

A survey of the effect of toluene on the impact of noise on hearing loss in workers

Ahmadi Asour A, MSPH^{1*}, Golbabaie F, PhD², Nassiri P, PhD³

1- Faculty Member, Dept. of Occupational Health, Sabzevar University of Medical Science, Sabzevar, Iran. 2- Professor, Dept. of Occupational health, Tehran University of Medical Science, Tehran, Iran. 3- Professor, Dept. of Occupational Health, Tehran University of Medical Science, Tehran, Iran

Abstract

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Background: Ototoxic chemicals can impair the sense of hearing and balance. In the past decades, the ototoxicity of solvents and their interaction with noise have become evident. This study has been carried out in the shoe manufacturing factory in Tehran (Iran) with the aim of evaluating the combined effects of noise and toluene on the workers' hearing.

Materials and Methods: This cross-sectional and analytical study was conducted on 64 workers selected through census. The participants were assigned to 3 groups according to their exposure to noise and toluene. Group 1 consisted of 33 workers who were exposed to noise, group 2 of 5 exposed to toluene, and group 3 of 26 exposed to noise and toluene. Toluene concentrations were measured in the workers' breathing zone as well as A-weighted sound pressure level (SPL), overall noise level (LpA) and equivalent continuous A-weighted SPL over 30 minutes, and the equivalent noise level A (LeqA) in the head position of workers. Then, the noise level was calculated and hearing thresholds were measured in 500-4000 Hz frequency range. The amounts of air and bone hearing loss were also calculated.

Results: The results indicated that the relationship between hearing loss caused by noise (group 1) and noise and toluene (group 3) were statistically significant ($P < 0.50$). Hearing loss due to toluene in midrange frequencies was more pronounced than in high frequencies.

Conclusions: The results of the study suggest that authorities should pay greater attention to agents such as noise which affect the hearing loss and health of employees, especially with respect to sensitivity of hearing system disorders. Moreover, individual characteristics should also be considered in employing future personnel.

Keywords: Noise, Toluene, Hearing Loss, Workers

Introduction

Noise and chemicals are the most common health hazards that are present simultaneously in many work environments. For instance, in the United States, approximately 10 million workers are exposed to organic solvents in the industrial sector, where there is also the possibility of frequent exposure to noise (1). Simultaneous exposure to noise and toluene, which is one of the most widely used organic solvents, has been clearly shown to interact in a synergistic adverse fashion on auditory functioning (2). Given that toluene is both ototoxic and neurotoxic, it has been suggested that such an adverse interaction of noise and

toluene on auditory functioning may result from a central action of toluene (3-5). If so, such an adverse synergistic interaction between noise and toluene may also alter other brain functions. This has been reported in a study by Morton et al. (6).

Exposure to noise may result in damage to the inner ear. Noise-induced hearing loss (NIHL) is a significant occupational health problem in industrialized countries (Alberti, 1998) (7). In addition to noise, a wide range of chemicals can impair the inner ear function. Among these

* **Corresponding author:** Akbar Ahmadi Asour, Dept. of occupational health, Sabzevar University of medical science, Sabzevar, Iran.
Email: asour50@yahoo.com

ototoxic agents are organic solvents, which are used as degreasers, adhesives, fuel additives, glues, and thinners. Human and animal studies have shown that several organic solvents can induce hearing loss in the midrange frequency region of the cochlea (e.g., Crofton and Morata) (7). This study was designed to determine whether an additive or synergistic interaction will occur after simultaneous exposure to the organic solvent of toluene and noise. Toluene is a colorless liquid at room temperature with the familiar odor of 'airplane glue'. Toluene is the most widely used substance in the world and it is often abused through inhalation for its euphoric effect. It is not considered carcinogenic (7). Toluene is a gas at body temperature, and thus, is removed quickly from animal or human tissues via the circulation. Solvents have long been suspected to be ototoxic agents. Human epidemiology studies have shown a greater risk for hearing loss among workers exposed to carbon disulfide (8) and toluene (9) than non-exposed workers. Our results confirm that sub chronic exposure to 40 ppm toluene significantly decreases hearing activity and leads to a sensitization to toluene-induced narcosis, as evaluated by loss of righting reflex (10).

