

Clinical performance of a preservative-free multipurpose solution with two SiH lenses

Howard Griffiths reviews the results of an independent clinical study on a preservative-free multipurpose solution used with two silicone hydrogel contact lenses



ome second generation silicone hydrogel lenses (SiHs) are being specifically introduced and increasingly prescribed for daily

wear (DW), despite having originally been developed for extended wear nearly a decade ago. Wearing SiHs for DW means patients benefit from high oxygen performance, without the increased risk of infection with overnight wear. The benefits of these novel materials do not come without some issues such as potential mechanical complications with higher modulus materials and differences in wettability compared to conventional hydrogels.^{1,2} Lower modulus materials are being introduced, and a range of material modification techniques are used - such as lens surface plasma oxidation or internal wetting agents-to overcome the hydrophobicity of the lens surface and improve wettability. The techniques vary in their effectiveness, with some areas on the lens remaining hydrophobic, affecting wettability and attracting lipid.

The increasing use of SiHs for DW, and hence the need for cleaning, storage and disinfection, means the compatibility of these materials with care products must be considered. There is increasing evidence of incompatibility between certain SiHs and care regimens, although the exact mechanism of the solution-induced corneal staining (SICS) seen is not known. Previous studies have shown certain preservative-based solutions caused SICS with lipid-attracting, neutral, high water content materials (FDA group II).³⁻⁸ One theory is that multipurpose solution (MPS) components bind to and are then released from lipid deposits on the lens surface,9 mimicking a drug delivery device, with the



pattern of lipid uptake being the same as the observed SICS. $^{10}\,$

More recent evaluations on solution interactions with SiHs have been carried out by Andrasko.11 These used a consistent testing methodology to determine which combinations successfully interacted without inducing excessive SICS, and led to the development of the staining grid. One of the most recent studies involved a range of SiHs and solutions worn for three months,¹² and showed that preservative-free systems, such as hydrogen peroxide, caused almost no SICS. It highlighted differences in response with certain MPS/SiH combinations, although there were differences in the levels of staining compared to Andrasko's work.

The levels of SICS are not always considered clinically significant and hence the exact significance of the staining is not generally agreed. In a recent retrospective analysis of contact lens patient records,¹³ Carnt *et al* showed wearers with low-grade, punctate, epithelial staining were three times more likely to experience a corneal

infiltrative event and to report lower subjective comfort. There appears to be no relationship between SICS and microbial keratitis risk - as there are many factors involved in infection other than staining - although this area has received significant coverage in the optical and lay press recently with the withdrawal of two MPS. The unusually high incidence of Fusarium keratitis with ReNu MoistureLoc and Acanthamoeba keratitis with Complete Moisture Plus was associated with the use of the two MPS but also with poor compliance.^{14,15} The apparent failure of the two MPS systems was felt to be due to a combination of effects:16 the ideal for lens wearers to have a more user-friendly disinfection system led to the introduction of no rub, and MPS reformulations to minimise their reaction with the ocular surface and improve comfort. It was concluded that, from a microbiological and safety point of view, rubbing should be reintroduced in lens disinfection.

SYNERGI - A PRESERVATIVE FREE MPS

In response to these issues, Sauflon launched Synergi in 2006 as a preservative-free MPS formulated for SiHs. It maintains high levels of efficacy, safety and convenience without the issues of preservative-uptake and subsequent incompatibility with certain contact lenses. The active ingredient is Oxipol, which combines cleaning, disinfecting and lubricating agents. The PVP lubricating agent ensures the lens surface is highly wettable to improve comfort on insertion. The poloxamer surfactant in the Synergi formulation is lipid specific to address the higher level of lipid binding associated with SiH lenses, yet the surfactant also ensures protein removal during the rub, rinse and soaking steps.¹⁷ Synergi also contains

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the viscosity-enhancing agent hydroxypropylmethylcellulose (HPMC) to improve comfort throughout the day.

Synergi's disinfecting component is a stable oxychlorite complex (sodium chlorite and hydrogen peroxide). Once placed in the lens case, a partial decomposition of the oxychlorite complex occurs, releasing low levels of chlorine dioxide and hydrogen peroxide, killing any microbial contamination on the lens or in the case. It is a highly effective antimicrobial agent against a broad range of ocular pathogens,17 with the requirements for primary criteria for stand-alone disinfection (ISO 14729, 2001) effectively achieved or exceeded in the six-hour recommended soak time (Figure 1). For additional patient safety, the lens case included with Synergi has antimicrobial properties that minimise organism transfer to the lens and eyes and help prevent the build-up of biofilm. It is promoted as a 'rub and rinse' MPS, shown to be important in enhancing disinfection performance, in addition to the benefits with certain patients that can be prone to lipid deposition with SiHs.

