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# The influence of in-eye cleaning/re-wetting drops on the performance of 30 day continuous wear silicone hydrogel contact lenses

## Abstract

30 patients were enrolled in a double blind study designed to determine the efficacy and subjective preferences in reducing deposit accumulation, both lipid and protein, between an in-eye cleaning/re-wetting drop and a control re-wetting drop while wearing silicone hydrogel contact lenses on a 30 day continuous wear schedule. The patients had previously worn these contact lenses on a continuous wear schedule for a minimum of two weeks prior to enrollment in this study, and were asked to determine their preferences based on comfort, vision, and contact lens cleanliness. 27 patients completed the study of two thirty day continuous wear periods. With regard to comfort, 55.56% preferred the control drops, 29.63% preferred the in-eye cleaning/re-wetting drops, and 14.81% had no preference. With regard to vision 33.33% preferred the control drops, 25.93% preferred the in-eye cleaning/re-wetting drops, and 40.74% had no preference. With regard to lens cleanliness 48.15% preferred the control drops, 25.93% preferred the in-eye cleaning/re-wetting drops, and the remaining 25.93% had no preference. Biomicroscopy results of contact lens wetting, deposits, and numbers of mucin balls were equivalent for the two drops. In-eye cleaning/re-wetting drops appear to be compatible with silicone hydrogel contact lenses worn on a continuous wear basis and are similar in performance to re-wetting drops.

## Degree Type

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## Degree Name

Master of Science in Vision Science

## Committee Chair

Peter Bergenske

## Keywords

in-eye cleaning/re-wetting drops, silicone hydrogel contact lenses, comfort, vision, cleanliness

## Subject Categories

Optometry

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THE INFLUENCE OF IN-EYE CLEANING/RE-WETTING DROPS ON THE  
PERFORMANCE OF 30 **DAY** CONTINUOUS WEAR SILICONE HYDROGEL  
CONTACT LENSES

By

**ANDREW ARMSTRONG**

**RITA WALLACE**

**A thesis submitted to the faculty of the**

**College of Optometry**

**Pacific University**

**Forest Grove, Oregon**

**for the degree of**

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**May 2004**

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## **Biographies**

**Andrew Armstrong** graduated from the University of Alberta in 1997 with a B.S. and Physics and Mathematics. **Andrew** found an interest in contact lenses during his studies at Pacific University College of Optometry which inspired his motivation in this study. He plans to practice primary care optometry in the Pacific Northwest.

**Rita Wallace** graduated from Pacific University in 2001 where she received a B.S. in Visual Science. She will graduate from Pacific University College of Optometry May 2004 and plans to practice in Beaverton, OR with a specialty in contact lenses.

## **Abstract**

30 patients were enrolled in a double blind study designed to determine the efficacy and subjective preferences in reducing deposit accumulation, both lipid and protein, between an in-eye cleaning/re-wetting drop and a control re-wetting drop while wearing silicone hydrogel contact lenses on a 30 day continuous wear schedule. The patients had previously worn these contact lenses on a continuous wear schedule for a minimum of two weeks prior to enrollment in this study, and were asked to determine their preferences based on comfort, vision, and contact lens cleanliness. 27 patients completed the study of two thirty day continuous wear periods. With regard to comfort, 55.56% preferred the control drops, 29.63% preferred the in-eye cleaning/re-wetting drops, and 14.81% had no preference. With regard to vision 33.33% preferred the control drops, 25.93% preferred the in-eye cleaning/re-wetting drops, and 40.74% had no preference. With regard to lens cleanliness 48.15% preferred the control drops, 25.93% preferred the in-eye cleaning/re-wetting drops, and the remaining 25.93% had no preference. Biomicroscopy results of contact lens wetting, deposits, and numbers of mucin balls were equivalent for the two drops. In-eye cleaning/re-wetting drops appear to be compatible with silicone hydrogel contact lenses worn on a continuous wear basis and are similar in performance to re-wetting drops.

## **Key Words:**

In-eye cleaning/re-wetting drops, silicone hydrogel contact lenses, comfort, vision, cleanliness

## Acknowledgments

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## **Introduction**

Practitioners have long been concerned over the increased rate of ocular complications associated with hydrogel contact lenses worn on an extended or continuous wear basis. While problems such as corneal edema and neovascularization resulting from hypoxia have decreased with the advent of silicone hydrogel contact lenses, other findings, such as surface deposits, are still a concern<sup>1-8</sup>.

Surface deposits may lead to decreased wettability of the contact lenses, decreased comfort, decreased visual acuity, and may potentially result in triggering an inflammatory response such as papillary conjunctivitis<sup>2-3, 9-11, 13-14</sup>. These findings could limit wear time, necessitate replacement of contact lenses more frequently, and perhaps lead to drop out from contact lens wear altogether<sup>10</sup>.

In-eye cleaning/re-wetting drops have been shown to be beneficial in HEMA-based contact lenses leading to fewer surface deposits, increased wettability, and increased patient comfort. These products utilize surfactants to reduce protein binding which increases both comfort and wettability<sup>12,15</sup>. The purpose of this study was to determine if the use of an in-eye cleaning/re-wetting drop with continuous wear of silicone hydrogel contact lenses influences subjective performance and surface characteristics. The aims of the study were:

- (1) To determine if the use an in-eye cleaning/re-wetting drop offered better subjective comfort and visual performance in comparison to a simple re-wetting drop with continuous wear of the lenses;

(2) **To determine if there was a difference in the amount and type of surface deposits on the lenses when using an in-eye cleaning/re-wetting drop versus a re-wetting drop; and,**

(3) **To determine if there was a difference in surface wettability with the use of an in-eye cleaning/re-wetting drop versus a re-wetting drop with continuous wear of the lenses.**

## Methods

**The study** was a randomized **double-blind** cross-over design in **which subjects wore** silicone **hydrogel** contact **lenses** on a continuous wear basis during two phases. Subjects used in-eye **cleaning/re-wetting** drops and **re-wetting drops** for **one month** each. **The subjects were asked to** wear the lenses, on a continuous basis for up **to one month and** instill **each** masked-label drop three times a day.

The **subjects were evaluated** at the following **intervals**:

- Dispensing visit
- **Two weeks**
- One month

Second dispensing visit

**Two weeks**

- One month

**Subjects** were initially randomly **dispensed** either **in-eye cleaning/re-wetting drops** or **re-wetting drops**. **Prior** to dispense each subject completed a "wash-out" period of **either spectacle lens wear** or daily disposable soft contact **lens** wear for **three days**. **Subjects** were **advised** to not use any lens **care** or lens drops during **wash-out** periods. **At the end** of one month (**28 days +/- 3 days**), the **subjects once again underwent** a three day "wash-out" period to ensure **that experiences** from Phase I did not influence Phase II. Each, **were** then dispensed **a new pair** of lenses and crossed-over to the second lens **drop for** the second **month long** phase.

For each phase, subjects returned on the 28<sup>th</sup> day (+/- 3 days) at which time the lenses were removed and collected by the investigators. The lenses were sent to the CCLR in Waterloo, Ontario where they will be assessed for surface deposition. The individuals assessing lens surface deposition were also masked to the lens drops utilized with each lens.

## **Subject Eligibility Criteria**

### **Inclusion Criteria**

Prior to consideration for this clinical investigation, each prospective subject must have met the following conditions:

1. The subject must have no known ocular or systemic allergies which might interfere with contact lens wear.
2. The subject must have no known systemic disease, or need for medication, which might interfere with contact lens wear, i.e. antihistamines.
3. The subject must have normal eyes (no ocular medications or ocular infection of any type).
4. The subject must have a visual acuity best correctable to 20/20 with spectacles for each eye.
5. The subject must be spherically correctable to a distance visual acuity of 20/30 or better for each eye.
6. The subject must read and sign the Statement of Informed Consent and be provided with a copy of the form.

7. The subject must appear and be willing to adhere to the instructions set forth in this clinical protocol.
8. The subject, based on their knowledge, must NOT be pregnant or lactating at the time of enrollment.
9. The subject, based on their knowledge, must NOT have an infectious disease (e.g., hepatitis, tuberculosis) or an immunosuppressive disease (e.g., HIV).
10. The subject, based on their knowledge, must NOT be diabetic.
11. The subject must have a contact lens prescription between +6.00 D Sph and -10.00 D Sph.
12. The subject must be corrected to 20/30 or better in each eye with the study contact lenses and satisfied with the vision and comfort of each lens.
13. The subject must be an adapted wearer of silicone hydrogel contact lenses (minimum of two weeks of previous successful continuous wear prior to study enrollment).

In an effort to standardize the sample population of subjects for this investigation, it was essential that subjects be carefully screened for any atypical condition. Therefore, in addition to satisfying the above criteria, subjects must have had a complete ocular examination in the last 12 months to ensure that none of the contraindications described below applied before being considered eligible to participate in this study.

## **Exclusion Criteria**

No subject was entered into this study who was known to have or currently exhibit any of the following conditions:

1. Ocular or systemic allergies which might interfere with contact lens wear.
2. Systemic disease or use of medication which might interfere with contact lens wear.
3. Clinically significant (grade 3 or 4) corneal edema, corneal vascularization, corneal staining, bulbar hyperemia, tarsal hyperemia or any other abnormality of the cornea which might cause unsafe contact lens wear.
4. Any active ocular infection or ocular surface disease.
5. Any corneal distortion resulting from previous hard contact lens wear.
6. Pregnancy or lactation.

## **Informed Consent**

If the subject was deemed eligible, the investigators or monitor explained in detail the nature of the study and the subject's requirements for participation in the two-month study. Interested subjects were asked to read the Statement of Informed Consent Form and the principal investigators and/or the study monitor answered any and all questions. All participants were required to sign both copies of the Statement of Informed Consent Form and were provided a copy of the consent form.

## **Ocular Examination**

Candidates for this study were screened from the outpatient clinic at Pacific University College of Optometry in Forest Grove, Oregon. All candidates for the study were required to have undergone a complete, dilated ocular examination within the past 12 months. Subject eligibility was established at the Enrollment Visit Examination and a total of 30 subjects were selected. The subjects were required to meet all of the previously described inclusion criteria to be considered eligible for this study.

A modified ocular examination was performed at the Enrollment Visit. The examination included the following:

- detailed patient history
- slit lamp examination, including NaFl evaluation
- habitual silicone hydrogel contact lens fit evaluation with the slit-lamp  
habitual contact lens spherical over-refraction

## **Lens Dispensing**

Eligible subjects were dispensed a new pair of lenses in the most appropriate lens parameters based on the lens-fit evaluation and over-refraction.

## **Study Lens Parameters**

<b>Silicon Hydrogel Contact Lenses:</b>	Base Curves: 8.4 and 8.6 mm
	Powers: +6.00 D to -10.00 D.
	Diameter: 13.8 mm

Detailed **oral and written** instructions **were given** to each **subject describing the study requirements**.

Subjects were instructed to:

- **wear** the same pair of lenses throughout **the course** of each **study** phase
- return for regularly scheduled follow-up **visits**
- immediately report any abnormalities, e.g., **ocular complications, lost** or uncomfortable **lenses to** the investigators or monitors
- instill the lens drops three **times** a day in both **eyes**
- **refrain from** instilling **a lens drop** within **one hour before scheduled study** visits

### **Adverse Reactions and Discontinuations**

**Subjects were** instructed that if **they experienced** ocular **irritation** or disturbance of vision, they should contact the investigator or monitor on-call for the study. Three **subjects** did not complete all **phases**. **Two** subjects **dropped out in** the first **two** week session as they **were** not comfortable with the silicone hydrogel contact **lenses**. The third **contracted an upper respiratory infection** between **the first** and **second** month **phases**, and **was discontinued due** to this unrelated **illness**.

If for any reason a lens needed to be removed, subjects were instructed to **rinsed** it for a minimum of 10 seconds with saline and then **reinsert**.



## **Two-Week Follow-Up Visit**

For both Period 1 and **Period 2**, at the **two-week** and one-month **follow-up** visits the subjects completed subjective questionnaires **assessing**: comfort and **lens-awareness** symptoms with the initial lens **drops**.

**An investigator masked to the type of lens drops the subject was using** performed an examination that included **the** following:

- distance **visual acuity**
- near **visual** acuity
- slit-lamp examination including surface deposit **assessment** and **grading** of posterior **debris (number of mucin balls)**
- spherical over-refraction in phoropter if **indicated by** entrance **visual acuity**

## **Phase II, Lens Drop Crossover**

**At the completion of the one-month visit each** subject completed a three-day "**wash-out**" period as previously described and was dispensed a new pair of **Focus** Night and Day lenses. The subjects were once again given **detailed** oral and written **instructions** on the **wearing** of the contact lenses,

**Subjects** were instructed to:

- wear **the** same **pair** of **lenses** throughout **the** **course** of the month
- return **for regularly scheduled follow-up visit** one month **later**

- immediately report **any** abnormalities, e.g., ocular complications, **lost or** damaged lenses, to the investigators or monitor.
- instill the lens **drops three times a day** in both eyes

**Along** with **standard one-month assessments**, at the final visit subjects were then **asked to complete** an additional **overall lens drop preference survey**.

