SciMedCentral

Journal of Substance Abuse & Alcoholism

Research Article

Biochemical Assessment of Inhalant Use among Adolescents: A Pilot Study from Tertiary De-Addiction Center of India

Roshan Bhad[1], Raka Jain[2]*, Anju Dhawan[3] and Manju Mehta[4]

[1]*Senior Resident, Department of Psychiatry and National Drug Dependence Treatment Centre, All India Institute of Medical Sciences, New Delhi-11029, India*
[2]*Professor, National Drug Dependence Treatment Centre and Department of Psychiatry, All India Institute of Medical Sciences, New Delhi-11029, India*
[3]*Professor, National Drug Dependence Treatment Centre and Department of Psychiatry, All India Institute of Medical Sciences, New Delhi-11029, India*
[4]*Professor, Department of Psychiatry, All India Institute of Medical Sciences, New Delhi-11029, India*

***Corresponding author**
Raka Jain, Rm. No. 4090, Department of Psychiatry, 4th floor, Teaching Block, All India Institute of Medical Sciences, New Delhi- 110029, India, Tel: +91-011-26593236; 26593595; Fax: 91-011-26588663, 26588641; Email: rakajain2009@gmail.com

Submitted: 16 October 2014

Accepted: 03 December 2014

Published: 05 December 2014

Copyright
© 2014 Bhad et al.

OPEN ACCESS

Keywords
- Inhalant abuse
- Adolescent substance use
- Toluene
- Biochemical validation
- Screening test

Abstract

Inhalant abuse is a serious problem worldwide, particularly in disadvantaged populations and among adolescents. However, very few studies are available on objective measurements of inhalant abuse among adolescents. A pilot study was conducted on twenty-three adolescent inhalant users with recent use within one month on self-report, with the aim of biochemical validation of inhalant use by objective method in a clinical setting. Urine hippuric acid level was measured using gas chromatography with NPD (Nitrogen Phosphorous Detector) detector as a part of biochemical validation. More than fifty percent of adolescents were confirmed positive for intentional exposure of toluene in urine. The study findings are indicative of feasibility of biochemical testing for assessment of inhalant use and envisage the development of screening test for inhalant abuse in near future. Such objective validation would be beneficial for management of inhalant abuse problem among adolescents.

ABBREVIATIONS

GLC: Gas Liquid Chromatography; NPD: Nitrogen Phosphorous Detector; TLC: Thin Layer Chromatography; UCL: Urine Creatinine Level; UHL: Urine Hippuric Acid Level; I.Q.: Interquartile Range

INTRODUCTION

In the last few decades inhalant abuse is on rise and has become an issue of great concern worldwide. Factors responsible for this increasing use include easy availability, accessibility and affordability. However among adolescents in India, inhalant abuse appears far more complex and multidimensional [1–5]. More challenging is the management of inhalant abuse, which is known to cause extensive medical, psychiatric, and psychological damage but there are hardly any pharmacological or non-pharmacological interventions available to tackle this problem [6–8]. There is a dearth of research in area of management of adolescent inhalant abuse. Additionally, objective assessment is limited by non-availability of any screening test to detect inhalant use.

Toluene, an important industrial organic solvent, is the most commonly abused inhalant across the world and in India [2,3,9–11]. Its exposure remains significant in an occupations involving manufacture of paints, glues and adhesives. Laboratory analysis of inhalant abuse requires the analysis of biological fluids, commonly using gas chromatography [12]. Hippuric acid, a primary urinary metabolite of toluene has been biochemically detected in urine for its occupational exposure in past [12–15]. However, there is paucity of literature for biochemical validation of toluene abuse among inhalant users in a clinical setting. We conducted a pilot study among adolescent inhalant users, which aimed at biochemical assessment of inhalant use by an objective method in a clinical setting.

