A Comparison of the Efficacy and Side Effects of Betoptic 0.5% and Betoptic S 0.25%

Authors:

Leslie K. Delemeester

Brian Pierce

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Introduction

Eye care professionals have used betaxolol solution in their armamentarium against glaucoma since its introduction in 1985.[1] However, a new vehicle for betaxolol has recently seen more use. Betoptic S 0.25% is a betaxolol suspension produced by Alcon Laboratories. It contains half the usual concentration of betaxolol and is a suspension rather than a solution. A solution is a homogeneous mixture of dissolved substances, it does not settle out. A suspension is noncolliodal dispersion of solid particles in a liquid, it will settle out.[2] In the case of Betoptic S 0.25% the drug is bound by polymer resin beads five micrometers in diameter.[3] The beads are in suspension. The benefits of this new suspension include greater bioavailability, hence lower concentration, and improved comfort upon instillation.

Betaxolol is a Beta blocker. Beta receptors are part of the sympathetic nervous system. They are located in the lungs, heart, liver, arterioles, veins, and ciliary body as well as other parts of the body. There are two forms of Beta receptors, B_1 and B_2.[4] Betaxolol reduces aqueous production and IOP by blocking B_1 receptors on the ciliary body. Betaxolol is cardioselective because it blocks B_1 receptors on the heart but does not block B_2 receptors in the lungs.[1] Cardioselectivity is beneficial because betaxolol can be more safely used than other Beta blockers in patients with pulmonary disease. Mild bradycardia is a reported side effect of Betoptic solution. Topical ophthalmic betaxolol can also lower both systolic and diastolic blood pressure.[5]

The intent of our research was to determine whether there was any difference in ability to lower intraocular pressure (IOP), affect blood pressure and heart rate, or cause ocular discomfort. The single most noted adverse effect of ocular betaxolol 0.5% solution is transient discomfort, reported to occur in 25 to 40% of patients.[1,6] "A Double-Masked Three-Month Comparison Between 0.25% Betaxolol Suspension and 0.5% Betaxolol Ophthalmic Solution", published in the August 15, 1990 issue of the American Journal of Ophthalmology reported no significant difference in IOP reduction, or effect on mean arterial pressure, or effect on pulse rate. However, ocular discomfort was significantly greater with the 0.5% solution. Greater comfort with the suspension can be attributed to the lower drug concentration and slower delivery from the vehicle.[3]

Methods

The subjects were optometry students and faculty who volunteered to participate. None of the subjects had glaucoma or were ocular hypertensive. Their ages ranged from approximately 21 to 55 years. Eighteen people were tested, of whom only two were subjects a second time and thereby tested with both drug forms. The data from one of the subjects tested a second time was discarded because the time constraints of the procedure were not followed. Hence, the results are compiled from 19 subject sittings.

Prior to the study the bottles of betaxolol were encased in white medical tape and labeled **A** and **B**. There were two bottles of

each drug form. Caps were switched because they were differing shades of blue.

The procedures outlined and the forms used throughout the study may be found on pages 9 through 12 of this paper. A consent form was used to screen patients for heart or lung anomalies which might preclude their participation in the study. It is important, however, to note that the chances of one administration causing an adverse reaction are remote. The subject's blood pressure was measured at the brachial artery using a sphygmomanometer and stethoscope. Pulse was calculated from a 15 second count at the wrist. The betaxolol drops were then instilled. Pulse and blood pressure were measured before the instillation of drops and tonometry so increases due to apprehension of these procedures would be at a minimum. Approximately three minutes were allowed to elapse after betaxolol instillation and before tonometry in order to keep the Fluress from washing out the Betoptic drops. Tonometry was performed using a Goldmann tonometer and Fluress. The second measurements of pulse, blood pressure, and IOP were taken two hours later because that is the time to maximum effect according to the drug inserts. A two hour wait was also most feasible for the schedules of ourselves and the subjects.

Results

Group **A** had an average IOP of 14.5 mm Hg at the first measurement, (14.5 in the right eye and 14.4 in the left eye). Two hours after the administration of Betoptic S 0.25% the IOP's were reduced to 13.0, (12.9 in the right eye and 13.1 in the left).