**Subject** participation in the **study** concluded **after** completion of the **two-month** visit.

## **Results**

### **Data Analysis**

#### **Statistical Method**

This study followed a 2x2 cross over design in which subjects were randomly assigned to in-eye cleaning/re-wetting drops (indicated in these analyses as “G”) or re-wetting drops (“W”). Due to the cross over design it was important to consider possible time and carry-over effects. A carry-over effect was not considered to be too great a concern due to the nature of the treatments, but was tested for nevertheless.

Time deserves careful consideration, as it is possible that ratings of comfort will be affected by adaptation to the lens wear.

Subjects were asked to rate comfort on a 100 point scale at each visit. They were asked to rate the comfort upon awakening, during the day, and in the evening before retiring. Higher scores indicate better comfort. We considered ratings of comfort obtained for three time-of-day categories: Upon awakening (AM), throughout the day (DAY) and in the late evening (EVE).

Analysis of comfort data was performed using NCSS Statistical Software (329 North 1000 East . Kaysville, Utah, 84037). The data were entered into three variables. The first variable contains the sequence number. For these analyses sequence “1” was used for subjects having the " G drops in the first phase (order is GW) and the " W in the second. “2” was used to indicate those using the " W drops in the first phase (order WG). The second variable contains the response in the first phase, and the third variable contains

the response in the second phase. Thus, each row of data represented the complete response for a single subject.

Cross over design analysis is designed to test primarily for equivalence. If equivalence is rejected, we can test further for relative superiority or inferiority.

We have chosen for analysis the responses at the end of each phase as it was felt these would best reflect the efficacy of the tested articles.

### AM Comfort

#### Cross-Over Analysis Summary Section: AM Comfort

Parameter	Estimated Effect	Standard Error	T Value (DF=24)	Prob Level	Lower 95.0% Upper 95.0% Confidence	
					Limit	Limit
Treatment	-2.43	4.09	-0.59	0.5587	-10.88	6.02
Period	12.02	4.09	2.93	0.0072	3.57	20.47
Carryover	4.44	18.48	0.24	0.8123	-33.70	42.58

#### Interpretation of the Above Report

The two treatment means in this 2x2 cross-over study are not significantly different at the 0.0500 significance level (the actual significance level was 0.5587). The average response to treatment G was 54.88 and the average response to treatment W was 52.45.

A preliminary test rejected the assumption of equal period effects at the 0.0500 significance level (the actual significance level was 0.0072). A preliminary test failed to reject the assumption of equal carryover effects at the 0.0500 significance level (the actual significance level was 0.8123).

**Cross-Over Analysis Detail Section: AM Comfort**

Seq.	Period	Treatment	Count	Least Squares	Standard	Standard
				Mean	Deviation	Error
1	1	G	17	47.76	27.42	6.65
2	2	G	9	62.00	19.07	6.36
1	2	W	17	57.35	27.20	6.60
2	1	W	9	47.56	16.12	5.37
1	Difference	(W-G)/2	17	4.79	8.82	2.14
2	Difference	(W-G)/2	9	7.22	11.85	3.95
1	Total	G+W	17	105.12	51.69	12.54
2	Total	G+W	9	109.56	26.16	8.72
		G	26	54.88		5.14
		W	26	52.45		4.96
1			34	52.56		
2			18	54.78		
	1		26	47.66		5.00
	2		26	59.68		5.11

**Interpretation of the Above Report**

This report shows the means and standard deviations of various subgroups of the data. The least squares mean of treatment G is 54.88 and of treatment W is 52.45. Note that least squares means are created by taking the simple average of their component means, not by taking the average of the raw data. No adjustment is made for the unequal sample sizes.

**Equivalence Based on the Confidence Interval of the Difference: AM Comfort**

	Lower	Lower 90.0%	Upper 90.0%	Upper	Equivalent
	Equivalence	Confidence	Confidence	Equivalence	at the 5.0%
Test Type	Limit	Limit	Limit	Limit	Sign. Level?
Shortest C.I.	-10.98	-9.43	4.58	10.98	Yes
Westlake C.I.	-10.98	-8.05	8.05	10.98	Yes

Note: Westlake's  $k_2 = -1.37$  and  $k_1 = 2.56$ .

**Interpretation of the Above Report**

Average bioequivalence of the two treatments has been found at the 0.0500 significance level using the shortest confidence interval of the difference approach since both confidence limits, -9.43 and 4.58, are between the acceptance limits of -10.98 and 10.98.

Average bioequivalence of the two treatments has been found at the 0.0500 significance level using Westlake's confidence interval of the difference approach since both confidence limits, -8.05 and 8.05, are between the acceptance limits of -10.98 and 10.98.

### **Equivalence Based on the Confidence Interval of the Ratio: AM Comfort**

	<b>Lower</b>	<b>Lower 90.0%</b>	<b>Upper 90.0%</b>	<b>Upper</b>	<b>Equivalent</b>
	<b>Equivalence</b>	<b>Confidence</b>	<b>Confidence</b>	<b>Equivalence</b>	<b>at the 5.0%</b>
<b>Test Type</b>	<b>Limit</b>	<b>Limit</b>	<b>Limit</b>	<b>Limit</b>	<b>Sign. Level?</b>
Shortest C.I.	80.00	82.81	108.34	120.00	Yes
Westlake C.I.	80.00	85.34	114.66	120.00	Yes
Fieller's C.I.	80.00	83.03	109.74	120.00	Yes

### **Interpretation of the Above Report**

Average bioequivalence of the two treatments has been found at the 0.0500 significance level using the shortest confidence interval of the ratio approach since both confidence limits, 82.81 and 108.34, are between the acceptance limits of 80.00 and 120.00.

Average bioequivalence of the two treatments has been found at the 0.0500 significance level using Westlake's confidence interval of the ratio approach since both confidence limits, 85.34 and 114.66, are between the acceptance limits of 80.00 and 120.00.

Average bioequivalence of the two treatments has been found at the 0.0500 significance level using Fieller's confidence interval of the ratio approach since both confidence limits, 83.03 and 109.74, are between the acceptance limits of 80.00 and 120.00.

Equivalence Based on Schuirmann's Two One-Sided Hypothesis Tests: AM Comfort

	Lower	Upper	5.0%		
	Test	Test	Cutoff		Equivalent
Test Type	T Value	T Value	T Value	DF	Sign. Level?
Schuirmann's 2 1-Sided Tests	2.09	-3.27	1.71	24	Yes

Interpretation of the Above Report

Average bioequivalence of the two treatments was found at the 0.0500 significance level using Schuirmann's two one-sided t-tests procedure. The probability level of the t-test of whether the treatment mean is not too much lower than the reference mean is 0.0238. The probability level of the t-test of whether the treatment mean is not too much higher than the reference mean is 0.0016. Since both of these values are less than 0.0500, the null hypothesis of average bioequivalence was rejected in favor of the alternative hypothesis of average bioequivalence.

Equivalence Based on Two One-Sided Wilcoxon-Mann-Whitney Tests: AM Comfort

	Lower	Lower	Upper	Upper	Equivalent
	Sum	Prob	Sum	Prob	at the 5.0%
Test Type	Ranks	Level	Ranks	Level	Sign. Level?
2 1-Sided MW Tests	265.00	0.0295	177.00	0.0025	No

Interpretation of the Above Report

Average bioequivalence of the two treatments was not established at the 0.0500 significance level using the nonparametric version of Schuirmann's two one-sided tests procedure which is



based on the Wilcoxon-Mann-Whitney test. The probability level of the test of whether the treatment mean is not too much lower than the reference mean is 0.0295. The probability level of the test of whether the treatment mean is not too much higher than the reference mean is 0.0025. Since at least one of these values is greater than 0.0500, the null hypothesis of average bioequivalence was not rejected.

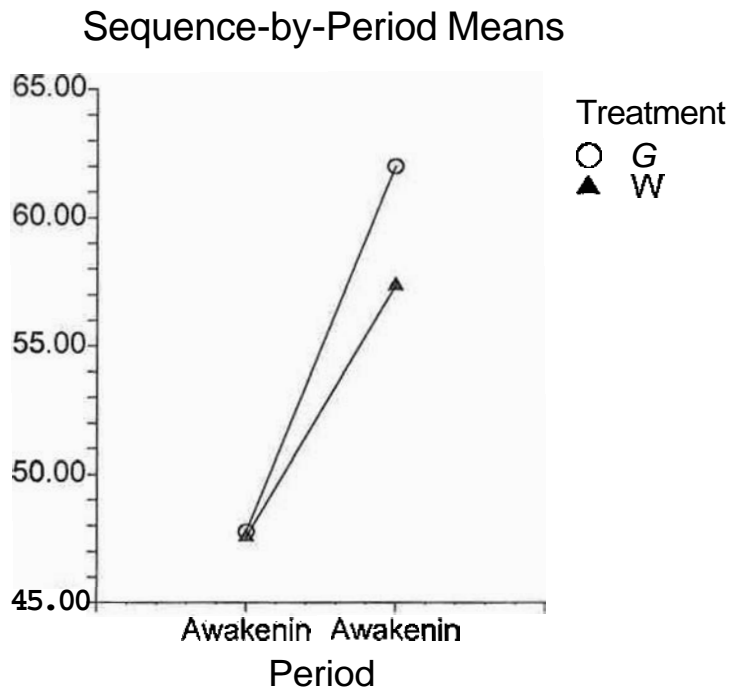
**Equivalence Based on Anderson and Hauck's Hypothesis Test: AM Comfort**

Test Type	Pr(-TL)	Pr(TU)	Equivalent	
			Prob Level	at the 5.0% Sign. Level?
Anderson and Hauck's Test	0.0238	0.0016	0.0222	Yes

**Interpretation of the Above Report**

Average bioequivalence of the two treatments was found at the 0.0500 significance level using Anderson and Hauck's test procedure. The actual probability level of the test was 0.0222.

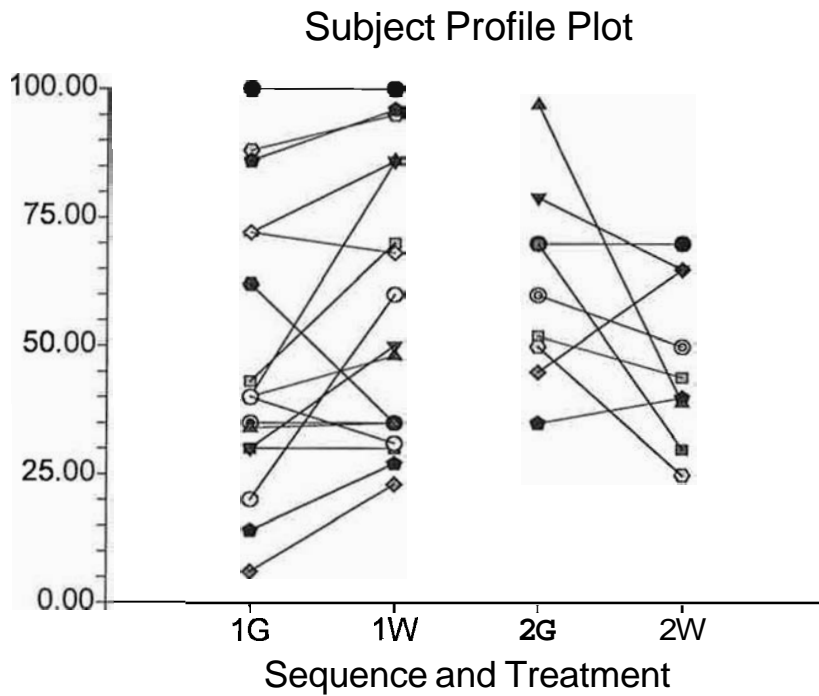
## Plot of Sequence-by-Period Means: AM Comfort



### Interpretation of the Sequence-by-Period Means

The sequence-by-period means plot shows the mean responses on the vertical axis and the periods on the horizontal axis. The lines connect like treatments. If there is no period, carryover, or interaction effects, two horizontal lines would be displayed. The distance between these lines represents the magnitude of the treatment effect. The tendency for both lines to slope up represents period and carryover effects. The fact that the lines do not cross represents absence of period-by-treatment interaction, a type of carryover effect.