As ototoxic substances are a heterogeneous group of chemicals that cause hearing impairment in various toxicological modes of action, risk identification and risk assessment present a challenge of their own (11).

Exposure to aromatic organic solvents may induce hearing loss in rats, the cochlea being the primary target. An issue of concern with ototoxic agents is that they may interact synergistically when administered in combination with noise. Barregard and Axelsson (12) suggested a synergistic interaction between noise and solvents in humans. They tested the hearing of shipyard painters who were exposed to noise as well as organic solvents. They reported a more pronounced hearing loss, based on tone audiograms, than the predicted hearing loss from noise exposure alone. Possible interactions between noise and organic

solvents were further investigated by a number of researchers (1,8,9,10). Despite these investigations, this is a controversial topic; some studies provided evidence that there is a synergistic interaction between noise and solvent exposure in humans, while others did not find any synergistic effect (12). Ziba Loukzadeh, in her study, showed that the mean hearing threshold at all frequencies among petrochemical workers was normal (below 25 dB) (13). She did not observe any significant association between solvent exposure and high-frequency or low-frequency hearing loss. This study showed that temporary exposure (less than 4 years) to a mixture of organic solvents, in the absence of noise exposure, does not affect workers' hearing threshold in audiometry tests (13).

In addition to the epidemiological results described above, animal studies have been performed to investigate the combined effects of noise and organic solvents on hearing. An interaction between noise and toluene was reported by Johnson et al (14). Rats were first exposed to 1000 ppm toluene (16 hours/day, 5 days/week for 2 weeks). This was followed by 100 dB of equivalent noise level (Leq) (10 hours/day, 5 days/week for 4 week). Hearing loss was determined by evaluating auditory brainstem responses (ABR). A synergistic interaction occurred after exposure to the combination of toluene and noise (15). However, when the sequence was reversed, with noise exposure preceding toluene exposure, the hearing loss in dB did not exceed the summation of losses caused by noise alone and toluene alone. Muijser et al. studied another ototoxic organic solvent; trichloroethylene (15). Rats simultaneously exposed to 3000 ppm of this compound and 95 dB SPL broadband noise (18 hours/day, 5 days/week, for 3 weeks) showed a significantly enlarged threshold shift at 4 kHz, measured with reflex modification audiometry, as compared to the summation of the threshold shifts in dB induced after exposure to noise alone and toluene alone. However, this synergistic effect was not observed at other

tested frequencies (8, 16, and 20 kHz). The effects of combined exposure to 750 ppm toluene and a 97 dB SPL octave band of noise centered at 8 kHz (6 hours/day, 5 days/week, for 4 weeks) on hearing were also examined in rats. The combination induced synergistic loss in the amplitudes of ABRs (16).

Ilhan Unlu et al. compared the effects of solvent and noise exposure on hearing, together and separately, and showed that combined exposure to solvents and noise can exacerbate hearing loss in workers and that together they are more ototoxic than noise alone (17). In addition to this, even the individual level of solvents is below acceptable levels; thus, if they are found together, they cause a cumulative effect and may damage the auditory system (17). The results of studies by Metwally et al. revealed that sensory neural hearing loss occurred earlier in subjects with combined exposure to noise and solvents at a mean duration of exposure of 16.38 ± 9.44 years compared to 24.53 ± 9.59 years in subjects with exposure to noise alone (18). The difference between the two groups was statistically significant regarding this type of hearing impairment ($P < 0.05$). There was a positive significant correlation between hearing impairment and duration of exposure in the two exposed groups (18).

For workers who are in contact with chemical solvents, noise is usually an integral part of the workplace. The aim of this study was to evaluate the combined effects of noise and toluene on workers' hearing.