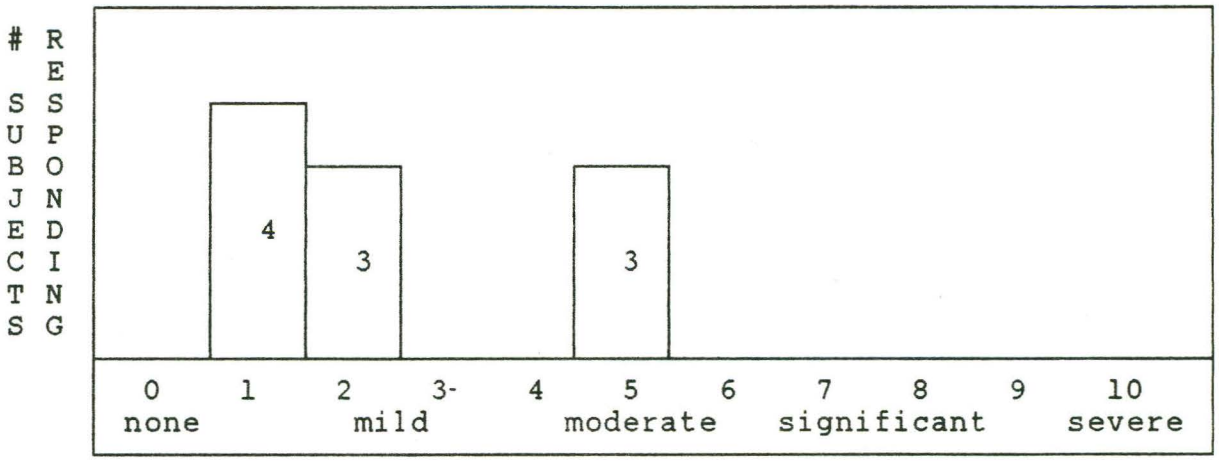
This difference was statistically significant in the right eye but not the left, (P=.016 and .090 respectively). The blood pressure went from an average of 122.2/81.1 to an average of 120.8/77.3 for a difference of 1.4/3.8 which was statistically insignificant. The pulse average stayed nearly the same also going from an average of 64.2 beats per minute to 64.6 beats per minute two hours after the administration of the drug.

Group **B** started with an average IOP of 14.6 mm Hg, (14.7 in the right and 14.4 in the left). Two hours after the administration of Betoptic 0.5% the IOPs dropped to an average of 10.7 mm Hg, (10.7 in the right and 10.8 in the left). The blood pressure average went from 117.7/75.6 to 114.8/75.6, a difference of 2.9/0. The pulse average stayed exactly the same, at 64.2 beats per minute before and after.

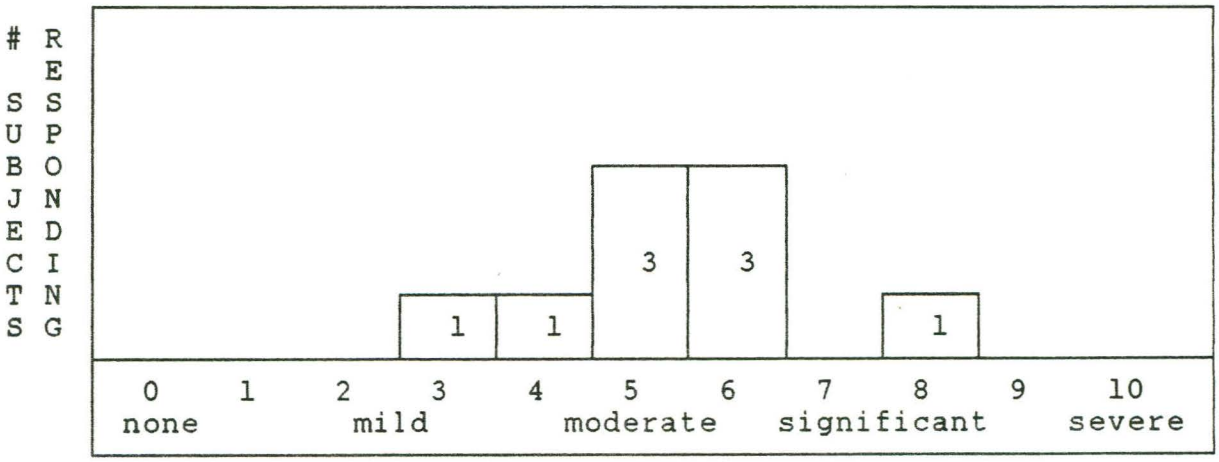
COMBINED RESULTS FOR IOP, BLOOD PRESSURE, PULSE, AND STING

	Betoptic S 0.25%	Betoptic 0.5%
Baseline IOP	14.5 mm Hg	14.6 mm Hg
IOP 2 hrs later	13.0 mm Hg	10.7 mm Hg
Baseline blood pressure	122.2/81.1	117.7/75.6
Blood pressure 2 hrs later	120.8/77.3	114.8/75.6
Baseline pulse	64.2 beats/minute	64.2 beats/minute
Pulse 2 hrs later	64.6 beats/minute	64.2 beats/minute
Sting	2.5	5.3

The sting of the drops was also recorded. The patient recorded a value of 0 to 10 corresponding to **no sting (0), mild (1-3), moderate (4-6), significant (7-9), and severe (10).** The subjective response form is located on page 12. Betoptic S 0.25% had a mean response of 2.5. Betoptic 0.5% had a sting recorded by the subjects of 5.3, more than two times that of Betoptic S.



