Effect of Ethambutol on Visual acuity, Contrast Sensitivity and Color Vision in the Tuberculosis Patients Visiting Allied Hospital Faisalabad

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ABSTRACT

Introduction: Due to increase in prevalence of tuberculosis worldwide, first line anti-tuberculosis drugs are widely utilized. Ethambutol is one of the first line anti-tuberculosis drug. Ocular side effects are frequently reported due to it. Visual functions i.e. visual acuity, color vision; contrast sensitivity and visual fields get disturbed. Blue-yellow color vision defects are detected at first and are thought to be the first symptom of Ethambutol toxicity. Methodology: A descriptive cross sectional study was carried out at outdoor patient department of Tuberculosis, Allied Hospital Faisalabad to study the frequency of Visual acuity, contrast sensitivity and color vision defects in Tuberculosis patients due to ethambutol. Age limit of patients was 15-45 year. Sample of 120 subjects was taken by convenient sampling method. Proper informed consent was taken from all subjects under study. After taking appropriate history, clinical examination was performed. Log Mar chart for visual acuity, Pelli robsin for contrast sensitivity and Fransworth Munsell D-15 for color vision testing was used. Subject responses were recorded on proforma. Data was analyzed by utilizing SPSS programming software. Results: Descriptive statistics of Mean visual acuity recorded was 1.3 and standard deviation was ±0.46. Mean contrast sensitivity was 1.84 and standard deviation was ±0.44. Mean value of color vision was 1.60 and standard deviation was ±0.492. Overall, the results have found that 36 (30%) patients had impaired visual acuity while in 84 (70%) patients visual acuity was not impaired. 23 patients had normal contrast sensitivity (19.2%), 93 patients had moderate impairment (77.5%) and 4 patients had severe impairment of contrast sensitivity (3.3%). Color vision defects were recorded in 72 (60%) patients whereas 48(40%) patients had normal color vision. Out of 120 patients, 50 (41.7%) had no color vision defect, 19 (15.8%) of them had proton defect, 10 (8.3%) were of Deutan and 41 (34.2%) had Tritan defect. In Chi-square test statistic of Duration of Ethambutol and Visual acuity results are found significant at the level of 0.001. Results of duration of Ethambutol and Contrast sensitivity are significant at the level of 0.001. In relation of duration of Ethambutol and color vision the results are found significant at the level of 0.05. Conclusion: This study suggests that patients on Anti-tuberculosis therapy (ATT) must be monitored regularly and the drug should be stopped immediately when any visual function defect is detected.

Keywords: Ethambutol, Visual acuity, color vision, contrast sensitivity, tuberculosis

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1. **INTRODUCTION**

Of all the human senses, sight is the most precious gift of nature. It’s a mighty process that images of the entire universe are stored in such a small space “The Eye”. Our impressions and ideas about the outside world are mainly stored in the form of visual images. So, a good vision is required for heading a normal life. Tuberculosis is a chronic bacterial infection caused by Mycobacterium tuberculosis, usually characterized pathologically by the formation of granulomas. Mycobacterium tuberculosis grows slowly and divides after every 16-20 hours. It has been estimated by the World health organization that M. tuberculosis has affected one third of the world’s population\(^1\).

The medications in the treatment of tuberculosis include isoniazid, rifampicin, pyrazinamide and ethambutol. Ethambutol is included in first line anti-tuberculosis drugs and was developed in 1960s. Since that time the most common side effects of ethambutol has been reported i.e. visual disturbances which includes decreased visual acuity, contrast sensitivity, visual field and color vision defects secondary to optic neuropathy including central and paracentral defects. It has been speculated in theories that ethambutol acts as a chelating agent and disrupts the metal carrying enzyme system in the nucleic acid structure of bacteria. Classically, Ethambutol toxicity is described as duration and dose related and restoration of vision after discontinuation of drug is not always achieved. The phenomenon of ocular toxicity is unpredictable and drug should be used cautiously with proper health education of patient. However, there are certain risk factors which increase the chances of ocular toxicity i.e. old age, renal disease and chronic smoking.1-5% patients develop ethambutol induced optic neuropathy and visual function defects under a standard dosage of 15 mg/kg\(^2\).

In addition to blue yellow color vision defects, red green defects have also been reported. Visual acuity loss starts with a hazy vision at the fixation point. This can further decline (20/40-20/200) and can lead to total blindness\(^3\).