## Plot of Subject Profiles: AM Comfort

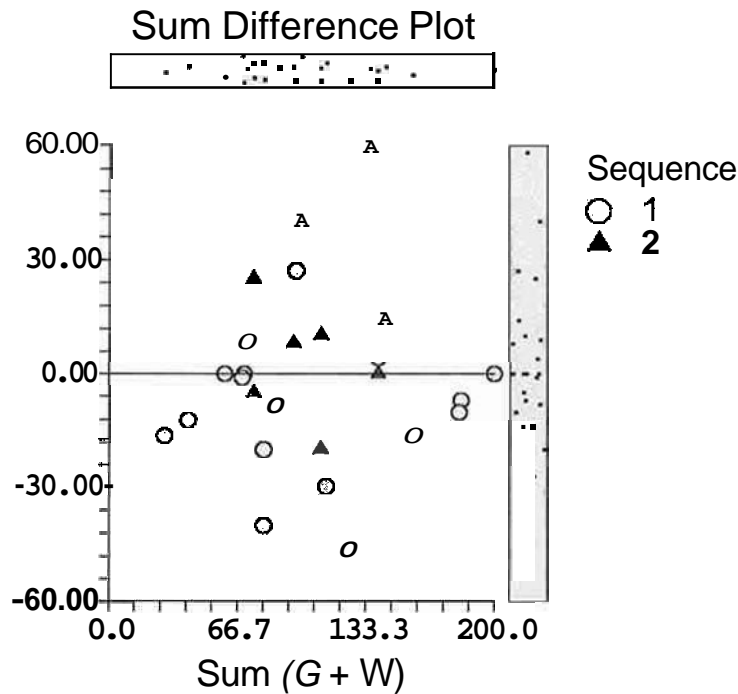


### Interpretation of the Profile Plot

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The profile plot displays the raw data for each subject. The response variable is shown along the vertical axis. The two sequences are shown along the horizontal axis. The data for each subject is depicted by two points connected by a line. The subject's response to the reference formulation is shown first followed by their response to the treatment formulation. Hence, for sequence 2, the results for the first period are shown on the right and for the second period on the left.

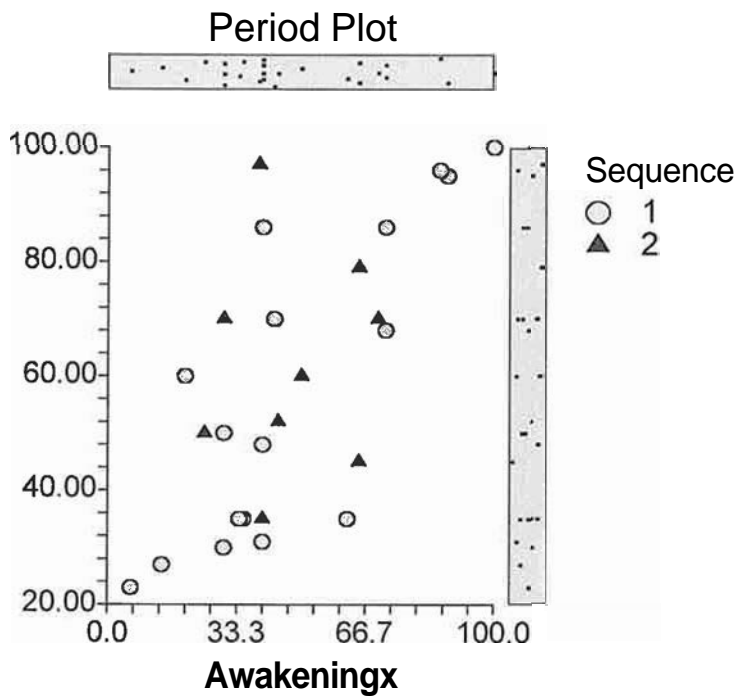
## Plot of Sums and Differences: AM Comfort



### Interpretation of the Sums and Differences Plot

The sums and differences plot shows the sum of each subject's two responses on the horizontal axis and the difference between each subject's two responses on the vertical axis. Dot plots of the sums and differences have been added above and to the right of the scatter plot, respectively. Each point represents the sum and difference of a single subject. Different plotting symbols are used to denote the subject's sequence. A horizontal line has been added at zero to provide an easy reference from which to determine if a difference is positive (favors treatment G) or negative (favors treatment W). The degree to which the plotting symbols tend to separate along the horizontal axis represents the size of the carryover effect. The degree to which the plotting symbols tend to separate along the vertical axis represents the size of the treatment effect.

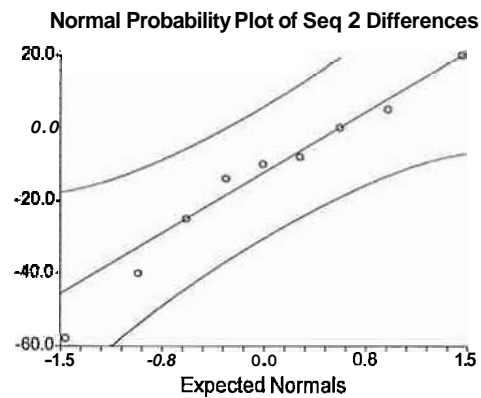
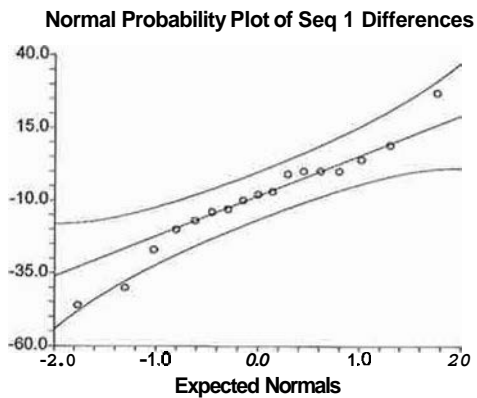
## Period Plot: AM Comfort



## Interpretation of the Period Plot

The Period Plot displays a subject's period 1 response on the horizontal axis and their period 2 response on the vertical axis. The plotting symbol is the sequence number.

## Probability Plots: AM Comfort



### Interpretation of the Probability Plots

These plots show the differences (P1-P2) on the vertical axis and values on the horizontal axis that would be expected if the differences were normally distributed. The first plot shows the differences for sequence 1 and the second plot shows the differences for sequence 2. The assumption of normality holds, as the points fall close to a straight line.

### DAY Comfort

#### Cross-Over Analysis Summary Section: DAY Comfort

					Lower 95.0% Confidence	Upper 95.0% Confidence
Parameter	Estimated Effect	Standard Error	T Value (DF=24)	Prob Level	Limit	Limit
Treatment	0.99	2.49	0.40	0.6944	-4.15	6.13
Period	7.66	2.49	3.07	0.0052	2.52	12.80
Carryover	-9.39	12.85	-0.73	0.4719	-35.91	17.13

### Interpretation of the Above Report

The two treatment means in a 2x2 cross-over study are not significantly different at the 0.0500 significance level (the actual significance level was 0.6944). The design had 17 subjects in sequence 1 (GW) and 9 subjects in sequence 2 (WG). The average response to treatment G was 71.19 and the average response to treatment W was 72.18.

A preliminary test rejected the assumption of equal period effects at the 0.0500 significance level (the actual significance level was 0.0052). A preliminary test failed to reject the assumption of

equal carryover effects at the 0.0500 significance level (the actual **significance level** was 0.4719).

**Cross-Over Analysis Detail Section: DAY Comfort**

Seq.	Period	Treatment	Count	Least Squares	Standard	Standard
				Mean	Deviation	Error
1	1	G	17	69.71	17.54	4.25
	2	G	9	72.67	17.28	5.76
	2	W	17	78.35	14.82	3.60
	1	W	9	66.00	17.98	5.99
	Difference	(W-G)/2	17	4.32	6.15	1.49
	Difference	(W-G)/2	9	3.33	5.81	1.94
	<b>Total</b>	<b>G+W</b>	<b>17</b>	<b>148.06</b>	<b>30.05</b>	<b>7.29</b>
	<b>Total</b>	<b>G+W</b>	<b>9</b>	<b>138.47</b>	<b>33.30</b>	<b>11.10</b>
		<b>G</b>	<b>26</b>	<b>71.19</b>		<b>3.60</b>
		<b>W</b>	<b>26</b>	<b>72.18</b>		<b>3.29</b>
			34	74.03		
			18	69.33		
	1		26	67.85		3.65
	2		26	75.51		3.23

**Interpretation of the Above Report**

This report shows the means and standard deviations of various subgroups of the data. The least squares mean of treatment G is 71.19 and of treatment W is 72.18. Note that least squares means are created by taking the simple average of their component means, not by taking the average of

the raw data.

**Equivalence Based on the Confidence Interval of the Difference: DAY Comfort**

	<b>Lower</b>	<b>Lower 90.0%</b>	<b>Upper 90.0%</b>	<b>Upper</b>	<b>Equivalent</b>
	<b>Equivalence</b>	<b>Confidence</b>	<b>Confidence</b>	<b>Equivalence</b>	<b>at the 5.0%</b>
<b>Test Type</b>	<b>Limit</b>	<b>Limit</b>	<b>Limit</b>	<b>Limit</b>	<b>Sign. Level?</b>
Shortest C.I.	-14.24	-3.27	5.25	14.24	Yes
Westlake C.I.	-14.24	-4.56	4.56	14.24	Yes

Note: Westlake's  $k_2 = -2.23$  and  $k_1 = 1.43$ .

**Interpretation of the Above Report**

Average bioequivalence of the two treatments has been found at the 0,0500 significance level using the shortest confidence interval of the difference approach since both confidence limits, -3.27 and 5.25, are between the acceptance limits of -14.24 and 14.24.

Average bioequivalence of the two treatments has been found at the 0.0500 significance level using Westlake's confidence interval of the difference approach since both confidence limits, -4.56 and 4.56, are between the acceptance limits of -14.24 and 14.24.



### **Equivalence Based on the Confidence Interval of the Ratio: DAY Comfort**

<b>Test Type</b>	<b>Lower Equivalence Limit</b>	<b>Lower 90.0% Confidence Limit</b>	<b>Upper 90.0% Confidence Limit</b>	<b>Upper Equivalence Limit</b>	<b>Equivalent at the 5.0% Sign. Level?</b>
Shortest C.I.	80.00	95.41	107.38	120.00	Yes
Westlake C.I.	80.00	93.59	106.41	120.00	Yes
Fieller's C.I.	80.00	94.62	108.67	120.00	Yes

### **Interpretation of the Above Report**

Average bioequivalence of the two treatments has been found at the 0.0500 significance level using the shortest confidence interval of the ratio approach since both confidence limits, 95.41 and 107.38, are between the acceptance limits of 80.00 and 120.00.

Average bioequivalence of the two treatments has been found at the 0.0500 significance level using Westlake's confidence interval of the ratio approach since both confidence limits, 93.59 and 106.41, are between the acceptance limits of 80.00 and 120.00.

Average bioequivalence of the two treatments has been found at the 0.0500 significance level using Fieller's confidence interval of the ratio approach since both confidence limits, 94.62 and 108.67, are between the acceptance limits of 80.00 and 120.00.

Equivalence Based on Schuirmann's Two One-Sided Hypothesis Tests: DAY Comfort

	Lower	Upper	5.0%		Equivalent
	Test	Test	Cutoff		at the 5.0%
Test Type	T Value	T Value	T Value	DF	Sign. Level?
Schuirmann's 2 1-Sided Tests	6.11	-5.32	1.71	24	Yes

Interpretation of the Above Report

Average bioequivalence of the two treatments was found at the 0.0500 significance level using Schuirmann's two one-sided t-tests procedure. The probability level of the t-test of whether the treatment mean is not too much lower than the reference mean is 0.0000. The probability level of the t-test of whether the treatment mean is not too much higher than the reference mean is 0.0000. Since both of these values are less than 0.0500, the null hypothesis of average bioequivalence was rejected in favor of the alternative hypothesis of average bioequivalence.

Equivalence Based on Two One-Sided Wilcoxon-Mann-Whitney Tests: DAY Comfort

	Lower	Lower	Upper	Upper	Equivalent
	Sum	Prob	Sum	Prob	at the 5.0%
Test Type	Ranks	Level	Ranks	Level	Sign. Level?
2 1-Sided MW Tests	302.00	0.0001	163.00	0.0002	Yes

Interpretation of the Above Report

Average bioequivalence of the two treatments was found at the 0.0500 significance level using the nonparametric version of Schuirmann's two one-sided tests procedure which is based on the

Wilcoxon-Mann-Whitney test. The probability level of the test of whether the treatment mean is *not too much* lower than the reference mean is 0.0001. The probability level of the test of whether the treatment mean is *not too much higher* than the reference mean is 0.0002. Since both of these values are less than 0.0500, the null hypothesis of average bioequivalence was rejected in favor of the alternative hypothesis of average bioequivalence.

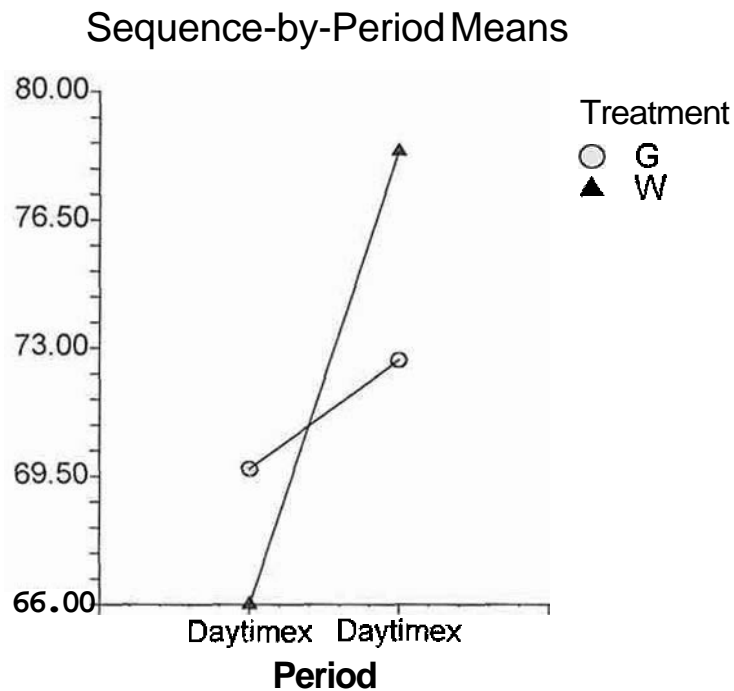
**Equivalence Based on Anderson and Hauck's Hypothesis Test: DAY Comfort**

Test Type	Pr(-TL)	Pr(TU)	Equivalent	
			Prob Level	at the 5.0% Sign. Level?
Anderson and Hauck's Test	0.0000	0.0000	0.0000	Yes

**Interpretation of the Above Report**

Average bioequivalence of the two treatments was found at the 0.0500 significance level using Anderson and Hauck's test procedure. The actual probability level of the test was 0.0000.