MATERIALS AND METHODS

The study was conducted over a six-month period (July 2010 to December 2010) at the National Drug Dependence Treatment Center, All India Institute of Medical Sciences (AIIMS), New Dehi, India. Ours is a tertiary care hospital in New Delhi, India, actively engaged in teaching, training and research activities and is an apex centre for management of substance related disorders. For the purpose of this study, consecutive adolescent male inhalant users in the age group 13 to 18 years, who reported current inhalant use in past one month, were recruited. The institutional ethics committee of AIIMS cleared the study protocol. Written informed assent/consent was taken from the participants and their parents/guardian. A total of twenty-three adolescent inhalant users were first examined by the clinician and thereafter 5 ml of urine was collected under close supervision and sent to Centre's laboratory for urinary hippuric acid (toluene) testing. Urinary hippuric acid level was measured using known technique of gas liquid chromatography equipped with Nitrogen phosphorus detector (NPD) as a part of biochemical assessment [16]. In the current study, a simplified, efficient method for separation of hippuric acid developed in our laboratory by gas liquid chromatography was used [17]. The gas Chromatograph (Model 7890A Agilent India Pvt. Ltd, USA) was equipped with Auto Sampler (7683B series), split/split less inlet, nitrogen phosphorus detector (NPD) and fused –silica capillary column coated with HP-5 cross-linked 5% diphenyl and 95% dimethylpolysiloxane (30m x 0.320 i.d., 0.25µm film thickness) [17]. Urinary creatinine was measured by Echoplus fully automated biochemistry autoanalyser (Logotech India, India). The ratio of urine hippuric acid level (UHL) to urine creatinine level (UCL) was calculated to detect toluene exposure [10,12].

RESULTS AND DISCUSSION

Mean age of the participants was 16 (S.D. = 1.859, I.Q. 14-18). All of the participants were male and from urban background. Most common inhalant product abused was typewriters fluid Eraz-Ex diluter and whitener, manufactured by Kores in 21/23 (91%) adolescents. Among study participants, mean age of initiation for inhalant use was 13.5 years. And total duration of inhalant use was 28.3 (SD=21.9) months. The last dose of inhalant use was between 1-3 days from the day of urine testing in 15/23 (65%) adolescents, 4-7 days in 3/23 (13%) adolescents, 8-15 days in 3/23 (13%) adolescents and > 15 days before in 2/23 (9%) adolescents respectively. Seven out of 23 adolescents (30.4%), urine toluene level was within normal range (UHL/UCL ratio < 1.5) whereas 13/23 (56.5%) detected positive for urine toluene level – intentional exposure (UHL/UCL ratio > 3) and 3/23 (13 %) detected positive for urine toluene level – exposure (UHL/UCL ratio >1.5 < 3) (Table 1) [15]. There was significant difference between last dose and urine hippuric/creatinine ratio Mann-Whitney U (U=0.000, p = 0.001). These finding suggests that if toluene level (UHL/UCL) is used as a screening test then most likely it will be applicable for the screening of recent use of inhalants however, more research is required to confirm this

Table 1: Results for Biomarker of toluene in urine.

Investigations	Normal (R) *	Inhalant users	Abnormal finding (n=23)
Urine hippuric acid level (UHL) mg/ml	0.34 -1.40	0.017-6.08	12 (52.2%)
Urine creatinine level (UCL) mg/dl	39-259	3.41-151.6	7 (30.4%)
UHL/UCL ratio	< 1.5	0.15-13.12	16 (69.6%)

As standardized by NDDTC laboratory [17].

