Visual functions of workers exposed to organic solvents in petrochemical industries

Abstract

Aim: The purpose of this study was to evaluate the visual functions of workers exposed to organic solvents in petrochemical industries. Materials and Methods: Thirty workers from the petroleum refinery and 30 age-matched controls (mean age) were recruited. Visual functions and occupational exposure levels were assessed among both the groups. Visual acuity, contrast sensitivity, color vision, and visual fields were evaluated at the workplace. The biological samples, namely blood and urine, were collected at the workplace and transported to the laboratory for analysis. The urinary excretion of hippuric acid and methylhippuric acid as well as creatinine was measured by high performance liquid chromatography. Results: The mean age of the workers and controls were 39.7 ± 7.6 years and 38.6 ± 8.1, years respectively. The mean years of experience of the workers were 15.6 ± 6.8 years. Visual acuity was >0.01 LogMAR among both the control and case groups. The contrast sensitivity was reduced at 12cpd among workers. Comparison between groups was done using independent sample t-test. The mean difference in color confusion index was 0.11 ± 0.05 (P = 0.037*). The mean difference in visual fields was −0.31 ± 0.36 dB (P = 0.933). The mean difference in urinary hippuric acid level (urinary metabolite of toluene) between the groups was 0.19 ± 0.96 g/g creatinine (P = 0.049*). The mean difference in the excretion of methylhippuric acid (urinary metabolite of xylene) was 0.06 ± 0.04g/g creatinine (P = 0.154). We also found that exposure was a significant risk factor for color vision defect with an odds ratio of 4.43 (95% CI: 1.36–14.4); P = 0.013. Conclusion: The study results showed that contrast sensitivity and color vision were affected among workers in petrochemical industry.

Key words: Exposure, hippuric acid, methylhippuric acid, petrochemical industry, toluene, xylene

INTRODUCTION

Petrochemical industry is one of the leading industries with a weightage of 14% in the industrial production index.[1] In India, over 11.5 lakh people are employed in this sector.[2] These industries are involved in the manufacturing of certain organic solvents such as benzene, toluene, xylene, ethyl benzene, and styrene.[3] Organic solvents are used in refining automotive gasoline, in the manufacture of rubber, paints, lacquers, inks, thinners, glues, reinforced plastics, detergents, and in organic synthesis of many other chemicals.[3]

Occupational exposure to these organic solvents damages central and peripheral nervous system, among which, visual system is susceptible.[3] The major route of entry for volatile organic solvents is inhalation. When these solvents are not metabolized by the liver, they penetrate into the central nervous system because of their high lipophilic properties. The mechanisms behind neurotoxicity are oxidative stress and neurotransmission.[5] The oxidative metabolism of benzene, toluene, xylene, ethanol, acetone, and trimethylbenzene generates and promotes the free radical or reactive oxygen species (ROS) (O₂⁻) formation.[6] These ROS settle in the central nervous system and cause neurobehavioural disturbances. Organic solvents in combination with dopamine in the nervous and the visual system cause neurotoxicity.[7,8]
People are more prone to exposure to organic solvents in petrochemical industries. Considering that this sector employs a large number of people, it is important to gather information regarding their visual functions. Previous studies done in the petrochemical industries have shown that acquired color vision defects are associated with organic solvents exposure. However, they did not mention whether it was done in a petrochemical industry with a protected environment. The purpose behind this study is to see the effect of organic solvents on the visual functions as well as relate the levels of exposure to these solvents in workers among the protected group or (organized sector).

MATERIALS AND METHODS

An observational cross-sectional study was conducted by Elite School of Optometry, a unit of Medical Research Foundation, Chennai during the period August 2013 to March 2014. The study was approved by the Institutional Review Board at the Vision Research Foundation and Ethics Committee and followed the principles of the Declaration of Helsinki. A written informed consent was obtained from all participants before enrolling in the study. Study sample included 60 participants, with 30 workers who were employees of petroleum manufacturing plant (cases), and 30 age-matched controls, who were workers from other office jobs. Some age-matched controls were from other industries such as hospital and office jobs who were not exposed to solvents. We excluded people who had congenital color blindness and ocular pathologies and people who were under medications for systemic illnesses such as diabetes mellitus, tuberculosis, and malaria, and were chronic consumers of alcohol and smokers.