The hydrogen peroxide in the oxychlorite complex assists antimicrobial activity in addition to stabilising the chlorite and preventing its decomposition in the bottle. Since chlorite is sensitive to UV light, the Synergi bottle uses plastic that does not allow UV light transmission. After disinfection, full decomposition of the partially decomposed components continues, leaving just salt, water and oxygen. Hence there is no stinging on lens insertion, since the stabilised oxychlorite complex and the decomposed components are nontoxic. Synergi can therefore be used for re-wetting during the day in addition to being indicated for sensitive eyes.

To assess Synergi's performance, in particular the short-term compatibility with SiHs, a study was conducted to investigate any SICS and subjective response using Synergi and Multi (a one-step peroxide) with two second generation SiHs. Although the Andrasko staining grid can be useful for practitioners in selecting the best SiH/ solution combination to minimise SICS, it does not include some care regimens widely used in the UK. Hence, the study with Synergi employed similar methodology used to generate the staining grid to give a more complete picture on SiH/ solution compatibilities for typical UK practitioners.

METHODS

The study was conducted by an independent clinical research group as a double-masked, bilateral, randomised,



Figure 1 Antimicrobial profile for Synergi

controlled crossover study at a single site. It evaluated the short-term clinical response to combinations of two lens types (Acuvue Oasys, AVO and Air Optix, AIRO) and two care systems (Synergi and Multi), with subjects wearing each of the four combinations for a two to three hour wearing period. Details of the study lenses and solutions are provided in Tables 1 and 2. Study lenses were stored overnight in solution in their respective cases (at least 12 hours, but no more than 72) before being worn.

At baseline, details were taken of the subject'socularand contactlens wearing history; their habitual lenses were not worn on the day of the visit. Slit lamp biomicroscopy included assessment of conjunctival redness, limbal redness, conjunctival staining and papillary changes and corneal staining. Corneal staining assessment (post-fluorescein instillation and with a yellow barrier filter) was graded to replicate that done to generate the Andrasko staining grid. A score was recorded for each of the five corneal zones (superior, inferior, temporal, nasal and central) and average taken to give the final score. Corneal staining type (0=none, 1=micropunctate, 2=macropunctate, 3=coalesced macropunctate, 4=patch >1mm) and depth (0=none, 1=superficial epithelial, 2=full epithelial, 3=stromal glow) were also recorded.

Study lenses were fitted and allowed to settle for five minutes; lens power was determined from the baseline visit. Both investigator and subject were masked from lens type and care system used. High contrast monocular logMAR VAs were recorded, and high and low contrast VAs with following over-refraction. Lens fit was assessed (horizontal and vertical centration, corneal coverage and movement) and subjects scored comfort, vision and overall score on visual analogue scales (VAS) and asked to return two to three hours later.

At the two-hour follow-up, VA and lens fit were measured as before. Subjects graded comfort after insertion, comfort before removal, dryness, grittiness, burning/stinging, vision and an overall score for each combination. Lenses were removed and discarded, and a biomicroscopic examination carried out as at baseline. All assessments with different lens/solution combinations were carried out on different days.

The study was randomised and rigorously masked such that any differences seen were unlikely to be due to methodology or investigator or subject bias.

RESULTS

Subject demographics

Twenty-one subjects were recruited, with 18 subjects completing the study. Three subjects were discontinued, although none were related to the study

TABLE 1

Lens parameters

Acuvue Oasys (AVO)	Air Optix (AIRO)						
Johnson & Johnson Vision Care	CIBA Vision Inc						
senofilcon A	lotrafilcon B						
38	33						
8.4	8.6						
14.0	14.2						
-0.50 to -10.00	-0.50 to -10.00						
	Acuvue Oasys (AVO) Johnson & Johnson Vision Care senofilcon A 38 8.4 14.0 -0.50 to -10.00						

TABLE 2

Solutions								
Solution name	Synergi	Multi						
Key disinfection component	Oxychlorite complex (Sodium chlorite & H ₂ O ₂)	Hydrogen peroxide						
Other components	Poloxamer, PVP, HMPC	Poloxamer						

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Figure 2 Subjective scores on insertion

lenses or solutions. Male to female ratio was 11:10, mean age 32.5 ± 9.3 years and mean lens power -3.56D (range -1.00D to -6.00D).

Comfort/subjective findings

There were no differences in subjective scores between the two solutions on insertion or after two hours wear (Figures 2 and 3). Overall, AVO was more comfortable than AIRO (P=0.02), although comfort scores were better after two hours when AIRO was used with Synergi, making it more comparable with the AVO scores. AVO also received a higher 'overall score' than AIRO.

