# The Systemic Effect Of Topical Timolol On Some Cardiovascular Parameters In Owerri Municipality

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**Abstract**

Timolol Maleate is a non-selective -adrenergic blocker used in ophthalmic medicine to manage glaucoma and raised intra-ocular pressure in general. The systemic effect of topical timolol was studied in fifty normotensive volunteers of mixed sexes (25 males, 25 females) in the Optometry Clinic of the College Of Medicine, Imo State University, Owerri. The subjects were aged 20-70 years, and were certified to be clinically healthy based on their medical history. The effect on Systolic (Sp) and Diastolic (Dp) blood pressure, as well as Heart Rate (HR) were studied using sphygnomanometer and stethoscope. The initial readings served as control. 0.5% solution of timolol was instilled via the conjuctiva. The B.P. and HR were taken at intervals of 30 minutes for 60 minutes. The result showed a mean decrease of 11.16 mmHg (22.3%) Sp ($P<0.057$), 8.40 mmHg (16.8%) Dp, and mean change in HR of 6.50 beats/minute (13% HR). No sex differences in B.P and HR were observed. The fall in B.P. was least in age (20-29) years and highest in (50-59) years age bracket. The fall in HR was not age related. We conclude that topical timolol decreases systemic B.P. and HR of subjects. It is suggested that adequate precaution be taken in the course of administering the drug to cardiovascular compromised patients. However, its possible benefits should be investigated in patients with tachycardia or raised B.P.

## INTRODUCTION

Timolol is a non-selective -adrenergic blocking agent that does not have intrinsic sympathomimetic, direct myocardial depressant, or local anaesthetic activity. Timolol and related ocular adrenergic antagonists block the sympathetic stimulation of the nervous system. Timolol blocks beta-receptors in the heart, lungs, and other organs of the body. This action lowers the heart rate and the force of contraction. As a result, the pressure at which blood is pumped out of the heart to the periphery is reduced.

Blood pressure is the pressure exerted on the blood vessel walls. It is usually referred to as the pressure within the arteries, which is measured in millimeters of mercury. It is an inherent physiologic characteristic that evaluates the general state of health of an individual. Blood pressure is usually denoted as a ratio of systolic pressure to diastolic pressure. Normal blood pressure in adults is about 120 mmHg during systole, and about 80 mmHg during diastole. In the Framinghan study, blood pressure was considered normal if systolic pressure was below 140 mmHg and diastolic below 90 mmHg. Hypertension was indicated for systolic pressure of 160 mmHg or greater and diastolic pressure of 95 mmHg or greater; and pressure between these values were considered as borderline (Guyton and Hall, 2000).

Heart rate measures the number of heartbeats in a minute and is recorded as beats per minute. The normal heart rate of adults falls within the limits of 60 and 80 beats per minute (Vaughan et.al.1999). Timolol maleate is a hypotensive beta-blocking agent, often used in the management of elevated intra-ocular pressure. When applied topically to the eye, timolol has the effect of reducing elevated, as well as normal intraocular pressure whether or not accompanied by glaucoma. It does this by predominantly decreasing aqueous formation and a slight increase in aqueous outflow. It blocks the sympathetic system to reduce the formation of excess fluid in the eyeball (Gerald, 1991). It also slows the heart rate and relaxes the smooth muscle of the blood vessels. This study aims at evaluating the systemic effect of topically applied timolol on the cardiovascular system, since there is the understanding that the drug may not have significant systemic effect especially on the cardiovascular system.

## MATERIALS AND METHODS

Sphygmomanometer, Stethoscope, Ophthalmascope, Schiotz tonometer, 0.5% Ophthalmic timolol eye drop and Stop watch for 50 normotensive adults subject of mixed doxes (25 males and 25 females) between the ages of 20 and 70 years were randomly selected. A case history of each subject was taken in order to rule out those who have history of allergic reaction to timolol, patients with bronchial asthma or a history of hypertension. The ophthalmoscope, was used to assess the fundus, the disc, cup-disc ratio, and optic-nerve head of the patients. Subjects with disc cupping, which meant suspected glaucoma, were not chosen for the study. Only subjects with normal blood pressure were chosen. This fell within the limits of 120 ± 15 - 80 ± 15 mmHg.

The intraocular pressure (IOP) of subjects were measured with the schiotztonometer. Subjects who have normal intraocular pressure between the ranges of 10-21 mmHg were chosen for the study. Subjects with normal heart rate which ranged from 60-80 beats per minute were also chosen.

Their age groupings were classified according to World Health Organization standard for categorizing age groups (Owie, 1999): 20-29 years, 30-39 years, 40-49 years, 50-59 years and 60-69 years.Each subject served as his or her own control throughout the study. The blood pressure and heart rate of subjects were recorded before the instillation of one drop of 0.5% timolol. The same parameters were recorded after 30 minutes of drug instillation and were measured again after another 30 minutes, making a total of 60 minutes. The research was carried out in Imo State University Optometry Clinic. Subjects were drawn from Owerri Municipality.

## RESULTS

Table 2 showed that the mean systolic blood pressure (SP) was decreased by 8.6% (P>0.05) after 60 minutes. 0.5% Timolol also decreased the diastolic blood pressure (Dp) in all cases.