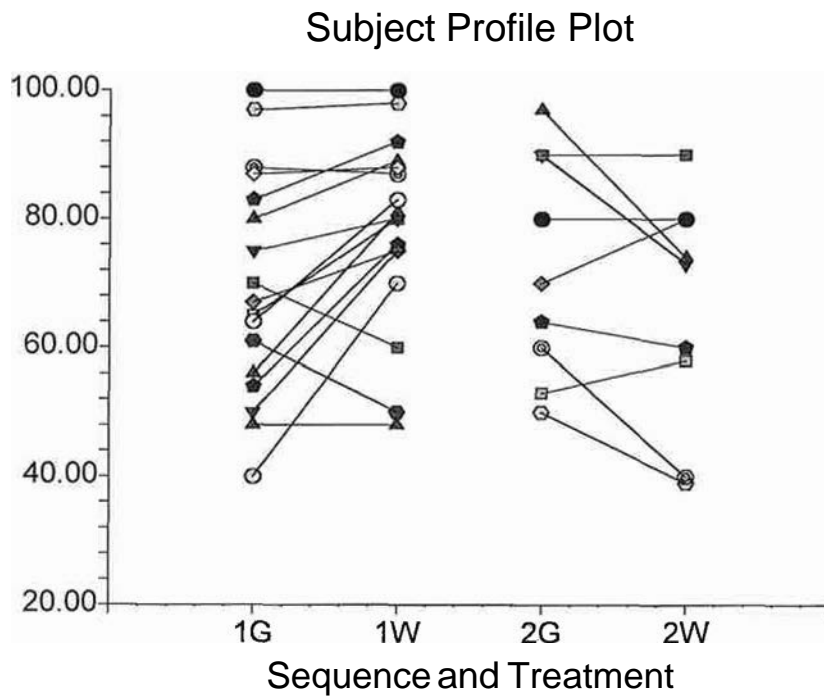
## Plot of Sequence-by-Period Means: DAY Comfort



### Interpretation of the Sequence-by-Period Means

The **sequence-by-period means plot** shows the **mean** responses on the **vertical axis** and the **periods** on the **horizontal axis**. The lines connect **like treatments**. If there **is no period, carryover,** or interaction effects, two horizontal lines **would be displayed**. The **distance** between these lines represents the **magnitude** of the **treatment** effect. The **fact** that both lines **slope up** represents **likely period** or **carryover** effects. The **fact** that the **lines cross** suggests **period-by-treatment** interaction, a type **of carryover** effect.

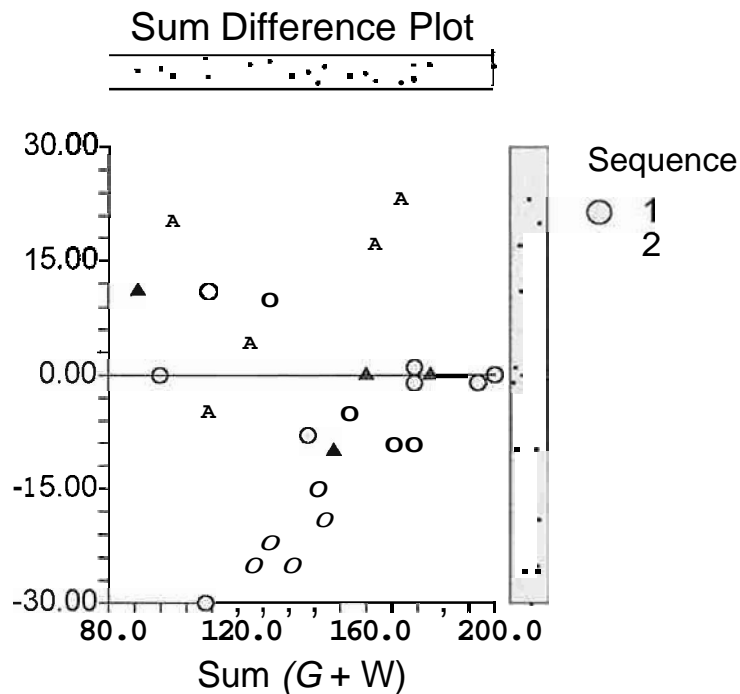
## Plot of Subject Profiles: DAY Comfort



### Interpretation of the Profile Plot

The **profile** plot displays the **saw** data for each subject. The **response variable** is shown **along the vertical axis**. The **two sequences** are **shown along the horizontal axis**. The data for each subject is **depicted by two points connected by a line**, The subject's response to the reference formulation is **shown first followed by their response to the treatment formulation**. Hence, for sequence 2, the results for the first period are shown on the right and for the second period on the left.

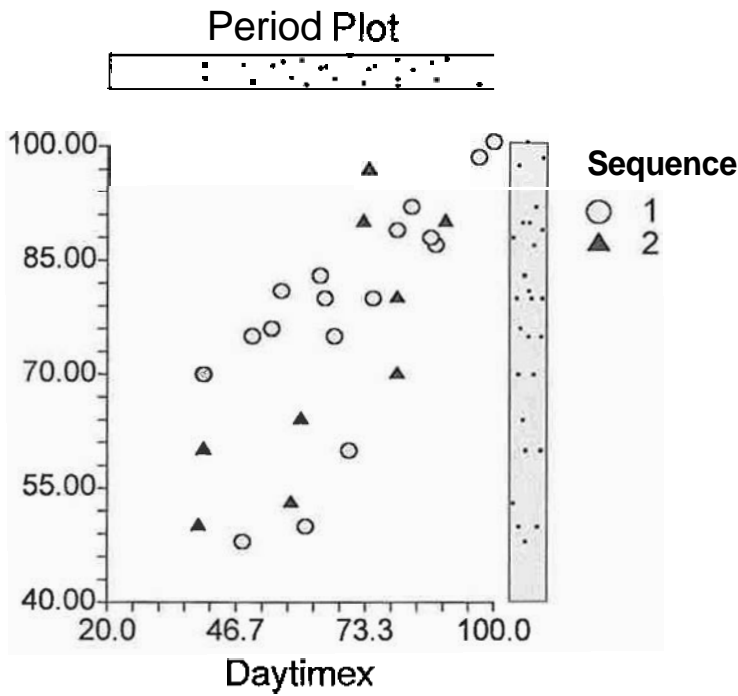
## Plot of Sums and Differences: DAY Comfort



### Interpretation of the Sums and Differences Plot

The sums and differences plot shows the sum of each subject's two responses on the horizontal axis and the difference between each subject's two responses on the vertical axis. Dot plots of the sums and differences have been added above and to the right of the scatter plot, respectively. Each point represents the sum and difference of a single subject. Different plotting symbols are used to denote the subject's sequence. A horizontal line has been added at zero to provide an easy reference from which to determine if a difference is positive (favors treatment G) or negative (favors treatment W). The degree to which the plotting symbols tend to separate along the horizontal axis represents the size of the carryover effect. The degree to which the plotting symbols tend to separate along the vertical axis represents the size of the treatment effect.

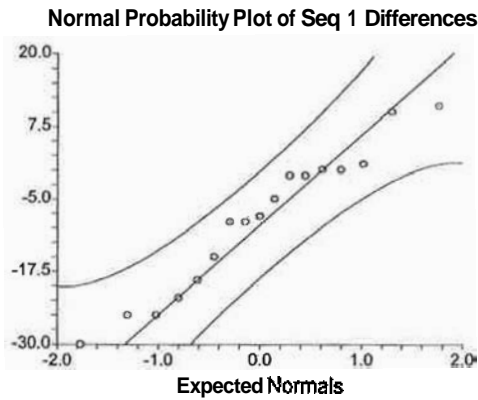
### Period Plot: DAY Comfort

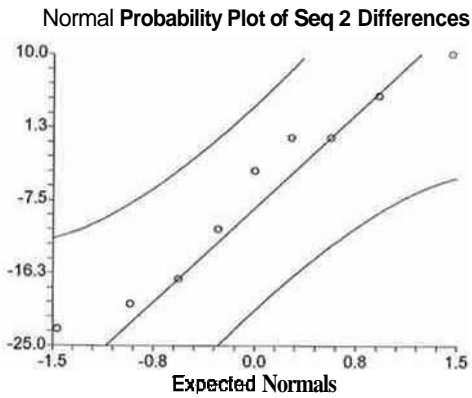


### Interpretation of the Period Plot

The Period Plot displays a subject's period 1 response on the horizontal axis and their period 2 response on the vertical axis. The plotting symbol is the sequence number.

### Probability Plots: DAY Comfort





### Interpretation of the Probability Plots

These plots show **the differences (P1-P2) on the vertical axis** and values **on the horizontal axis that would be expected if the differences were normally distributed**. **The first plot shows the differences for sequence I and the second plot shows the differences for sequence 2**. The **assumption of normality holds, as the points fall close to a straight line**.

### EVE Comfort

#### Cross-Over Analysis Summary Section: EVE Comfort

	Estimated	Standard	T Value	Prob	Lower 95.0% Confidence	Upper 95.0% Confidence
Parameter	Effect	Error (DF=24)		Level	Limit	Limit
Treatment	4.83	3.23	1.50	0.1477	-1.83	11.49
Period	3.94	3.23	1.22	0.2342	-2.72	10.60
Carryover	-17.03	15.61	-1.09	0.2861	-49.23	15.18



### **Interpretation of the Above Report**

The **two treatment means** in a **2x2** cross-over study are not **significantly** different at **the 0.0500** significance level (the **actual** significance level was **0.1477**). The treatment **order** designated sequence 1 (GW) and 9 subjects in sequence 2 (WG). The **average response** to treatment G was 60.07 and the **average response** to treatment W was **64.89**.

**A preliminary** test **failed to reject** the assumption of equal period effects at the **0.0500** significance level (the actual significance level was 0.2342). **A preliminary test** failed to **reject** the assumption of **equal** carryover effects at the **0.0500** significance level (the actual significance level was 0.2861).

### Cross-Over Analysis Detail Section: EVE Comfort

Seq.	Period	Treatment	Count	Least Squares Mean	Standard Deviation	Standard Error
1		G	17	62.35	22.12	5.36
2		G	9	57.78	24.32	8.11
2		W	17	71.12	18.31	4.44
1		W	9	58.67	16.64	5.55
	Difference	(W-G)/2	17	4.38	9.01	2.19
	Difference	(W-G)/2	9	-0.44	4.63	1.54
	Total	G+W	17	133.47	36.39	8.82
	Total	G+W	9	116.44	40.64	13.55
		G	26	60.07		4.71
		W	26	64.89		3.66
			34	66.74		
			18	58.22		
1			26	60.51		4.22
2			26	64.45		4.23

### Interpretation of the Above Report

This report shows the means and standard deviations of various subgroups of the data. The least squares mean of treatment G is 60.07 and of treatment W is 64.89. Note that least squares means are created by taking the simple average of their component means, not by taking the average of the raw data. No adjustment is made for the unequal sample sizes.

## Equivalence Based on the Confidence Interval of the Difference: EVE Comfort

Test Type	Lower Equivalence Limit	Lower 90.0% Confidence Limit	Upper 90.0% Confidence Limit	Upper Equivalence Limit	Equivalent at the 5.0% Sign. Level?
Shortest C.I.	-12.01	-0.69	10.35	12.01	Yes
Westlake C.I.	-12.01	-9.08	9.08	12.01	Yes

Note: Westlake's  $k_2 = -4.31$  and  $k_1 = 1.32$ .

### Interpretation of the Above Report

Average bioequivalence of the **two** treatments has been found at the **0.0500** significance level using **the shortest** confidence interval of **the difference approach** since **both confidence limits**, -0.69 and 10.35, are between **the acceptance** limits of -12.01 and 12.01.

Average bioequivalence of the **two** treatments has been found at the **0.0500** significance level using **Westlake's** confidence interval of **the difference approach** since both confidence limits, -9.08 and 9.08, are between **the acceptance** limits of -12.01 and 12.01.

### **Equivalence Based on the Confidence Interval of the Ratio: EVE Comfort**

<b>Test Type</b>	<b>Lower Equivalence Limit</b>	<b>Lower 90.0% Confidence Limit</b>	<b>Upper 90.0% Confidence Limit</b>	<b>Upper Equivalence Limit</b>	<b>Equivalent at the 5.0% Sign. Level?</b>
Shortest C.I.	80.00	98.84	117.23	120.00	Yes
Westlake C.I.	80.00	84.88	115.12	120.00	Yes
Fieller's C.I.	80.00	95.80	122.16	120.00	No

### **Interpretation of the Above Report**

Average bioequivalence of the two treatments has been found at the 0.0500 significance level using the shortest confidence interval of the ratio approach since both confidence limits, 98.84 and 117.23, are between the acceptance limits of 80.00 and 120.00.

