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Editor
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Dear Sir

FURTHER UPDATE ON THE PHARMACOLOGICAL TREATMENT OF MYOPIA PROGRESSION IN CHILDREN

We refer to the article, “Update on treatment of childhood myopia progression”, by Saw et al. published in the July – September issue of The Singapore Family Physician. Since the submission of that article for publication, several local research developments have occurred leading to important clinical implications in myopia treatment. As such, we wish to provide family physicians with a further update on the pharmacological control of myopia progression.

While well-designed randomised controlled trials (RCTs) of various optical means aimed at controlling myopia such as bifocals, progressive addition lenses and contact lenses have all yielded disappointing results,[1-4] pharmacological interventions have met with greater success.[1,5-8] Atropine, a non-selective muscarinic antagonist, remains the most promising treatment available at present for preventing the progression of myopia in children. While several clinical trials on atropine have suggested its efficacy, these trials have had some limitations in methodology, including low compliance rates and sample size. The Singapore Eye Research Institute (SERI) therefore embarked on a major 3-year randomized, double masked, placebo-controlled clinical trial known as the ATOM (Atropine in the Treatment of Myopia) Study, in which we evaluated the use of 1% atropine eye drops in 400 local Singaporean schoolchildren, and this study has just been completed.

The ATOM Study revealed that uniocular treatment with 1% atropine eye drops achieved about 77% reduction in progression of myopia over a 2-year period compared with placebo treatment.[5] This study provides the strongest evidence to date that human myopia can be controlled pharmacologically. This study, which had a high retention rate of 87%, also found that long-term atropine treatment was well tolerated and there were no serious adverse events directly related to atropine.[6] Nevertheless, the treatment regimen adopted in the study has two drawbacks.

Firstly, long-term uniocular treatment of myopia was necessary in order to have the other eye as a control, but is quite impractical and obviously unsatisfactory in the clinical setting, because the myopia in the untreated fellow eye may continue to progress thus resulting in anisometropia and aniseikonia. Moreover, the risk of myopic complications in the untreated eye remains undiminished.

Secondly, while treatment with 1% atropine was relatively safe, it can nonetheless produce unwanted short-term side effects such as glare and photophobia because of pupillary dilatation, as well as a theoretical risk of excessive light entering the eye causing chronic photic damage. In the ATOM study, glare and photophobia, and excessive light entry were effectively minimised through the use of photochromatic lenses.

Another side-effect of 1% atropine is the blurring of near vision due to induced cycloplegia (paralysis of accommodation) from which binocular treatment will have functional consequences such as difficulty with near work activity e.g., reading and writing. To overcome this problem the use of either bifocal or progressive addition lenses may be prescribed.

The limitations and problems associated with monocular 1% atropine treatment have led us to plan a second RCT designed to evaluate lower doses of atropine for the binocular treatment of myopia progression. The study, named ATOM II, will compare the efficacy and safety of 0.5%, 0.1% and 0.01% atropine in retarding progression of myopia in primary school children with myopia of -2.0 dioptres (200 degrees) or more. One of the objectives of this trial is to find an optimal dose of atropine that has clinically significant beneficial effects without the accompanying side effects of pupillary dilatation and cycloplegia. Upon completion of this trial, we will be close to ascertaining clinical guidelines on the best approach towards the effective and safe, use of atropine eyedrops in reducing myopia progression in children.

One further myopia drug trial deserves mention. SERI is currently involved in a multicentre Asian trial on the use of pirenzepine eye gel. Similar studies are currently underway in the US. Like atropine, pirenzepine eye gel is a muscarinic antagonist and is currently an investigational drug and as such not available to the family physician nor public. Results from two multi-centre phase II RCTs were released this year and they appear to be promising.[7,8] Children on a twice a day dosing regimen of 2% pirenzepine for one year had between 40-50% reduction in progression of myopia compared to placebo treatment. Pupillary dilatation and accommodative effects were present although they were relatively mild, as were adverse events.

More data on long-term treatment with pirenzepine are forthcoming and should provide us with more information on the effects of pirenzepine treatment beyond one year. In addition, further phase III RCTs are being planned.

In summary, there is good evidence from several RCTs that pharmacological intervention with antimuscarinic agents like atropine and pirenzepine is both effective and safe in retarding the progression of childhood myopia over 1-2 year period. While further basic research and clinical trials are still required to elucidate the mechanisms of action and long-term efficacy and safety profiles, we now have two promising treatment modalities in our armamentarium and perhaps the fight against rapid myopia progression is finally turning the corner.

Yours sincerely

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