**Figure 1**

Table 1: Age Distribution of Subjects

| Age Group (Years) | Frequency | Percentage% |
|---|---|---|
| 20 – 29 | 16 | 32 |
| 30 – 39 | 8 | 16 |
| 40 – 49 | 10 | 20 |
| 50 – 59 | 10 | 20 |
| 60 – 69 | 6 | 12 |
| Total | 50 | 100 |

**Figure 2**

Table 2: Mean Systolic Pressure (mmHg) before and after Drug Administration (N=50).

| Age group (yrs) | Mean initial systolic Pressure(mmHg) | Mean final systolic pressure mmHg | Change |
|---|---|---|---|
| 20-29 | 113.13 | 106.44 - 6.69 | |
| 30-39 | 130.63 | 117.75 - 12.88 | |
| 40-49 | 134.30 | 124.50 - 12.80 | |
| 50-59 | 136.50 | 121.70 - 14.80 | |
| 60-69 | 133.33 | 121.33 - 11.00 | |
| Mean | | | - 11.16 |

**Figure 3**

Table 3: Mean Diastolic Pressure (mmHg) before and after Drug Administration according to Age (N = 50)

| Age group (yrs) | Mean initial diastolic Pressure (mmgh) | Mean final diastolic Pressure mmgh | Change |
|---|---|---|---|
| 20-29 | 69.06 | 62.81 | - 6.25 |
| 30-39 | 77.50 | 65.63 | - 11.87 |
| 40.49 | 83.50 | 75.00 | - 8.50 |
| 50-59 | 82.50 | 73.50 | - 9.00 |
| 60-69 | 85.00 | 76.67 | - 8.33 |
| Mean | | | -8.4 |

**Figure 4**

Table 4: Mean Heart Rate (Beats/Minutes) before and after Drug Administration

| Age group (yr) | Mean initial H/R | (n = 50) Mean final H/R | Change |
|---|---|---|---|
| 20-29 | 72 | 68 | - 4.00 |
| 30-39 | 70.88 | 62.75 | - 8.13 |
| 40-49 | 70.70 | 63.70 | - 7.00 |
| 50-59 | 70.00 | 62.40 | - 7.60 |
| 60-69 | 68.83 | 60.50 | - 8.33 |
| Mean | | | - 6.5 |

## DISCUSSION

50 subjects of mixed sexes were randomly selected and assigned to the respective groups. The majority of the subjects used belong to the age group 20 – 29 years (32%). Age group 60 – 69 years were the least (12%) (Table 1). This is because the subjects were screened to obtain only normotensive (non-glaucomatous and non-susceptible to hypertension) individuals, which naturally belong to the former age bracket, unlike the latter age group who are elderly subjects and susceptible to glaucoma and hypertension, and other geriatric prone sicknesses.

Table 2 showed that 0.5% topical timolol significantly reduced the systolic blood pressure of the subjects. ($p<0.05$). It also showed that the mean decrease in systolic pressure after instillation of 0.5% topical timolol was 11.16 mmHg, representing a decrease of 22.32% in systolic blood pressure. The significant reduction of blood pressure is an indication that the drug was absorbed systemically and blocked the sympathetic nervous system, bringing about a reduction in blood pressure. A similar observation was made by Shield (1980) who showed that timolol, as a non-selective -blocker was associated with progressive fall in blood pressure after an initial peripheral compensatory vasoconstriction. The mechanism by which this occurs is obscure (Shield, 1980 and Lawrence et al., 1997). However, Mcmahon (1979) thinks that fall in blood pressure may result from the blockage of -mediated cardiovascular constriction which leads to the dominance of systemic cholinergic activities (Mcmahon 1979 and Goldstein 1977), and the attendant fall in blood pressure. 0.5% timolol has a significant reduction in the diastolic blood pressure of adult subjects (Table 3).

Ophthalmic solution of sterile timolol has been shown to have some systemic effects (Hugues et al., 1985). Systemic Timolol as a beta-adrenergic blocking agent acts by inhibiting some actions of the sympathetic nervous system. It reduces the contraction of the vascular smooth muscles of the heart (Bobi et al., 1979). In the same vein, Timolol has been found to induce bradycardia and to lowers fast heartbeats.

Data analysed from the study population showed that mean decrease in diastolic blood pressure was 8.40 mmHg (Table 3) representing 16.8% fall in diastolic blood pressure ($P<0.05$). The reason for the reduction is because topical timolol is absorbed through systemic circulation and as a cardiorascular -blocker caused the overwhelming of vasodilatory action and fall in blood pressure and negative chronotropic effect, a condition which may lead to overwhelming vagal activities. This possibly explains the reason for the fall in heart rate observed in subjects after instillation of timolol. This study supports the work of Diggory et al. (1998) who observed a mean reduction of heart rate in patients administered with timolol. The works of Botef and Benito (1986), Hong et al. (1995) and Diggory et al. (1998) support these finding. From these findings, it is suggested that regular spirometry, resting pulse rate and blood pressure checks should be undertaken for all patients receiving topical timolol. The investigation should be extended to other topical -adrenergic blockers.

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