Average bioequivalence of the two treatments has been found at the 0.0500 significance level using Westlake's confidence interval of the ratio approach since both confidence limits, 84.88 and 115.12, are between the acceptance limits of 80.00 and 120.00.

Average bioequivalence of the two treatments has not been established at the 0.0500 significance level using Fieller's confidence interval of the ratio approach since both confidence limits, 95.80 and 122.16, are not between the acceptance limits of 80.00 and 120.00.

### Equivalence Based on Schuirmann's Two One-Sided Hypothesis Tests

	Lower	Upper	5.0%		Equivalent
	Test	Test	Cutoff		at the 5.0%
Test Type	T Value	T Value	T Value	DF	Sign. Level?
Schuirmann's 2 1-Sided Tests	5.22	-2.23	1.71	24	Yes

### Interpretation of the Above Report

Average bioequivalence of the two treatments was found at the 0.0500 significance level using Schuirmann's two one-sided t-tests procedure. The probability level of the t-test of whether the treatment mean is not too much lower than the reference mean is 0.0000. The probability level of the t-test of whether the treatment mean is not too much higher than the reference mean is 0.0178. Since both of these values are less than 0.0500, the null hypothesis of average bioequivalence was rejected in favor of the alternative hypothesis of average bioequivalence.

### Equivalence Based on Two One-Sided Wilcoxon-Mann-Whitney Tests: EVE Comfort

	Lower	Lower	Upper	Upper	Equivalent
	Sum	Prob	Sum	Prob	at the 5.0%
Test Type	Ranks	Level	Ranks	Level	Sign. Level?
2 1-Sided MW Tests	303.00	0.0000	192.00	0.0230	Yes

### Interpretation of the Above Report

Average bioequivalence of the two treatments was found at the 0.0500 significance level using the nonparametric version of Schuirmann's two one-sided tests procedure which is based on the

Wilcoxon-Mann-Whitney test. The probability level of the **test** of whether **the** treatment mean is **not too much lower** than **the reference mean** is 0.0000. The probability level of the test of **whether** the treatment mean **is** not too much higher **than** the **reference** mean is 0.0230. Since both of these **values are less than 0.0500**, the **null hypothesis** of **average bioinequivalence was** rejected in **favor** of the alternative hypothesis of **average bioequivalence**.

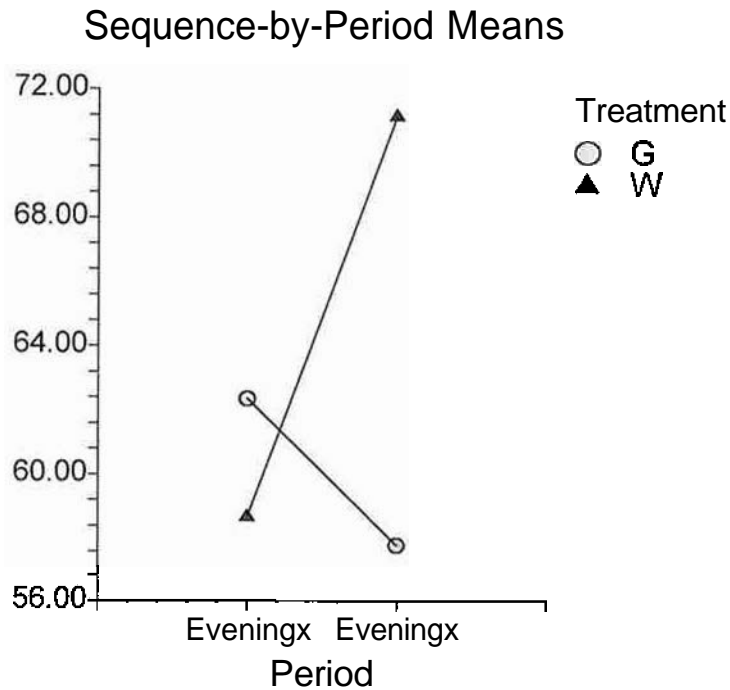
### **Equivalence Based on Anderson and Hauck's Hypothesis Test**

<b>Test Type</b>	<b>Pr(-TL)</b>	<b>Pr(TU)</b>	<b>Equivalent</b>	
			<b>Prob Level</b>	<b>at the 5.0% Sign. Level?</b>
Anderson and Hauck's Test	0.0000	0.0178	<b>0.0178</b>	Yes

### **Interpretation of the Above Report**

**Average bioequivalence of the two** treatments **was found at the 0.0500 significance level using Anderson and Hauck's test procedure**. The actual probability level of **the test was 0.0178**.

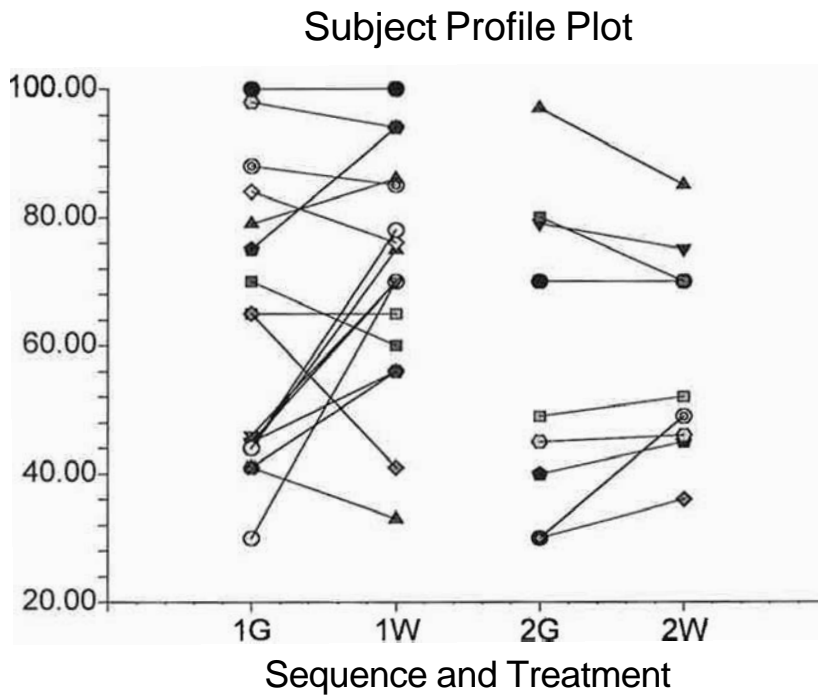
## Plot of Sequence-by-Period Means



### Interpretation of the Sequence-by-Period Means

The **sequence-by-period means** plot shows the mean responses on the **vertical axis** and the **periods** on the **horizontal axis**. The lines connect **like treatments**. **If there is no period, carryover, or interaction effects, two horizontal lines would be displayed.** The distance between these lines represents **the magnitude** of the treatment effect. The **fact that both lines slope up** represents **likely period or carryover effects**. The **fact that the lines cross** suggests **period-by-treatment interaction, a type of carryover effect**.

## Plot of Subject Profiles: EVE Comfort

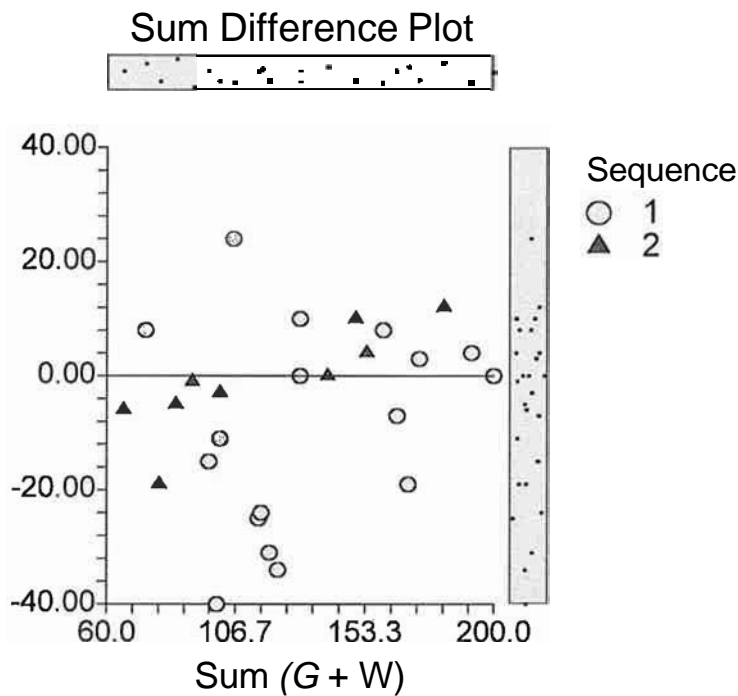


### Interpretation of the Profile Plot

**The profile plot displays the raw data for each subject. The response variable is shown along the vertical axis. The two sequences are shown along the horizontal axis. The data for each subject is depicted by two points connected by a line. The subject's response to the reference formulation is shown first followed by their response to the treatment formulation. Hence, for sequence 2, the results for the first period are shown on the right and for the second period on the left.**



## Plot of Sums and Differences: EVE Comfort

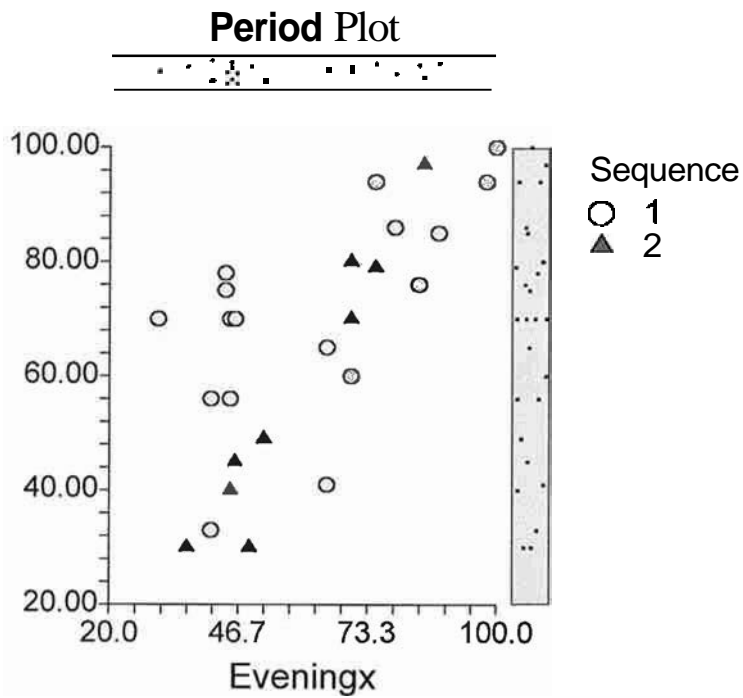


### Interpretation of the Sums and Differences Plot

The sums and differences plot shows the sum of each subject's two responses on the horizontal axis and the difference between each subject's two responses on the vertical axis. Dot plots of the sums and differences have been added above and to the right of the scatter plot, respectively.

Each point represents the sum and difference of a single subject. Different plotting symbols are used to denote the subject's sequence. A horizontal line has been added at zero to provide an easy reference from which to determine if a difference is positive (favors treatment G) or negative (favors treatment W). The degree to which the plotting symbols tend to separate along the horizontal axis represents the size of the carryover effect. The degree to which the plotting symbols tend to separate along the vertical axis represents the size of the treatment effect.

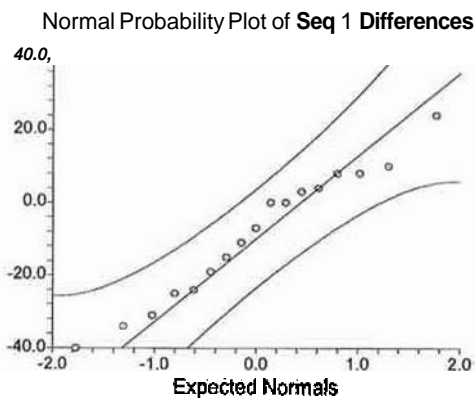
## Period Plot: EVE Comfort

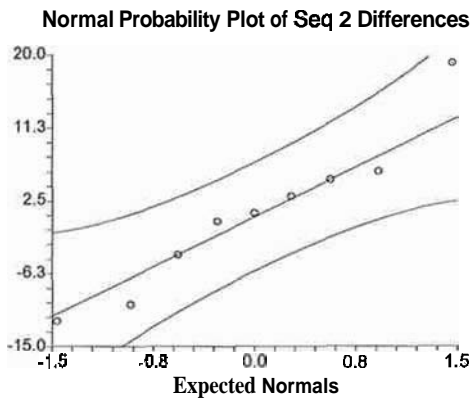


## Interpretation of the Period Plot

The Period Plot displays a subject's period 1 response on the horizontal axis and their period 2 response on the vertical axis. The plotting symbol is the sequence number.