Comprehensive eye examination included eliciting detailed medical, ocular history, personal history, occupational history (years of experience, hours of work, and use of personal protective equipment), visual acuity testing, refraction, cover test, pupillary examination, color vision (using Ishihara pseudoisochromatic plates), slit lamp biomicroscopic examination, intraocular pressure measurement (air puff tonometer), and fundus evaluation (non-mydriatic fundus camera). All the tests were performed in standard lighting conditions and environment. Visual acuity was assessed with internally illuminated LogMAR chart, contrast sensitivity with Functional Acuity Contrast Test chart, color vision with Farnsworth Munsell (FM) 100 hue test, and fields using Frequency Doubling Perimeter. The biological samples (molecular markers) from both the groups were collected and analyzed based on the protocol proposed by the National Institute of Occupational Safety and Health (NIOSH) using high performance liquid chromatography (HPLC).[9]

Biological analysis

Liver and kidney function tests: All the parameters including creatinine were analyzed in clinical analyzer (Dade Behring).

For HPLC analysis of hippuric acid and methylhippuric acid, 1 mg of hippuric and 1 mg of methylhippuric acid were taken separately in 1.5 ml Eppendorf vials. This was made to 1 ml with the buffer, mixed well, and kept aside. Different concentrations of hippuric and methylhippuric acid were taken as 2, 4, 6, 8, and 10 µg/ml, and a preparation was made with the buffer. A total of 20 µl of standards was injected on the same day as well as on different days, and the standard graphs were plotted for different concentrations against the area in milli absorbance units. Control urine with negligible hippuric acid and methylhippuric acid content was also spiked along with the hippuric and methylhippuric acid working standards to assess recovery with biological matrix.

Statistical analysis

All the parameters and patient details were entered in MS excel 2003. Statistical analysis was performed using SPSS (Statistical Package for Social Sciences, Version 12.0, SPSS Inc., Chicago). All the parameters were checked for normality using Kolmogrov–Smirnov’s (KS), test and it was found that all the parameters were normally distributed. For parameters that showed statistical significance with KS test, Mean ± SD was given. Only two-tailed tests were performed. P value of less than 0.05 was considered to be statistical significance. Inferential statistics were performed accordingly.

RESULTS

Visual acuity

All the workers in the two groups had a visual acuity of more than 0.01 LogMAR units.

Contrast sensitivity function

The mean difference at 12cpd was 0.29 ± 0.0089 and 0.29 ± 0.089 among controls and workers respectively (P = 0.025*). Other spatial frequencies (1.5, 3, 6, 18) cpd were the same among the workers and controls.

Visual fields between workers and control groups

The mean difference and the standard error between the protected group and controls in mean deviation was −0.31 ± 0.36 dB, with a P value of 0.933.

Color vision function among workers and controls

Blue yellow colour vision defects were found in 16 workers and red green defects were found in 3 workers as explained in the Figure 1. The difference in total error score and colour confusion index was noted between the groups. The
mean difference and standard error between the groups for total error score were found to be 15.36±6.98 (0.032*) and 0.11±0.05 (0.037*) for colour confusion index as explained in Table 1.

**DISCUSSION**

In this study, the visual functions of workers in the protected environment (organized sector) and the effect of exposure of organic solvents were studied. To the best of our knowledge, this is the first study in India to examine change in visual functions when exposed to organic solvents. The individual level of exposure to organic solvents can be assessed by molecular markers. This will help in providing guidelines for personal protective equipment and to emphasize safe working environment in this and other allied industries.

As part of a systematic prospective study, after ruling out abnormal liver functions by laboratory investigations and other systemic diseases based on workers’ history, documented using a proforma, we estimated the levels of hippuric acid and methylhippuric acid among the groups. In parallel, visual function tests were performed for both the groups. Age-matched controls were also subjected to all the analysis similar to the workers.

The observations in the study included visual functions and biological parameters. Our results suggest that there was a change in both the chromatic and achromatic attributes of vision. The effect of organic solvents on the visual acuity of an individual has not been reported in the literature, except by Costa et al. Our study showed the best corrected visual acuity of ≥0.01 LogMAR units and near vision of N6 in workers and age-matched controls, suggesting that vision was not affected, which is in agreement with Costa et al.

