), and dizziness (1%). 1

In 2018, Pearce et al. 2 first described as a unique pigmentary maculopathy affecting six patients with known diagnosis of IC/PBS being treated with PPS. Their median exposure to PPS was 186 months (range 144 -240 months).

Subsequently, a multi-institutional larger retrospective case study found an additional 35 cases among a cohort of 404 patients with a median PPS exposure of 15 years duration. 3More recently, a case cohort study of over 1,600 patients from a large U.S. insurer claims database found that women exposed to PPS were more likely to develop macular changes at 7 years compared to controls (odds ratio 1.41, CI 1.09–1.83).4 Vora et.al. looking at a Kaiser data base of patients with greater than 500 g of life time exposure (approximately 4.6–9.1 years at a typical 100 mg three times daily dosage regimen) found that 12.7% manifested the characteristic maculopathy, whereas 41.7% of those with more than 1,500 g of life time exposure were affected.5

Patients, who developed maculopathy, presented with symptoms of difficulty seeing in dim lighting and decreased visual acuity with reading. In more advanced cases, degeneration of the macula resulted in legal blindness.

Recommendations for clinical practice:

- Prescribers should include discussion of possible visual side effects when using PPS for women with IC/BPS. Patients should be made aware of the possibility of permanent visual changes and/or the progression of visual symptoms following cessation of the medication.
- Baseline ophthalmologic evaluation with fundus photography is recommended at initiation of medical treatment with PPS and should be repeated within 5 years of initiating treatment and then yearly afterwards. 6
- Providers should be cognizant to screen patients for any changes in visual symptoms while on the medication and refer for evaluation.
- Practitioners should prescribe the medication at the lowest necessary dose and the shortest duration trying to keep the overall dose at <500 grams or 5 years to therapy.

Conclusion:
There is a growing body of evidence linking long term PPS exposure to a unique form of maculopathy. The relationship between this unique form of degenerative maculopathy and long term use (greater than 4-6 years at 100 mg TID) of PPS warrants further investigation. Visual side effects should be discussed with patients before initiating PPS therapy. Clinicians taking care of patients who are taking PPS should pay attention to

visual complaints and, if present, refer them to an ophthalmologist or retinal specialist for further evaluation. This should also be discussed with patients before initiating therapy with PPS.

References:

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4. Jain M, Li AL, Yu Y, et al. Association of macular disease with long-term use of pentosan polysulfate sodium: Findings from a U.S. cohort. Br J Ophthalmol 2019 Nov 6. bjophthalmol-2019-314765.doi: 10.1136/bjophthalmol-2019-314765. [Epub ahead of print].
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