## Probability Plots: EVE Comfort





### Interpretation of the Probability Plots

These **plots** show the differences (P1-P2) on the **vertical axis** and **values** on the horizontal **axis** that would be **expected** if the **differences were normally distributed**. The first plot **shows** the differences **for** sequence 1 and **the second plot shows** the differences for sequence 2. The assumption of normality holds, **as the points fall** close to a **straight** line.

### Subjects

Twenty **seven** subjects **completed** both **phases of the** study. **Two subjects were** discontinued secondary to **lens** awareness or **discomfort with the** study contact lenses and one subject lost a **lens** from the **eye** during **sleep** and **was** also suffering from an **upper respiratory** infection. **Data was considered** only **from** the subjects **completing all** phases.

**Subject age ranged** from 21-52 years and refractive **error ranged** from +3.00 D to -6.00 D.

Ten males and 20 females **participated in** the study.

## **Habitual Lens Drops**

Prior to study enrollment 7 subjects habitually used lens drops.

## **Objective Findings**

### **Biomicroscope Examination and Adverse Events**

A biomicroscope examination was performed at each visit using a 0-4 scale for each observation. A copy of the examination form is attached. None of the biomicroscopy scores showed a difference between the two types of drops at any point or in either phase.

No adverse responses occurred during the study.

### **Visual Acuity**

No statistical or clinical difference in visual acuity between lens drops was observed at any point.

### **On-Eye Surface Deposition and Wetting**

No clinical or statistical difference could be detected in the grading of front surface wetting, front surface deposits, posterior lens debris or number of mucin balls.

Lenses were collected at the completion of each four week interval and have been sent to the CCLR at the University of Waterloo for laboratory analysis.

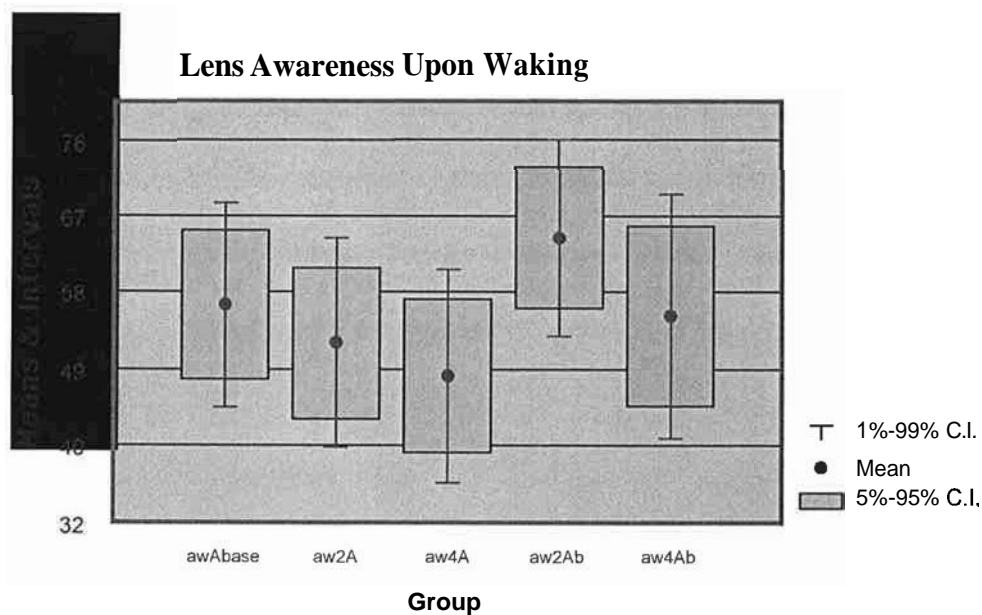
### **Comfort and Awareness: Evidence of Adaptation, Change with time**

**Comfort and awareness scores were very similar and thus we chose to analyse the comfort scores in the previous section on subjective responses. We noted an apparent effect of adaptation, such that subjects tended to be more comfortable in the second phase, regardless of drop sequence. To illustrate this, an analysis is presented using the Lens Awareness data, combining all subjects in each phase regardless of drops used in that phase.**

### **Lens Awareness**

**Lens awareness was rated for awakening, daytime and evening at each interval. At no point was there a difference in awareness scores for the two drops. As with comfort ratings, there were changes noted with time.**

## Lens Awareness Upon Awakening.

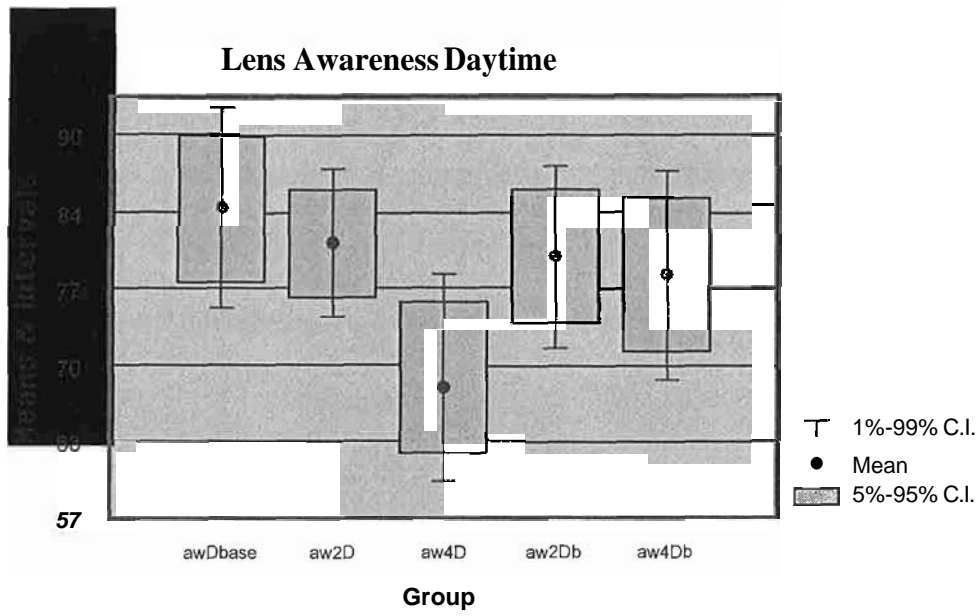


Lens awareness upon awakening, change with time

Lens awareness upon awakening was significantly better in the second phase, regardless of drop type ( $p < 0.01$  comparing the 2 week of the second phase to either interval in the first phase.  $p < 0.05$  comparing the 4 week visit of the second phase to the 4 week interval in phase one). Note the only baseline data was obtained prior to phase one.

## Lens Awareness During the Day

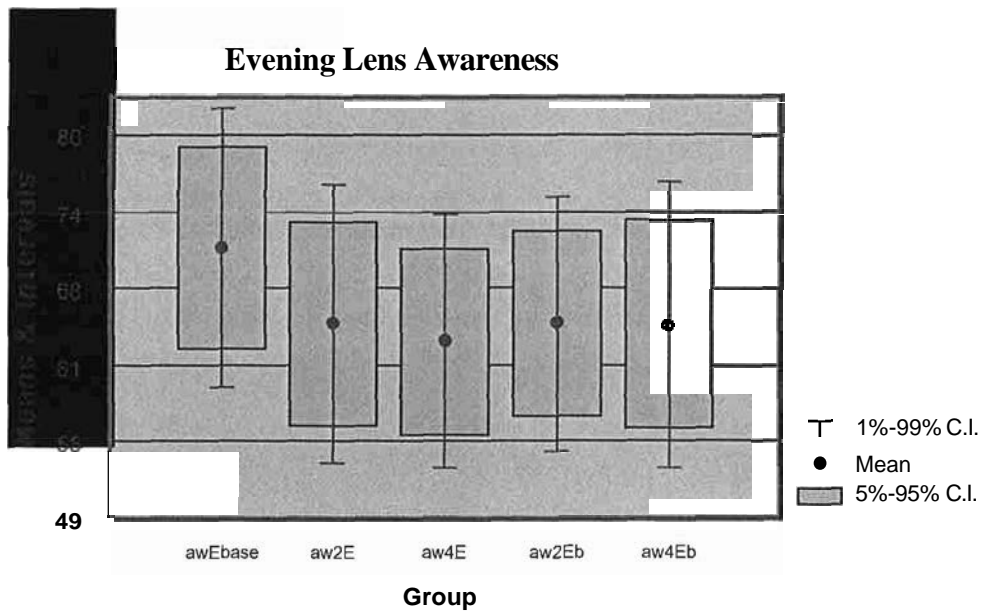
Lens awareness during the day was different ( $p < 0.01$ ) from other intervals and baseline only at the 4 week interval of the first phase.



Lens awareness Daytime, change with time

### Lens Awareness in the Evening

Evening lens awareness was equal for the two drop types. There was a small but significant ( $p < 0.05$ ) difference in awareness scores for evening for both intervals of the first phase when compared to baseline.



## **Lens Awareness Evening, Change with time**

### **Subjective Questionnaires**

**Subjects** responded to the following 10 questions **at** each of the four intervals:

1. **My lenses feel** comfortable upon **awakening**.
2. **My lenses feel** comfortable **all day** long.
3. **My** lenses **feel** comfortable **at the end of** the **day**.
4. **My vision** is not **blurry** upon **awakening**.
5. My eyes do **not** feel dry **during** the lens wearing **day**.
6. These drops **keep my** lenses clean.
- 7, These **drops** are **easy to** use.
8. **I like these drops**.
9. **My** contact lenses **feel more** comfortable **after** the **use of the** drops.
10. The **drops** keep my lenses clear.

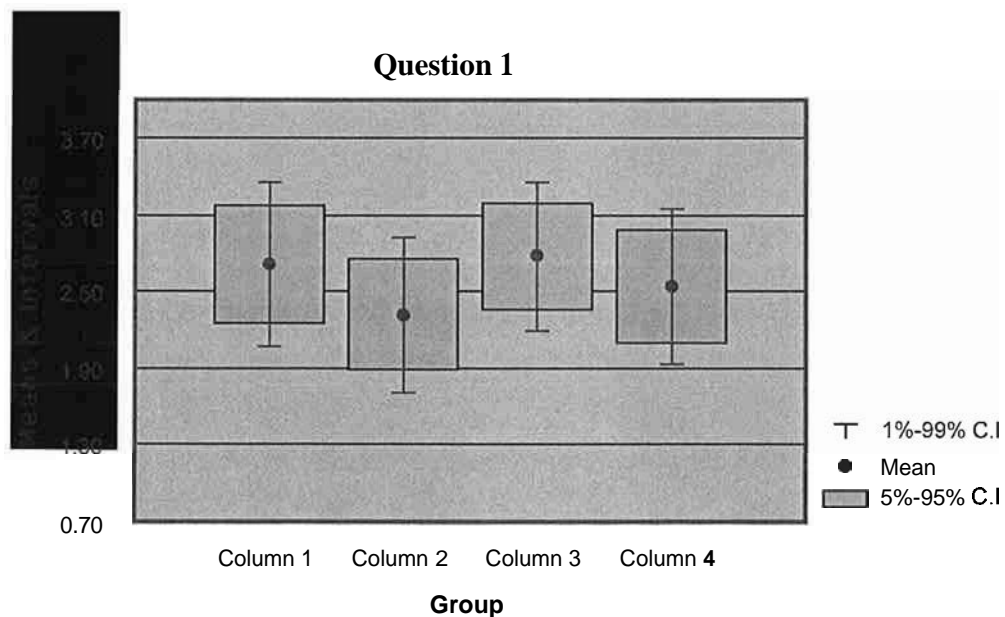
**Answers were on a ranked scale of 1 (strongly disagree) to 5 (strongly agree).**

**The table below shows the p values for difference between the two types of drops when comparing the answers to each of these questions at each interval. There were no significant differences noted.**

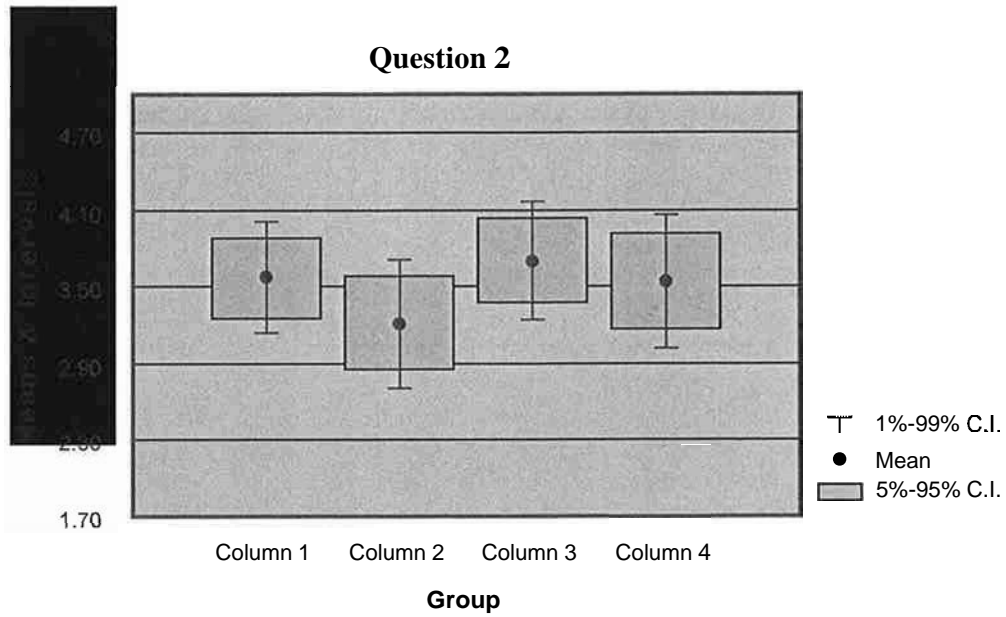


	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10
Phase 1: 2 week	.50	.74	.52	.42	.54	.51	.83	.25	.6	.139
Phase 1: 4 week	.25	.80	.09	.45	.81	.076	.94	.59	.58	.25
Phase 2: 2 week	.93	.16	.49	.47	.67	.57	.81	.06	.23	.33
Phase 2: 4 week	.76	.43	.44	.68	.69	.24	.90	.10	.06	.33