![Figure 1: Color vision defects among groups](image)

The mean contrast sensitivity scores of the protected group were almost similar to the age-matched controls at all the spatial frequencies. Gong et al., Boeckelman et al., and Costa et al. have reported that contrast sensitivity was reduced at all spatial frequencies from 1.5 cpd to 20 cpd among furniture factory workers and painters. The contrast sensitivity function was reduced in the worker group compared to controls at 42 cpd. Although the difference was statistically significant, it was not clinically significant because the mean difference was less. A study done among gas station workers showed that the contrast sensitivity function was reduced in high spatial frequencies 20 and 30 cpd. However, here, the loss among workers were at higher spatial frequency. The minor differences at each spatial frequency could not be noted, which could be attributed to the methodology of testing among our groups. Though computerized psychophysical method performs precise measurement, FACT picked up differences in contrast sensitivity in our study, and hence, it can also be used as a screening tool.

We examined color confusion which is a tendency of an individual to mix up colors while arranging in a panel color vision test. We found that, among the 30 workers, 16 had blue yellow color confusion and 3 had red green confusion, which was more when compared to controls. Mutray et al. and Paramei et al. have reported blue yellow color confusion exclusively among print shop workers and painters. A study performed by Zalvic et al. among printing press workers reported that 62.2% had blue-yellow dyschromatopsia. The blue yellow defects are present even at low level of exposure among workers exposed to organic solvents. The blue yellow confusion in workers could be attributed to their years of exposure in this industry. Our study also showed few red green color confusion despite ruling for congenital color defects.

The difference in color vision parameters such as color confusion index and the total error score was done between the groups. There was a difference in total error score and the color confusion index between groups in the organized sector and their age-matched controls in our study. A similar study done in Africa among crane operators in the refinery showed that approximately 26% of the people had blue yellow dyschromatopsia among 30 people; however, they did not compare it with age-matched normal population. Another study done by Kaur et al. reported that there was both blue yellow and nonpolar defects found in workers exposed to organic solvents when compared to controls. The change in

| Parameters                  | Workers (n=30) | Controls (n=30) | Mean difference±std error | P*          |
|-----------------------------|---------------|----------------|--------------------------|-------------|
| Total error score           | 53.5±23.40    | 37.14±29.96    | 15.36±6.98               | 0.032*      |
| Color Confusion Index       | 1.40±0.18     | 1.28±0.21      | 0.11±0.05                | 0.037*      |
color vision could be attributed to more number of exposure years in the same environment.

Mergeler et al., Cavalleri et al., and Campagna et al. reported that there was an increase in color confusion index among people who were exposed to organic solvents,\(^{[19-21]}\) which is similar to our study; however, they did not compare it with age-matched normals to prove the hypothesis. Other studies reported by Gong et al. and Costa et al. showed similar results on comparison with age-matched controls.\(^{[10,11]}\) Although the calculation of the color confusion index was based on a quantitative method proposed by Vingrys in all the studies, the method of color vision testing was different.\(^{[21]}\) We used FM 100 Hue, which is based on hue discrimination, whereas other studies used Lanthony Desaturated panel 15 tests, which are based on unsaturated color caps.

When we examined the risk factors for color vision defect after adjusting for age, we found that the place of work (or exposure) was a major risk factor with an odds ratio of 4.43, however, the excretion of hippuric acid among the workers was not a risk factor for color vision defect but was an indicator for exposure [Table 2]. Although few of the controls had color vision defects, it was not associated with age. This could be attributed to any other early changes at the retinal level. An electrophysiological study could possibly provide the reason for the changes in both the workers and controls.

This change in color vision could be attributed to the reasons suggested by Gobba et al. and Muttray et al. of bring due to direct influence of the organic solvent on photoreceptors.\(^{[14,20]}\) Edling et al. reported that changes in the neurotransmitter system at the retinal or cortical level due to glutamate, dopamine, and acetylcholine can cause color vision defects.\(^{[22]}\)

On examining the effects of solvents on visual fields in our study, there was no significant difference in the mean deviation between the groups. Lacerda et al. reported that there was a decrease in the mean detection threshold observed among gas station workers in 10\(^{\circ}\) and 60\(^{\circ}\) eccentricity when compared to age-matched controls.\(^{[13]}\) A study done by Costa et al. showed that there was a difference in mean deviation \(-1.80 \pm 2.16\) and \(-0.30 \pm 0.94\) among the exposed and control group, respectively.\(^{[20]}\) The reason for this disagreement could be the methodology of testing.