Visual field defects include central scotomas most commonly, but peripheral field constriction and bitemporal field defects are also reported\(^4\).

Contrast sensitivity testing is also found significant in detecting the ethambutol induced toxicity as contrast also compromises. International guidelines on early detection and prevention of ethambutol induced toxicity and visual function defects have been published. No specific treatment is available other than stopping the drug. Once the drug is discontinued, many patients will recover in weeks to months but full recovery is not always achieved. Despite of this, there are some reports which showed vision will still decline even after the cessation of the drug if the damage is intense and patient has presented too late\(^5\).

The visual symptoms can occur from a few days to 2 years after the initiation of treatment. The visual function defects improved after the patient had stopped taking ethambutol. Despite of the fact that the dose of the medication patient took was high, but clinical side effects appeared were serious. In some extreme cases, visual field examination through perimetry showed bitemporal hemianopia, which may occur because of involvement of optic chiasm due to advanced stage of ethambutol-induced optic neuropathy\(^6\).

2. **METHODOLOGY**

Descriptive Cross sectional study.

**Study setting:** Study was carried out at outdoor patient department of Tuberculosis, Allied Hospital Faisalabad, Pakistan.

**Study Duration:** January 2017 to May 2017

**Sample Size:** 120 Patients.

**Sampling Technique:** Convenient sampling technique was used to collect data of 120 subjects. Convenient sampling is a type of non-probability sampling in which individuals are selected because of their access and proximity to the investigator/researcher. In this technique, data is easily collected through a known group.

**Sample Selection:**

*Inclusion Criteria:*

• Patients aging from 20 to 50 years of age diagnosed with Pulmonary Tuberculosis.

• Patients taking Ethambutol for atleast 2-3 months in combination with other 1st line Anti-tuberculosis drugs.

*Exclusion Criteria:*

• Those who already had some disease contributing to Visual dysfunction.

• Patients having refractive error.

• Patients having any systemic diseases other than Tuberculosis

**Data collection Procedure:** Study was carried out at outdoor patient department of Tuberculosis Allied Hospital Faisalabad, Pakistan to study the frequency of Visual acuity, contrast and color vision defects in patients having Pulmonary Tuberculosis diagnosed and treated with Ethambutol in combination with other first line Anti tuberculous agents.

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Tuberculosis patients due to ethambutol. Age limit of patients was 20-50 years. Proper informed consent was taken from all subjects under study and detailed history was recorded. History contained the fundamental points as personal, ocular, Medical history, duration of Tb drugs and dosage. After taking appropriate history, clinical examination was performed. A room for examination was chosen, having proper arrangement of lights, chairs, and appropriate distance for charts. Data was entered and analyzed in computer program SPSS version 22.

3. RESULTS

No. of subjects in study were n=120. Of those, 52 (43.3%) were male and 66 (55%) were female patients. 83 were in first age group (15-25 years). 20 patients were included in second age group that is 26-35 years and 15 patients in third age group i.e. 36-45 years. Mean visual acuity recorded was 1.3 and standard deviation was 0.46. Minimum value was 1.0 and maximum was 2.0. 79 patients were taking Ethambutol for 2-3 months. Of those 70 patients had no Visual impairment and 9 patients had impairment of vision? 35 patients were taking Ethambutol for 3-6 months. Out of those 35 patients 22 had visual impairment and 13 had normal vision. 6 patients were on Ethambutol treatment for 6-9 months. Significant impairment of vision was recorded in these patients. 5 patients had visual impairment, whereas 1 patient had normal vision.

<table>
<thead>
<tr>
<th>Age groups</th>
<th>Frequency</th>
<th>Percent</th>
<th>Valid Percent</th>
<th>Cumulative Percent</th>
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</thead>
<tbody>
<tr>
<td>Valid</td>
<td>15-25 years</td>
<td>83</td>
<td>69.2</td>
<td>69.2</td>
</tr>
<tr>
<td></td>
<td>26-35 years</td>
<td>20</td>
<td>16.7</td>
<td>16.7</td>
</tr>
<tr>
<td></td>
<td>36-45 years</td>
<td>15</td>
<td>12.5</td>
<td>12.5</td>
</tr>
<tr>
<td></td>
<td>4.0</td>
<td>2</td>
<td>1.7</td>
<td>1.7</td>
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<tr>
<td>Total</td>
<td>120</td>
<td>100.0</td>
<td>100.0</td>
<td></td>
</tr>
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</table>