Corneal staining

There were no significant differences in overall extent or depth of corneal staining scores for lenses or solutions (Figures 4 and 5). Staining types (Table 3) were mostly micro- or macro-punctate.

Bimicroscopy - other signs

Of the other biomicroscopic signs, no differences were evident between solutions.

Lens fit

Lens fits were generally good, with all fits being at least 'acceptable'. There were no differences between lenses for proportion optimum fits at either visit.

Visual acuity

Visual acuity was good throughout the study, with no differences at either visit between lenses or solutions.

Adverse events

There were no serious adverse events,

lenses or solutions. DISCUSSION

Synergi performed well with the two second-generation SiHs for shortterm ocular response with minimal SICS; there was a similar performance from the one-step peroxide, Multi. If these results are compared to those of Andrasko's staining grid,¹¹ the low level of staining seen with the preservative free systems Multi and Synergi MPS would warrant both products having a 'green' background on the grid (signifying less than 10 per cent staining area, or insignificant staining). Although the methods used here were similar to the staining grid work, some caution should be applied when directly comparing data from different sites and investigators.

and two significant adverse events, both

for foreign body staining and as such,

were not directly related to the study

AIRO = Air Optix; L = lens; S = solution

Corneal staining due to certain solution/lens combinations is primarily caused by the solution components, probably preservatives, absorbed by the lens overnight and released on to the eye during wear.⁹ The majority of SICS is micro-punctate, although there is also a wide variation in the reporting of staining levels due to differences in methodology and staining grading.¹⁸ Other reasons for corneal staining include lens fit, design, modulus, dehydration and inter-subject differences.

There is much debate currently about the clinical significance of SICS. Although corneal staining is a wellestablished clinical technique to assess ocular surface integrity, there is no definitive evidence of a deleterious effect on wearer comfort or an association with more sinister adverse events. SICS is not thought to increase the risk of microbial keratitis, perhaps since the staining is mostly superficial and shortlived. Although staining indicates that the epithelial barrier has been compromised, laboratory evidence suggests that damage needs to extend into the corneal stroma to lead to bacterial infections.¹⁹⁻²² There is however evidence that patients with SICS are more likely to experience inflammatory events,13 hence it would seem prudent to minimise staining to reduce the risk of

TABLE 3

Type of corneal staining									
		Staining Type (Grade 0 - 4)							
Solution	Lens	0 = None	1 = Micropunctate	2 = Macropunctate	3 = Coalesced macropunctate	4 = Patch (>1mm)			
Synergi	AVO	15%	55%	15%	15%	0%			
	AIRO	15%	50%	5%	25%	5%			
Multi	AVO	26%	37%	32%	5%	0%			
	AIRO	20%	45%	15%	10%	10%			





Mean depth of corneal staining (0-3) 0.3 0.2 0.1 0 Synergi

1

0.9

0.8

0.7

0.6

0.5

0.4

Figure 4 Overall extent corneal staining (% cornea stained) There were no differences in corneal staining depth between solutions or lenses

Figure 5 Depth of corneal staining results

📕 Acuvue Oasys 📕 Air Optix

0.5

0.5

adverse events, even if the staining does not appear to be problematic.

Previously there have been differences in findings of the effect of SICS on comfort, with some reporting it to be asymptomatic^{3,5,7,23} and others finding an inverse relationship between staining and comfort.4,11,24 In this study, there were no differences in subjective performance between solutions and there were no differences in comfort between lenses when used with Synergi. This suggests Synergi performs well with both SiHs, highlighting how careful solution selection can lead to subjective performance improvements.

The results emphasise the importance of examining all SiH wearers early in the day for SICS, even if asymptomatic, to identify and remedy solution/lens compatibility issues. Between two and four hours post-insertion has been shown to be the most sensitive time period for assessing SICS.23 Sodium fluorescein, a cobalt blue excitation filter and a yellow barrier filter should be used to improve the visibility and if clinically unacceptable staining levels are seen, a new lens/solution combination should be chosen for better biocompatibility. Patients should be educated about potential consequences of switching solutions, with studies highlighting differences in performance with subtle differences in solution formulation with some lenses

Conclusion

The preservative-free MPS Synergi performed well when used with two second-generation SiHs for shortterm ocular response and subjective performance. The corneal staining data generated by the study will be helpful when selecting a solution that safely complements the SiH brand fitted. For practitioners wanting to recommend a convenient MPS with the benefits of continuous disinfection and no risk

of inserting non-neutralised contact lenses, Synergi provides biocompatible, effective disinfection for SiH DW patients.

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Multi

0.5

0.5

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