In addition to the visual functions, we analyzed biological parameters in all the groups. Liver function test revealed that there was no difference between the workers and age-matched controls, which indicated that the liver functioned normally [Table 3]. The urinary metabolites of toluene and xylene were also studied among the groups. There was a significant difference in the excretion level of hippuric acid between the workers in the protected group and the controls (\(P < 0.049\)), with a mean hippuric acid level of 0.49 ± 0.41 g/g creatinine and 0.30 ± 0.31 g/g creatinine, respectively [Table 4]. Steenkamp et al. also showed a spike in the urinary hippuric acid level associated with postshift among refinery workers. However, their study did not compare the levels with age-matched controls.\(^{[17]}\) This study indicates that exposure to organic solvents can result in increased urinary excretion of hippuric acid. Further studies are required to validate this as a marker of exposure. The increase in the urinary metabolite was seen in all the workers, however, it was not more than the threshold level value proposed by the National Institute for Occupational Safety and Health (NIOSH) guidelines, which is 1.65 g/g creatinine for hippuric acid and 1.5 g/g creatinine for methylhippuric acid.\(^{[20]}\) Thus, we found that the blue yellow color confusion was present among workers in a petrochemical refinery plant, though they were protected, however, low levels of exposure can cause changes and neurobehavioral disturbances.

CONCLUSION

Blue yellow confusion was seen among workers when compared

### Table 2: Age adjusted risk factors for color vision defects among the workers and controls

| Parameters                              | Age adjusted odds ratio | 95% confidence intervals | \(P\)  |
|------------------------------------------|-------------------------|--------------------------|-------|
| Exposure                                 | 4.43                    | 1.36–14.4                | 0.013 |
| Excretion of Hippuric acid g/g creatinine | 2.67                    | 0.51–13.76               | 0.240 |

### Table 3: Difference in liver function test parameters in the groups

| Parameters with units | Mean difference±std error | \(P\) | Difference between two groups |
|-----------------------|---------------------------|-------|------------------------------|
| Total bilirubin (mg/dL) | 0.11±0.91                 | 0.244 |
| Alkaline phosphatase (U/L) | 2.03±4.71               | 0.186 |
| ALAT (U/L)            | 0.103±2.54                | 0.080 |
| Total protein (g/dL)  | 0.20±0.86                 | 0.063 |
| Albumin (g/dL)        | –0.03±0.056               | 0.277 |
| Globulin (g/dL)       | 0.203±0.71                | 0.946 |
| SGOT (U/L)            | –0.414±1.59               | 0.923 |
| GGTP (IU/L)           | 0.241±4.03                | 0.917 |
| Urine creatinine (mg/dL) | 0.024±0.114              | 0.925 |

### Table 4: Hippuric acid levels between the workers and controls

| Parameters                             | Workers (n=30) | Controls (n=30) | Mean difference±std error | \(P\)  |
|----------------------------------------|----------------|----------------|--------------------------|-------|
| Hippuric acid g/g creatinine           | 0.49±0.41      | 0.30±0.31      | 0.19±0.96                | 0.049* |
| Methyl hippuric acid g/g creatinine    | 0.16±0.17      | 0.10±0.12      | 0.06±0.04                | 0.154  |