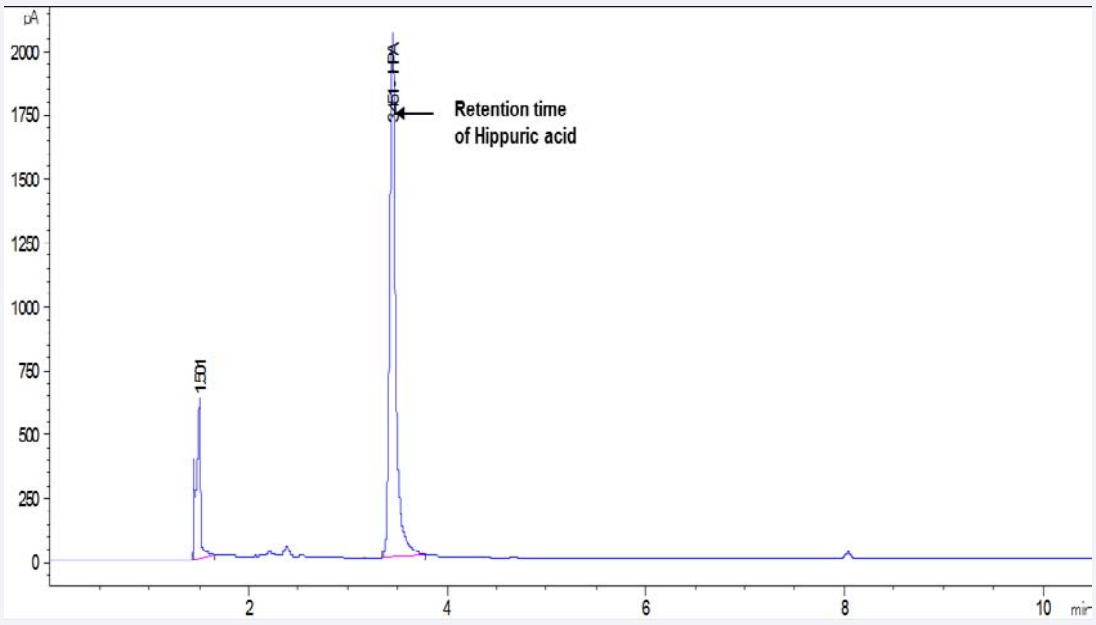

Figure 1 GLC chromatogram of Hippuric acid in control urine.

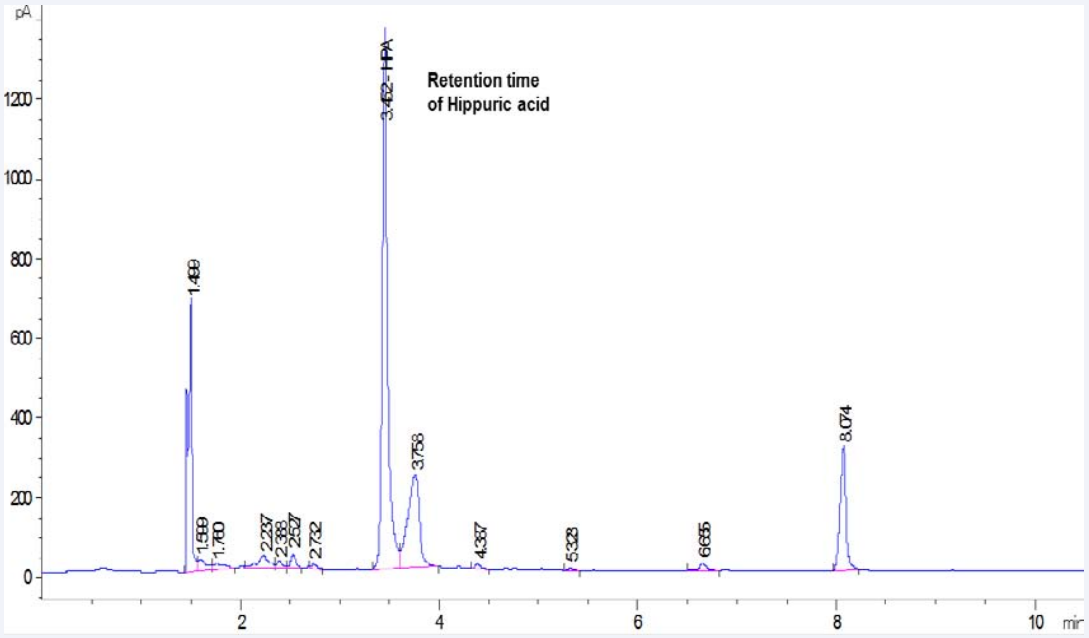

Figure 2 GLC chromatogram of Hippuric acid in adolescents urine sample.
Abbreviations: GLC: Gas Liquid Chromatography

finding. Figure 1 and 2 shows the gas liquid chromatography (GLC) chromatogram of hippuric acid in control urine and in adolescents urine sample respectively. In the present study, 50% of individuals were detected positive for toluene in urine, suggestive of intentional exposure in individuals using inhalants within last one to three days before testing. The difference in percentage of detection of toluene could be due to different group of population i.e. homeless adolescents street children in previous study and treatment seeking adolescents in the present study [16].