Table 1: frequency distribution of age

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<tr>
<th>DESCRIPTIVE STATISTIC</th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual acuity</td>
<td>120</td>
<td>1.3000</td>
<td>.46018</td>
<td>1.00</td>
<td>2.00</td>
</tr>
</tbody>
</table>

Table 2: descriptive statistics of visual acuity

<table>
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<tr>
<th>Duration of Ethambutol Visual acuity Cross tabulation</th>
<th>Visual acuity</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>6/6-6/18 No impairment</td>
<td>&lt;6/18-6/60 Visual impairment</td>
</tr>
<tr>
<td>Duration of Ethambutol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-3months</td>
<td>70</td>
<td>9</td>
</tr>
<tr>
<td>3-6months</td>
<td>13</td>
<td>22</td>
</tr>
<tr>
<td>6-9months</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>84</td>
<td>36</td>
</tr>
</tbody>
</table>

Table 3: cross tabulation of visual acuity and duration of ethambutol

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4. DISCUSSION

It has been demonstrated through this study that Ethambutol can cause ocular toxicity and there is a strong positive correlation of Ethambutol toxicity with duration of its usage. Previously, the research study of Nair at the University of Southern California has suggested that a significant number of patients in his research study had visual problems due to Ethambutol and they were referred to ophthalmology department of Seoul National University Hospital, Korea. The study comprised of 857 subjects. Diminished visual acuity was present in (39.4%) and abnormal color perception was detected in (61.5%) of the patients(7).

Our study strongly agrees with the research study of Nair. The study consisted of 120 subjects. Of those 52 (43.3%) were male and 66 (55.5%) were female patients. The age groups under study were 15-25 years, 26-35 years, 36-45 years. 83 patients were included in first age group, 20 patients were included in second age group and third age group comprised of 15 patients. Out of 120 patients, 72 (60%) patients reported with color vision defects whereas, 48 (40%) patients had normal color vision. So the results are in correspondence with the above research study as they detected color vision defects in 61.5% of patients. In case of visual acuity, 80 (70%) had no visual impairment, whereas 36 patients had visual impairment (30%). In the research study of Nair, diminished visual acuity was present in 39.4% of the patients.

In our study, Red green defects were less common and were more frequent in patients taking Ethambutol for 6-9 months. During 2-3 months, 13 out of 79 patients reported with red green defects, during 3-6 months of ethambutol treatment 1 out of 35 patients was found to have red green color defect and in patients taking ethambutol for 6-9 months, 5 out of 6 patients had red green color defect whereas, one patient had normal color vision. This research study is also in accordance with the research study of Polak, conducted at Hong kong. He concluded that blue yellow color vision defects are the earliest symptoms of Ethambutol toxicity. The most common color vision defect was blue yellow, followed by confusion and then red green defects. Red green color vision defect is less common and is a sign of more advanced toxicity(8).

The main aim of this research was to study the effect of Ethambutol on visual acuity, color vision and contrast sensitivity and Ethambutol is found to be ocular toxic in relation to its duration of usage. However, there were certain limitations of the study. A significant number of patients above the age of 40 years had hypertension and diabetes which was in our exclusion criteria. We also excluded the patients of ocular pathology and cataract from our study. Cataract and lenticular changes were found prevalent above the age of 50 years so, the age of patients in our inclusion criteria was 15-45 years. The patients with renal insufficiency were at great risk of ethambutol toxicity, so we had to exclude all the patients who had any systemic or ocular disease previously. So, this was found quite challenging to collect the sample of such filtered patients. Moreover, the time duration for this descriptive study was short.

5. CONCLUSION

This study was conducted to investigate the effect of Ethambutol on Visual acuity, contrast sensitivity and color vision in Tuberculosis patients. From the findings of the study it has been concluded that Ethambutol is oculo-toxic and duration of drug is a risk factor of ocular toxicity. Patients who were taking ethambutol treatment for a long duration presented more frequently with visual function defects. Whereas, less visual function defects were recorded in patients who were taking Ethambutol for 2 months. Blue-yellow color vision defect is the earliest sign of toxicity. So, the study suggests that patients on Anti-tuberculosis therapy (ATT) must be monitored regularly. On every follow up visit to DOT centre there must be a follow up visit to optometrist and visual functions must be assessed. This study also emphasizes that health education must be given to the patients before initiation of ATT, so that patient must be aware of all possible side effects of the Anti-tuberculosis drugs.
REFERENCES