Is intraocular pressure lowering drop persistence improved by adding 0.4% Sodium Hyaluronate? The 'Five Minute' technique.

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INTRODUCTION

The glaucomas are a group of diseases that are characterised by changes in the optic nerve and subsequently in the visual field. The only risk factor for glaucoma that can be manipulated is the intraocular pressure (IOP). Lowering the IOP has been shown to reduce the risk of getting glaucoma and of slowing the disease when it is established[1,2,3]. There are a number of ways the IOP can be lowered but currently topical eye drops are the mainstay and have been shown in large RCTs to significantly slow the disease[1,2].These drops need to be taken at least once and day and some patients can subsequently become sensitive to their drops. This is more likely the longer the patient has taken the drops, the more drops they take and the amount of preservatives the drops contain[4,5,10,11]. This may manifest at one extreme as a pure allergy to the drop (usually to the preservative but sometimes to the active ingredient itself) but more commonly patients have mild irritation for variable amounts of time after drop instillation. Even though this irritation is mild and short lived it can reduce the likelihood of patients taking their drops. This could be stopping completely or reducing the frequency of the pressure lowering drops – neither of these situations is ideal for long term glaucoma control and preservation of visual function. For the drops to work the patient has to acquire the drops and use them as directed – this is named persistence[6,7,8]. Lack of persistence can be caused by a number of factors e.g. cost of medication or inability to instill drops but one of the commonest is irritation from the drops. Glaucoma is an asymptomatic disease until its very late stages, so the patient has to understand the need for daily drops to protect future vision. Drops that irritate erode this understanding and so potentially could lead to blindness. It is logical that anything that will reduce drop irritation will make a patient more likely to use their IOP lowering drops. In the ophthalmic unit the audit was conducted in, patients having this problem are asked to use dry eye drops five minutes after installation of their glaucoma drop. Five minutes is used as a convenient time gap but long enough to prevent the dry eye drop washing out the glaucoma medication and reducing its effect. This intervention is not used when patients have clinical signs of an allergy to their medication as the drops would then be changed but when they have symptoms of irritation but no signs of allergy or ocular surface damage. The aim of this study was to ascertain if this method gave relief to patients with drop intolerance and so making it more likely they persist with their glaucoma drops. We conducted as a prospective audit.

METHOD

Twenty consecutive patients who, during their glaucoma review, mentioned drop irritation but who had no clinical signs of allergy or serious ocular surface damage were included in the audit. To try to standardise the intervention each one was given Preservative Free 0.4% Sodium Hyaluronate in the form of Eyezin XL™ (Aspire Pharma, UK) and asked to use it five minutes after instillation of their glaucoma medication. If they used two or more IOP lowering drops, they were asked to use five minutes after the final drop was instilled. Combination drops were counted as a single drop. If the patient was using dry eye drops already, they were allowed to use them as often as they needed during the rest of the day or the night but to only use the Eyezin XL™ at the five-minute point. Patients were asked after one month of this regime:

1. If their eyes were less irritable following their IOP lowering medications.
2. Whether they had persisted with their IOP lowering medications for the entire month
3. How often they had needed to use other ocular lubricants.

Patient No	Age	M/F	Number Glaucoma drops	No dry eye drops/ ointment	Dry Eye Drop given	Drop irritation reduced?	Glaucoma drop Persistence?	Need for other DED or ointment?
1	82	F	1	2	Eyezin XL	Yes	Yes	No
2	76	F	2	2	Eyezin XL	Yes	Yes	No
3	84	M	1	1	Eyezin XL	Yes	Yes	No
4	66	F	3	0	Eyezin XL	Yes	No	N/A
5	76	F	2	2	Eyezin XL	Yes	Yes	No
6	61	F	2	2	Eyezin XL	Yes	Yes	No
7	82	F	1	2	Eyezin XL	Yes	Yes	No
8	85	F	1	1	Eyezin XL	Yes	No	No
9	82	M	3	0	Eyezin XL	Yes	Yes	N/A
10	75	F	2	2	Eyezin XL	Yes	No	No
11	76	M	1	2	Eyezin XL	Yes	Yes	Yes
12	69	F	1	0	Eyezin XL	Yes	Yes	N/A
13	64	F	1	2	Eyezin XL	Yes	Yes	No
14	81	F	2	0	Eyezin XL	Yes	No	N/A
15	74	M	1	1	Eyezin XL	Yes	Yes	No
16	78	F	2	2	Eyezin XL	Yes	No	Yes
17	70	M	1	0	Eyezin XL	Yes	Yes	N/A
18	82	F	3	1	Eyezin XL	Yes	Yes	No
19	84	F	1	2	Eyezin XL	Yes	Yes	No
20	71	M	2	1	Eyezin XL	Yes	Yes	No