This is one of the few studies to use biochemical method for assessing recent inhalant use in a clinical setting. Results are indicative of relationship between last dose of exposure and urine toluene level. All adolescents with the use of inhalants in last 1-3 days were detected positive for the exposure of the inhalants. As the self- report is questionable among substance users [18], it is possible that actual time of exposure to toluene in all such adolescents was within 24 hours of urine testing. It would be interesting to see the similar relationship between dose of inhalant use and urine toluene level. Considering the fact that toluene is primarily excreted in the urine as the metabolite, hippuric acid and excretion of hippuric acid is usually complete within 24 hours after exposure which is related to the level of exposure, urine hippuric acid level would be good screening test to detect recent and heavy inhalant use in clinical samples [19–22]. However, the study findings need to be validated in larger sample, before advocating routine use of such screening test in management of inhalant abuse problem. In the current study gas liquid chromatography equipped with Nitrogen phosphorus detector (NPD) was used which is quite specific and sensitive for toluene assay and can be used both for qualitative (screening and confirmation) as well as quantitative purposes. Urine hippuric acid level adjusted with creatine level is the best expression of crude values for the exposure of toluene [23].

This study had certain limitations. The small sample size may limit the generalizability of its findings. In addition, the study group was selected by self- report and no control group was used. Also, no dietary history details were recorded. Benzoate in foods and drinks is one of the major confounder in hippuric acid evaluation. The level of markers urine in non- exposed subjects may vary depending on local dietary customs and it may have affected the results of the present study [24,25]. Also, possible differences in metabolism of toluene were not accounted for which may influence the findings to some extent. It would be worthwhile to conduct similar study taking into consideration dietary details in larger sample size.

CONCLUSION

Overall the results indicate feasibility of biochemical testing for assessment of inhalant use. A future study with a larger sample size could confirm role of urine hippuric acid level as a screening test for adolescent inhalant use in a clinical setting. Non-invasive and easy collection of sample will make it more suitable for routine clinical use. These observations warrant further studies on other metabolites of toluene like benzoyl glucuronide, p-cresol and o-cresol for their potential role as a screening test for inhalant abuse.

ACKNOWLEDGEMENTS

The authors acknowledge Mr. Nizamuddin Saifi, laboratory technician, National Drug Dependence Treatment Centre (NDDTC), AIIMS, New Delhi, India for providing technical assistance for the study.

REFERENCES

1. Gigengack R. “My body breaks. I take solution.” Inhalant use in Delhi as pleasure seeking at a cost. Int J Drug Policy. 2014; 25: 810-818.

2. Seth R, Kotwal A, Ganguly KK. Street and working children of Delhi, India, misusing toluene: an ethnographic exploration. Subst Use Misuse. 2005; 40: 1659-1679.

3. Sharma S, Lal R. Volatile substance misuse among street children in India: a preliminary report. Subst Use Misuse. 2011; 46 Suppl 1: 46-49.

4. Basu D, Jhirwal OP, Singh J, Kumar S, Mattoo SK. Inhalant abuse by adolescents: a new challenge for Indian physicians. Indian J Med Sci. 2004; 58: 245-249.

5. Verma R, Balhara YP, Deshpande SN. Inhalant abuse: a study from a tertiary care de-addiction clinic. East Asian Arch Psychiatry. 2011; 21: 157-163.

6. MacLean S, Cameron J, Harney A, Lee NK. Psychosocial therapeutic interventions for volatile substance use: a systematic review. Addiction. 2012; 107: 278-288.

7. Garland EL, Howard MO. Volatile substance misuse: clinical considerations, neuropsychopharmacology and potential role of pharmacotherapy in management. CNS Drugs. 2012; 26: 927-935.