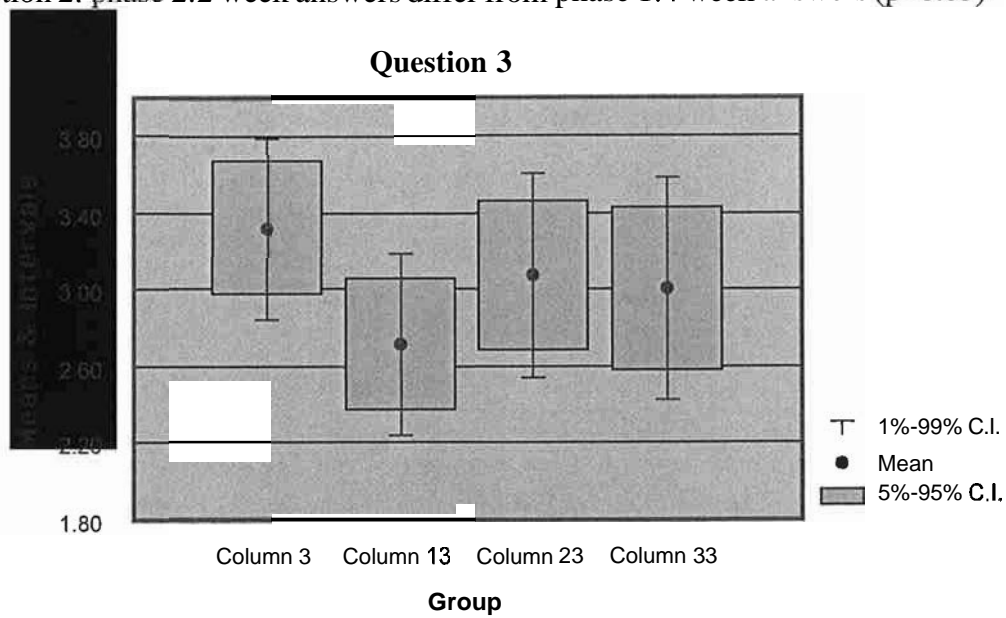
As changes with time had been noted in the rating scales, the questions were evaluated for a similar trend. Small differences were noted comparing responses at different intervals. No differences were noted with respect to time for questions 4, 5, 7, 9 and 10. The differences for the other questions are depicted graphically in the next several figures. The “column” indications from left to right indicate phase 1:2 week ; phase 1:4 week; phase 2:2 week; and phase 2:4week.



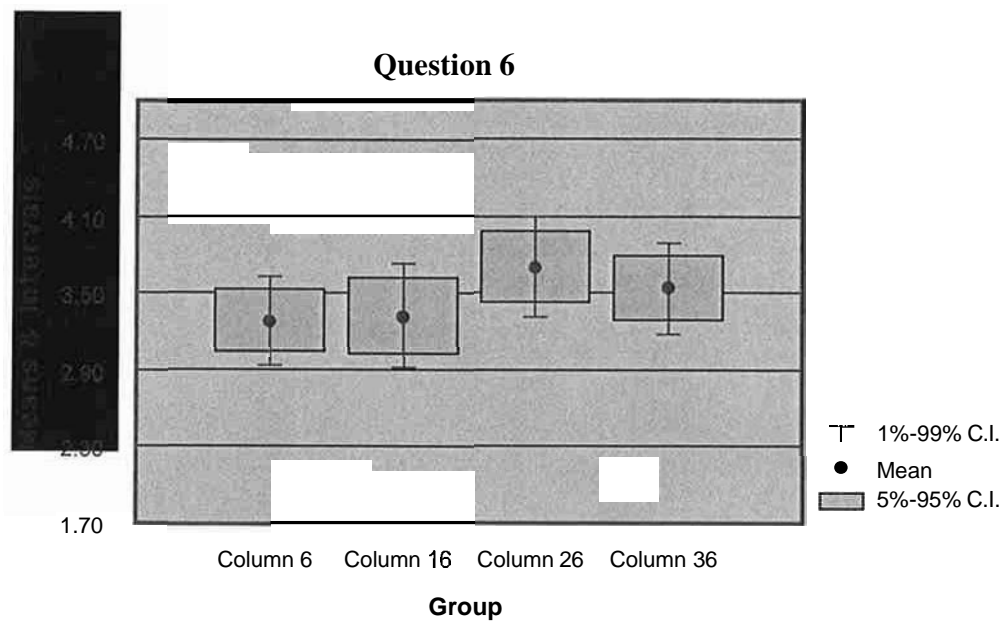
Question 1: phase 2:2 week answers differ from phase 1:4 week answers ( $p < 0.05$ )



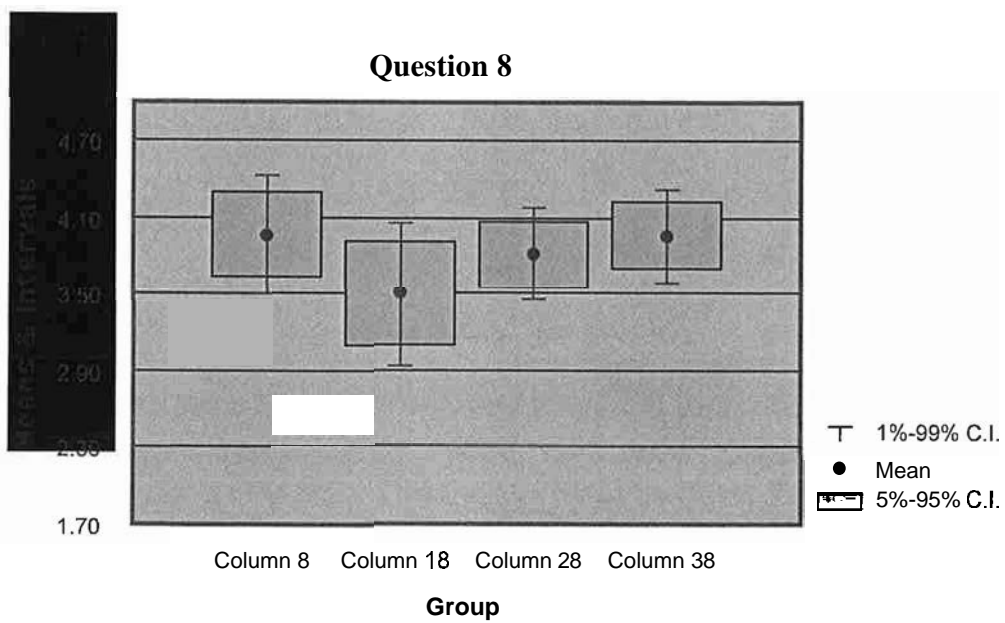
Question 2: phase 2:2 week answers differ from phase 1:4 week answers ( $p < 0.05$ )



Question 3: phase 2:2 week answers differ from phase 1:2 week answers ( $p < 0.05$ )



Question 6: phase 2:2 week answers differ from phase 1:2 week answers ( $p < 0.05$ )



Question 8: phase 1:4 week answers differ from phase 1:2 week answers ( $p < 0.05$ )

## Subject Preferences

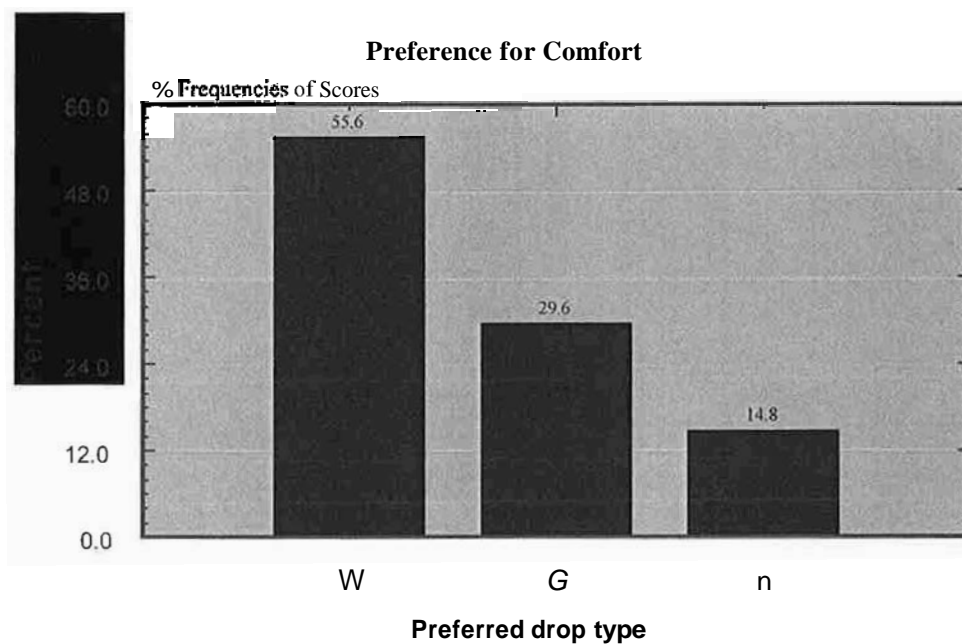
At the end of the study subjects were asked to respond to the following questions:

For each of the following questions, please circle your overall preferences.

(1) With regard to comfort, I prefer:

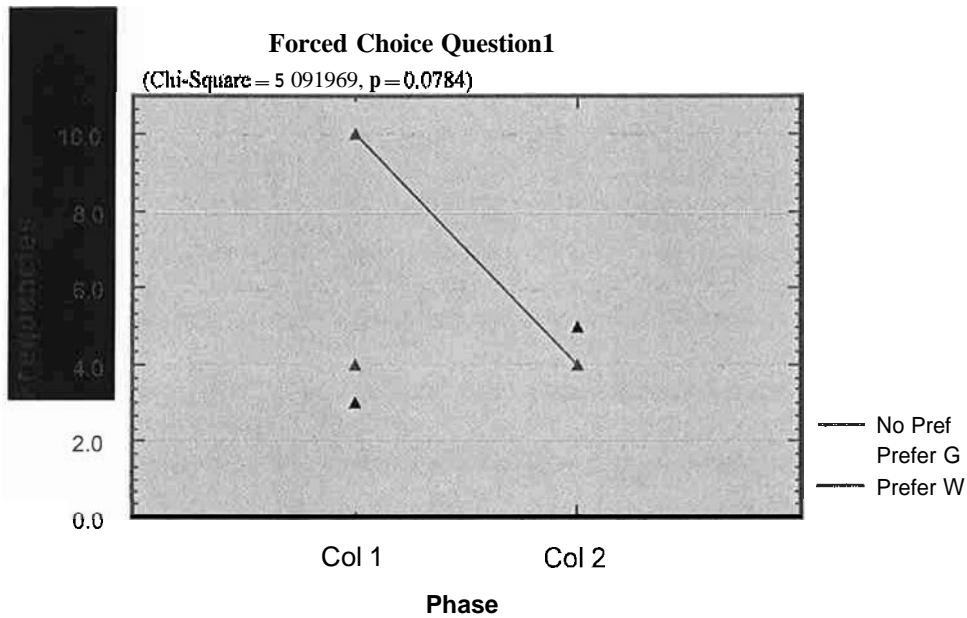
- a. Phase I Drops
- b. Phase II Drops
- c. I have no preference

The control drop was preferred 2 to 1 over the in-eye cleaningre-wetting drop. The following chart illustrates the insignificant difference between choice frequencies. " G indicates the in-eye cleaningre-wetting drop. "W" indicates the control drop.