RESULTS

Table 1 contains the results of the audit.

20 patients were asked to use the five-minute regime. All did so for at least a month and none reported any problems using the Eyezin XL™. The average age of the patients was 76. 14 out of 20 patients were female. 10 patients were taking one IOP lowering drop per day (this included combination drops), 7 patients were taking two drops per day, 3 were taking 3 drops a day. 15 patients were already taking dry eye drops or ointment – 10 were taken ointment at night and lubricating drops during the day. All 20 patients stated that their eyes were more comfortable when taking the Eyezin XL™ 5 minutes after instillation of their glaucoma drops. 18 out of 20 patients (90%) were happy to persist with their glaucoma medications when using this regime. Of the patients who were taking eye drops prior to the audit only two reported requiring extra lubricants during the day. Eyezin XL™ is indicated for day and night use and appeared to give sufficient relief for the vast majority of patients without needing extra lubrication over 24 hours.

DISCUSSION

IOP lowering medications have been shown to reduce the rate of visual field loss in patients with glaucoma and ocular hypertension[1,2,3]. Self-evidently these drops need to be used as prescribed to have the desired effect. Patients' non-persistence with their eye drops can be for a number of reasons[4,5,6,8,9,11]. One of the most important is that the drops irritate their eyes. When an asymptomatic disease becomes symptomatic because of drop intolerance compliance is far more likely to reduce with all the implications this has. There are a number of ways to address this compliance/concordance issue. Patient understanding of their disease, trusting their practitioner and regular visits showing good IOP control are very important. But just as important is patient comfort hence the use of the 'Five Minute Technique' described above. The audit results show excellent improvement in patient comfort with the Eyezin XL™ drops five minutes post antihypertensive drop. All 20 patients reported decreased ocular irritation. 18 of the 20 patients were happy to persist with their glaucoma medication using this technique – and this is a very important finding. Only two of the patients needed extra dry eye drops during the audit period – this is probably because the Eyezin XL is 0.4% Sodium Hyaluronate (and also contains lipid) so is likely to persist on the ocular surface for some hours. Only one of the patients who was taking nighttime ointment needed to take it when using the Eyezin XL. This was an unexpected finding and perhaps indicates that patients on glaucoma medications do need the higher concentrations of hyaluronate to make them comfortable. It also suggests that many patients could be managed with a single Eyezin XL type drop rather than drops during the day and ointment at night. This has cost and convenience implications. Certainly the fewer drops patients take the better – not least from the compliance point of view[4,5,6,8,9]. This was only a pilot study and to show true efficacy of the five-minute technique a randomised trial would be required. The results do indicate though that this trial would be worth doing. The positive features of this audit are that patients were standardised to one lubricating drop and that they all saw the same practitioner at each visit. This does not of course discount other dry eye medications being equally efficacious or that the practitioner themselves had an influence upon the patient's subjective outcomes. These points could all be addressed by an adequately designed and powered RCT. IOP level was not measured before and after the technique as all patients were adequately controlled prior to the audit.

In summary, this audit indicates that patients were more likely to persist with their IOP lowering medications even when they caused ocular irritation if they instilled Eyezin XL five minutes after their glaucoma drops. This has positive implications for their long-term disease and practitioners should consider utilising this technique in patients with drop irritation including those who potentially wish to stop their medications because of this irritation. A month's trial of 0.4% Sodium Hyaluronate five minutes after drops instillation may be all that is needed to preserve an acceptable IOP level and inevitably visual function.

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