*\(P\) values \(< 0.05\) are considered significant.
to age-matched controls. The contrast sensitivity function was decreased at 42 cpd spatial frequency among workers. The urinary metabolite, hippuric acid, excretion was more among workers, although it was within the threshold level. A worker exposed to organic solvents in a petrochemical industry has a risk of developing color vision defects. Thus, we recommend that the visual functions and biological markers should be monitored and the effect of these solvents in the long term should be studied. Similarly, a study to assess the chronic and long-term exposure among unprotected groups should be conducted.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Available from: http://www.dnb.co.in/Chemical/overview.asp. [Last accessed on 1/4/2014].
2. Available from: Web page of reliance industries -www.ril.com. [Last accessed on 25/2/2014].
3. Dick FD. Solvent Neurotoxicity. Occup Environ Med 2006;63:221-6.
4. Available from: http://www.dnb.co.in/Chemical/overview.asp. [Last accessed on 01/4/2014].
5. International Programme on Chemical Safety (IPCS). Chemical Environmental Health Criteria 52: Toluene. Geneva: WHO, 1986.
6. Martinez-Alfaro M, Alcaraz-Contreras Y, Cárabez-Trejo A, Leo-Amador GE. Oxidative stress effects of thinner inhalation. Indian J Occup Environ Med 2011;15:87-92.
7. Win-Shwe TT, Fujimaki H. Neurotoxicity of toluene. Toxicol Lett 2010;198:93-9.
8. Gralewicz S, Dyzma M. Organic solvents and the dopaminergic system. Int J Occup Med Environ Health 2005;18:103-13.
9. National Institute of Occupational Safety and Health Manual of Analytical Methods (NMAM). 4th ed. Atlanta, USA: DHHS (NIOSH) Publication 98-119; 2003. p. 154.
10. Costa TL, Barboni MT, Moura AL, Bonci DM, Gualtieri M, de Lima Silveira LC, et al. Long-Term Occupational Exposure to Organic Solvents Affects Color Vision, Contrast Sensitivity and Visual Fields. Plos One 2012;7:e42961.
11. Gong Y, Kishi R, Kasai S, Katakura Y, Fujiwara K, Umemura T, et al. Visual Dysfunction in Workers Exposed to a Mixture of Organic Solvents. Neurotoxicology 2003;24:703-10.
12. Boeckelmann I, Pfister EA. Influence of occupational exposure to organic solvent mixtures on contrast sensitivity in printers. J Occup Environ Med 2003;45:25-33.
13. Lacerda EM, Lima MG, Rodrigues AR, Teixeira CE, de Lima LJ, Ventura DF, et al. Psychophysical Evaluation of Achromatic and Chromatic Vision of Workers Chronically Exposed to Organic Solvents. J Environ Public Health 2012;2012:784390.
14. Muttray A, Wolff U, Jung D, Konietzko J. Blue-yellow deficiency in workers exposed to low concentrations of organic solvents. Int Arch Occup Environ Health 1997;70:407-12.
15. Paramei GV, Meyer-Baron M, Seeber A. Impairments of color vision induced by organic solvents: A meta-analysis study. Neurotoxicology 2004;25:803-16.
16. Zavalic M, Mandic Z, Turk R, Bogadi-Sare A, Plavec D, Gomzi M, et al. Assessment of color vision impairment in male workers exposed to toluene generally above occupational exposure limits. Occup Med 1988;48:175-80.
17. Steenkamp MKJ. An investigation into visual problems of crane operators at a petrochemical factory and possible link with hydrocarbons. South Africa: Masters thesis, Potchefstroom University; 2004.
18. Sharanjeet-Kaur, Mursyid A, Kumaruddin A, Ariffin A. Effect of petroleum derivatives and solvents on colour perception. Clin Exp Optom 2004;87:339-43.
19. Mergler D, Bélanger S, De Grosbois S, Vachon N. Chromal focus of acquired chromatic discrimination loss and solvent exposure among print shop workers. Toxicology 1988;49:341-8.
20. Cavalleri A, Gobba F, Nicali E, Fiochi V. Dose-related color vision impairment in toluene-exposed workers. Arch Environ Health 2000;55:399-404.
21. Campagna D, Stengel B, Mergler D, Limasset JC, Diebold F, Michard D, et al. Color vision and occupational toluene exposure. Neurotoxicol Teratol 2001;23:473-80.
22. Vingrys AJ, King-Smith PE. A Quantitative Scoring Technique For Panel Tests of Color Vision. Invest Ophthalmol Vis Sci 1998;29:50-64.
23. Edling C, Hellman B, Arvidson B, Andersson J, Hartzog P, Lilja A, et al. Do organic solvents induce changes in the dopaminergic system? Positron emission tomography studies of occupationally exposed subjects. Int Arch Occup Environ Health 1997;70:186-90.