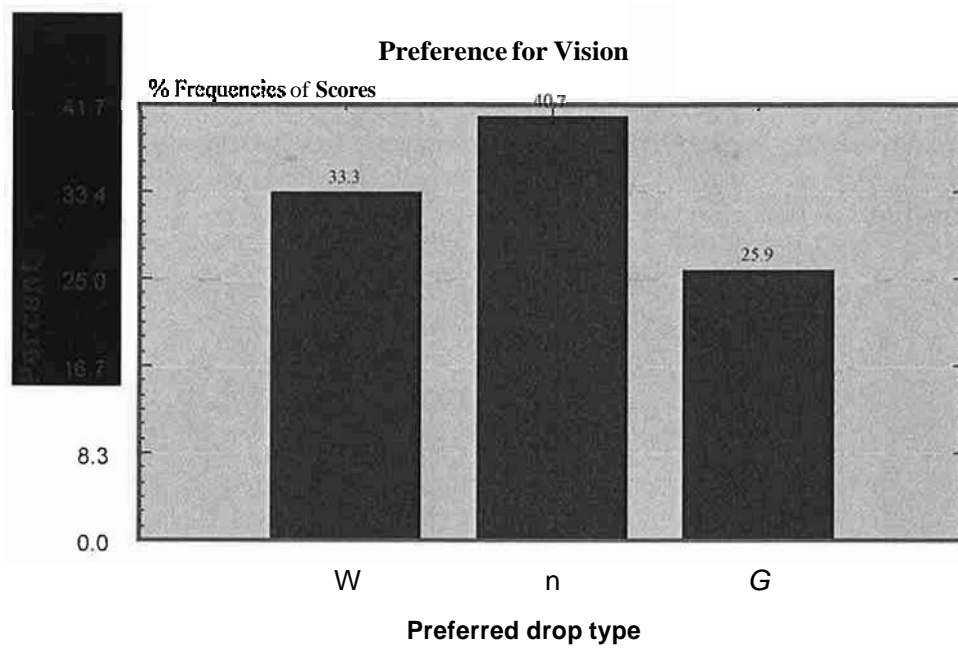
Bivariate chi-square analysis of the responses to each question were performed in order to test for significance of differences and for sequence effect. The following plot represents the responses by phase.

Note "Col 1" indicates subjects following "G W" sequence, and "Col 2" represents subjects in "WG" sequence. There appears to be an effect such that subjects tended to prefer the drop they finished with. As there were more subjects in the "G W"

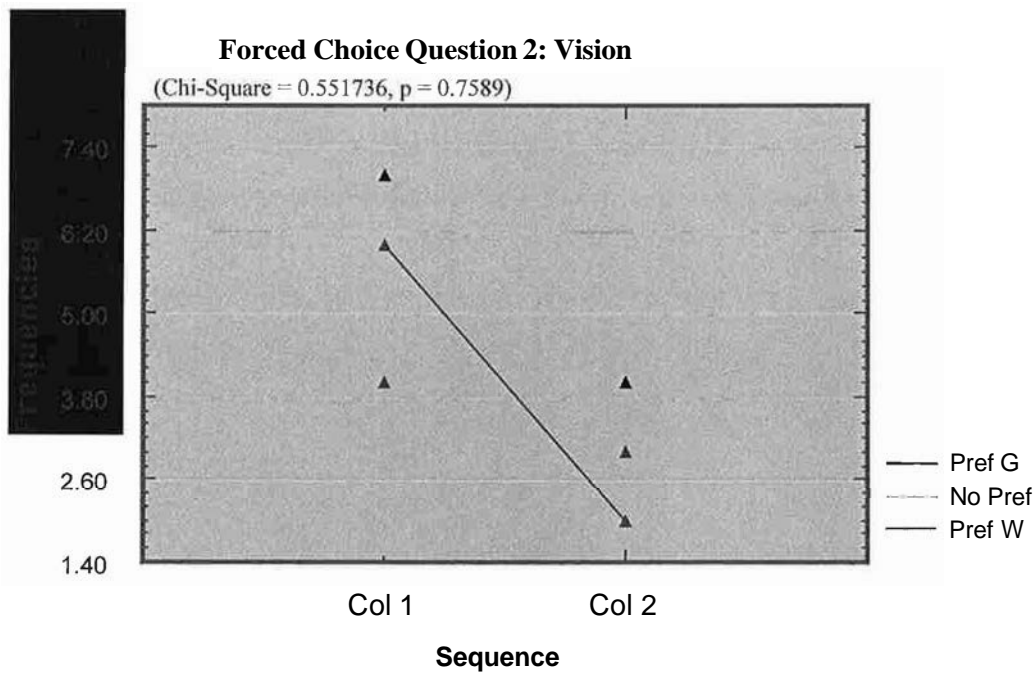
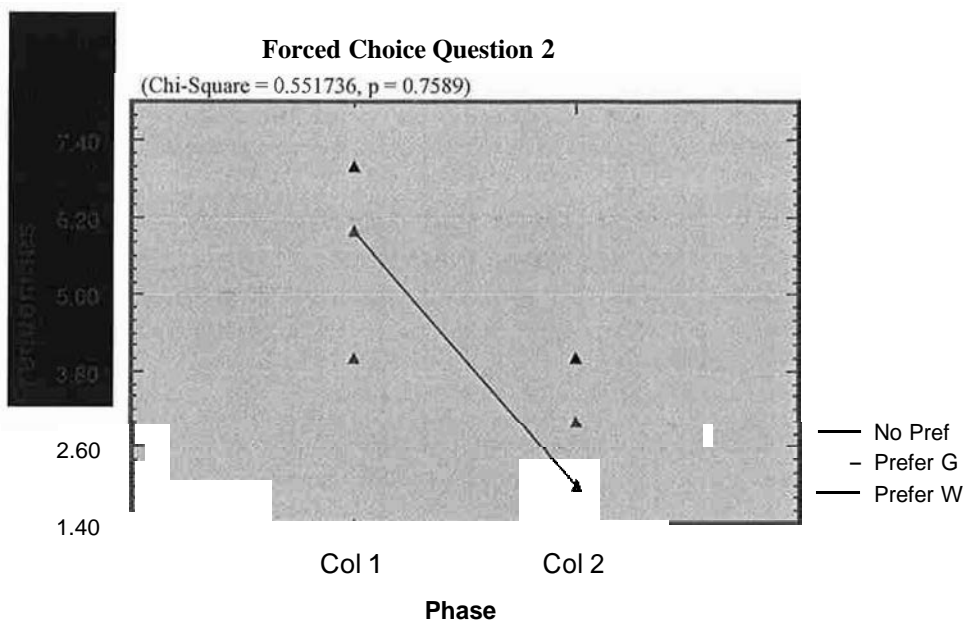


group, this gives rise to the appearance that W was strongly preferred, when there does seem to be a substantial sequence effect.

- (2) With regard to vision, I prefer:
- a. Phase I Drops
  - b. Phase II Drops
  - c. I have no preference



This table indicates a majority had no preference with regard to vision.



Note "Col 1" indicates subjects following " G W sequence, and "Col 2" represents subjects in " W G sequence. A majority had no preference regardless of sequence. Among those that did, there again appears to be an effect such that subjects tended to prefer the drop they finished with. As there were more subjects in the " G W group, this gives rise to the appearance that W was somewhat preferred, when there does seem to be a sequence effect.

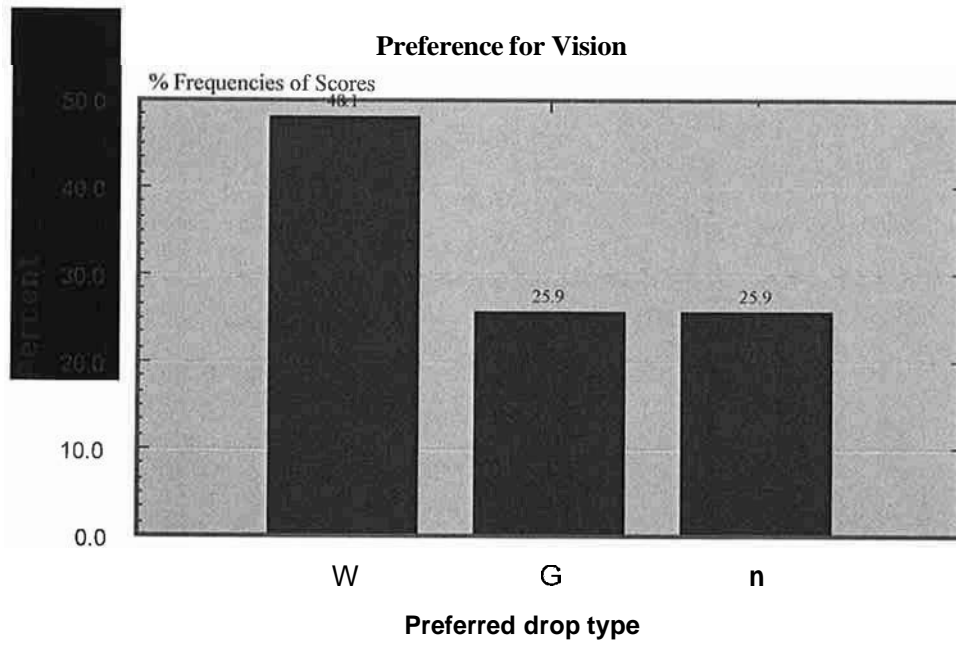
(3) With regard to lens cleanliness, I prefer:

a. Phase I Drops

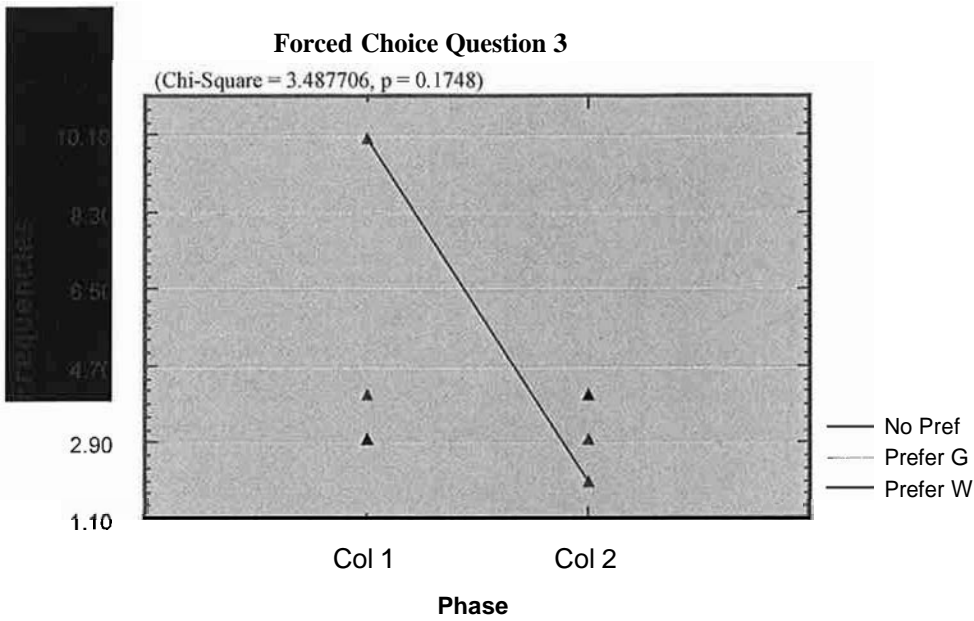
b. Phase II Drops

c. I have no preference

The following table shows a preference for the control drops:







Note "Col 1" indicates indicates subjects following "GW" sequence, and "Col 2" represents subjects in "WG" sequence. There appears to be an effect such that subjects tended to prefer the drop they finished with. As there were more subjects in the "GW" group, this gives rise to the appearance that W was strongly preferred, when there does seem to be a substantial sequence effect.

## **Discussion**

This study evaluated the subjective performance and surface characteristics of in-eye cleaning/re-wetting drops with continuous wear of silicone hydrogel contact lenses. In-eye cleaning/re-wetting drops have been shown to be beneficial in HEMA-based contact lenses leading to fewer surface deposits, increased wettability, and increased patient comfort.

The aims of the study were:

- (1) To determine if the use of an in-eye cleaning/re-wetting drop offered better subjective comfort and visual performance in comparison to a simple re-wetting drop with continuous wear of the lenses;
- (2) To determine if there is a difference in the amount and type of surface deposits on the lenses when using an in-eye cleaning/re-wetting drop versus a re-wetting drop;
- (3) To determine if there is a difference in surface wettability with the use of an in-eye cleaning/re-wetting drop versus a re-wetting drop with continuous wear of the lenses.

We were unable to detect any difference in subjective comfort or lens awareness for the two drops tested. Overall comfort scores were quite good, although two subjects dropped out due to inability to achieve acceptable comfort with the lenses. This appeared to be much more of a lens related issue than anything related to the drops.

A trend towards decreased comfort and increased lens awareness with time was observed, particularly in the first month phase. There appeared to be evidence of adaptation in the second phase, where comfort and awareness were notably better at the four week visit of phase two than they had been at this point in phase one. This is consistent with clinical observation.

The differences described above were elicited via the grading scales. Less substantial differences with time were noted via the questionnaire. The questionnaire also failed to show any difference with regard to the type of drops used.

Observation of slit-lamp findings, and in particular on-eye observation of lens wetting, deposits, numbers of mucin balls were all equivalent for the two drops. In general, wetting and deposition were graded very favorably. No significant changes in slit-lamp findings were observed in either phase.

It is to be noted that all lenses were collected at the conclusion of each phase and have been sent to University of Waterloo where they await analysis for any difference in quantity or nature of deposits.

## **Conclusions**

It appears the use of in-eye cleaning/re-wetting drops is compatible with silicone hydrogel contact lenses worn on a 30 night continuous wear basis, and performance is equivalent to re-wetting drops under these circumstances.

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