8. Ridenour TA. Inhalants: not to be taken lightly anymore. Curr Opin Psychiatry. 2005; 18: 243-247.

9. Bruckner JV, Peterson RG. Evaluation of toluene and acetone inhalant abuse. I. Pharmacology and pharmacodynamics. Toxicol Appl Pharmacol. 1981; 61: 27-38.

10. Narayanaswamy JC, Viswanath B, Ravi M, Muralidharan K. Inhalant dependence: data from a tertiary care center in South India. Indian J Psychol Med. 2012; 34: 232-236.

11. Praharaj SK, Verma P, Arora M. Inhalant abuse (typewriter correction fluid) in street children. J Addict Med. 2008; 2: 175-177.

12. Kawai T, Mizunuma K, Okada Y, Horiguchi S, Ikeda M. Toluene itself as the best urinary marker of toluene exposure. Int Arch Occup Environ Health. 1996; 68: 289-297.

13. Kawai T, Yasugi T, Mizunuma K, Horiguchi S, Iguchi H, Uchida Y. Comparative evaluation of urinalysis and blood analysis as means of detecting exposure to organic solvents at low concentrations. Int Arch Occup Environ Health. 1992; 64: 223-234.

14. Ukai H, Kawai T, Inoue O, Maejima Y, Fukui Y, Ohashi F. Comparative evaluation of biomarkers of occupational exposure to toluene. Int Arch Occup Environ Health. 2007; 81: 81-93.

15. Broussard LA. The role of the laboratory in detecting inhalant abuse. Clin Lab Sci. 2000; 13: 205–209.

16. Thiesen FV, Noto AR, Barros HM. Laboratory diagnosis of toluene-based inhalants abuse. Clin Toxicol (Phila). 2007; 45: 557-562.

17. Jain R. An efficient screening method for detection of toluene -based inhalant abuse in urine by Gas Chromatography-Nitrogen Phosphorous Detector. Addict Disord. Their Treatment. 2014 doi: 10.1097/ADT.0b013e31829bb3d0.

18. Jain R. Self-reported drug use and urinalysis results. Indian J Physiol Pharmacol. 2004; 48: 101-105.

19. Löf A1, Wigaeus Hjelm E, Colmsjö A, Lundmark BO, Norström A, Sato A. Toxicokinetics of toluene and urinary excretion of hippuric acid after human exposure to 2H8-toluene. Br J Ind Med. 1993; 50: 55-59.

20. Wilczok T, Bieniek G. Urinary hippuric acid concentration after occupational exposure to toluene. Br J Ind Med. 1978; 35: 330-334.

21. Cok I1, Dagdelen A, Gökçe E. Determination of urinary hippuric acid and o-cresol levels as biological indicators of toluene exposure in shoe-workers and glue sniffers. Biomarkers. 2003; 8: 119-127.

22. Raikhlin-Eisenkraft B1, Hoffer E, Baum Y, Bentur Y. Determination of urinary hippuric acid in toluene abuse. J Toxicol Clin Toxicol. 2001; 39: 73-76.

23. Nicolli A1, Chiara F2, Gambalunga A3, Carrieri M4, Bartolucci GB5, Trevisan A6. Reliability of urinary excretion rate adjustment in measurements of hippuric acid in urine. Int J Environ Res Public Health. 2014; 11: 7036-7044.

24. Ong CN. Reference values and action levels of biological monitoring in occupational exposure. Toxicol Lett. 1999; 108: 127-135.

25. Inoue O, Seiji K, Watanabe T, Kasahara M, Nakatsuka H, Yin SN. Possible ethnic difference in toluene metabolism: a comparative study among Chinese, Turkish and Japanese solvent workers. Toxicol Lett. 1986; 34: 167-174.

Cite this article

Bhad R, Jain R, Dhawan A, Mehta M (2014) Biochemical Assessment of Inhalant Use among Adolescents: A Pilot Study from Tertiary De-Addiction Center of India. J Subst Abuse Alcohol 2(3): 1021.