BETOPTIC S 0.25% FREQUENCY OF STING RATINGS



BETOPTIC 0.5% FREQUENCY OF STING RATINGS

Conclusion

Our data support previous research which found a significant difference between the sting upon administration of Betoptic 0.5% and Betoptic S 0.25%. Those patients who would avert therapy rather than instill the 0.5% solution may benefit from changing to the 0.25% suspension. However, our research showed the solution to reduce IOP much more significantly than the suspension. This does not correspond to previous research, but the difference in the drugs' abilities to reduce IOP may be related to our method. Insignificant changes in pulse and blood pressure did correlate to the present literature.

There are three possible errors in our method. Because the suspension releases the drug more slowly than the solution the three minute wait between betaxolol instillation and Fluress instillation may have been too short. The suspension may indeed have been washed out by the Fluress. It is also possible that while both drugs are reported to attain maximum effect on IOP two hours after instillation that the suspension really does not. And finally, we may have underestimated the amount of shaking necessary to fully mix the suspension. To the practitioner who is using Betoptic S 0.25% we advise careful selection of patients who will follow directions to always shake the drops vigorously and for a prolonged period of time.

Acknowledgements

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PROCEDURES

A. 1. Check the participant's history for heart or lung anomalies by having them read the consent form.

2. Put the participant's name, the date, and the drug used, (A or B, 1 or 2), on both the sting response form and the vital statistics form.

3. Measure and record blood pressure and pulse.

4. Instill one drop (same drug in each eye), in the lower cul de sac of each eye. SHAKE THE DRUGS WELL. ADVISE THE PARTICIPANT THAT THEY WILL BE ASKED TO MEASURE THE STING. Record the time.

5. After 3 minutes have elapsed measure the IOP of each eye using the Goldman tonometer. Record the pressures.

Approximately 2 hours later...

B. 1. Measure and record blood pressure and pulse.

2. Again measure the IOP of each eye using the Goldman tonometer. Record the pressures and the time.

I, _____, agree to participate in a study comparing the efficacy of two ophthalmic drugs used to reduce intraocular pressure. I do not have a history of either lung or heart problems. This includes but is not limited to asthma, emphysema, chronic obstructive pulmonary disease, bronchitis, heart block, congestive heart failure, and cardiomyopathy. Further, I understand that the information obtained from this research will be used for educational purposes.

_____ _____
signature date

I, _____, agree to participate in a study comparing the efficacy of two ophthalmic drugs used to reduce intraocular pressure. I do not have a history of either lung or heart problems. This includes but is not limited to asthma, emphysema, chronic obstructive pulmonary disease, bronchitis, heart block, congestive heart failure, and cardiomyopathy. Further, I understand that the information obtained from this research will be used for educational purposes.

_____ _____
signature date

I, _____, agree to participate in a study comparing the efficacy of two ophthalmic drugs used to reduce intraocular pressure. I do not have a history of either lung or heart problems. This includes but is not limited to asthma, emphysema, chronic obstructive pulmonary disease, bronchitis, heart block, congestive heart failure, and cardiomyopathy. Further, I understand that the information obtained from this research will be used for educational purposes.

_____ _____
signature date

NAME:_____

DATE:_____

DRUG A or B

BEFORE

IOP: OD_____, OS_____

PULSE:_____ BLOOD PRESSURE:_____

TIME OF ADMINISTRATION:_____

AFTER

IOP: OD_____, OS_____

PULSE:_____ BLOOD PRESSURE:_____

TIME ELAPSED:_____

NAME:_____

DATE:_____

DRUG A or B

BEFORE

IOP: OD_____, OS_____

PULSE:_____ BLOOD PRESSURE:_____

TIME OF ADMINISTRATION:_____

AFTER

IOP: OD_____, OS_____

PULSE:_____ BLOOD PRESSURE:_____

TIME ELAPSED:_____

NAME:_____

DATE:_____

DRUG A or B

I would rate the sting of this drop on a scale of 0 to 10 to be:

0 1 2 3 4 5 6 7 8 9 10

no sting mild moderate significant severe sting

NAME:_____

DATE:_____

DRUG A or B

I would rate the sting of this drop on a scale of 0 to 10 to be:

0 1 2 3 4 5 6 7 8 9 10

no sting mild moderate significant severe sting

NAME:_____

DATE:_____

DRUG A or B

I would rate the sting of this drop on a scale of 0 to 10 to be:

0 1 2 3 4 5 6 7 8 9 10

no sting mild moderate significant severe sting

NAME:_____

DATE:_____

DRUG A or B

I would rate the sting of this drop on a scale of 0 to 10 to be:

0 1 2 3 4 5 6 7 8 9 10

no sting mild moderate significant severe sting