Material and Methods

This cross-sectional and analytical study was carried out in the shoe manufacturing factory in Tehran (Iran). The solvent toluene is used to make shoes and workers exposed to its vapors during work. Based on census method, 64 workers were selected and divided into 3 groups, which were exposed to noise, toluene, and noise plus toluene. Group 1 consisted of 33 workers (code1), group 2 of 5 workers

(code2), and group 3 of 26 workers (code3). They were considered together as case and control groups. The participants were assured that their information would remain confidential. The exclusion criteria were a history of hereditary hearing loss and ear surgery. The inclusion criteria were exposure to noise and toluene in combination and alone. The limitation of this study was the sample size. No data were available for estimating the impact of hearing loss due to exposure to toluene alone. This study consisted of several parts, which are described below.

1: Measurement and determination of toluene in the workplace and respiratory zone

Supplies and equipment for sampling vapors of toluene:

- a) Toluene detector tubes and piston pump with a detector tube for pretest manufactured by GASTEC
- b) Activated charcoal sampling tubes with maintenance and limiting orifice
- c) Low flow sampling pump

To ensure the level of toluene, pretest was conducted in different parts of the plant using a toluene detector tube. After ensuring the presence of toluene, activated charcoal tubes made by the laboratory of the Department of Occupational Health, School of Public Health of Tehran University of Medical Sciences (Iran) were used for the sampling of toluene vapors in order to determine Time-Weighted Average (TWA). For personal and environmental sampling, pump model 222-3 S.K.C. with flow rate of 50-200 ml/m was used. Toluene concentration was measured using a combination of ASTM method no. d3687 and d3686, the National Institute for Occupational Safety and Health (NIOSH) method No. 1501, and the Occupational Safety and Health Administration (OSHA) method No. S343. After calibration of the equipment based on the recommendations of NIOSH, the samples were taken into the respiratory zone of workers with the flow rate of 100 ml/minute.

2: Sample collection and preparation

Based on the conducted test, the calculated sampling time was 1 and 1.5 hours. To collect environmental samples, activated, charcoal sampler was placed on a tripod at the height of the respiratory area and connected by pipe to the pump. In total, 150 samples were collected, and 3 samples were excluded from the study because of breakthrough. In this study, toluene was reabsorbed from activated charcoal through the chemical method using carbon disulfide. The samples were transported to the laboratory and analyzed with gas chromatograph (GC) model Varian 3600.

The analysis of samples was performed by GC with the following characteristics:

Column: SE-30 temperature: 38 °C 3m D = 3 mm

Detect. = FID: 200 °C

FlowN2 = 30 ml/minute

Pn2 = 80 PSI

Ph2 = 40 PSI

Sensitivity = 8

3: Sample volume correction

To correct the volume of air samples based on the standard conditions, Temperature, Relative Humidity (RH), and air pressure were measured. Concentration of toluene was calculated in ppm using the following formula:

$$C = \frac{24.45 \times m}{M_w \times V}$$

where C is the concentrations of pollutants (ppm), M the total weight of the desired substance (mg), Mw the molecular weight of solvent (g/me), 24.45 is the molecular volume in 25 °C and 760 mmHg 760 (l/mol), and v the volume of air samples (l/minute).

4: Noise measurement

To measure the overall noise level (LpA) and Leq in different parts of the plant, the sound level meter (CEL model, Casella co. England) along with the noise analyzer were used. The noise analyzed was in the frequency range of 250-8000 Hz.

5: Personal noise exposure measurement (dosimeter)

To measure the rate of personal exposure to noise during a work shift, personal dosimeter (CEL-272model) was used after calibration for the first and third groups.

6: Audiometry

To determine the type of hearing impairment and hearing loss, an audiometric device (Midmied model, Madsen co. Germany) was used. Audiometry was performed in air way and bone way at different frequencies, and audiograms were drawn for left and right ears. The percentage of disability was calculated for each ear separately and also both ears. RLA and RLB codes of analysis were allocated to the disability of air and bone. Workers with hearing loss were clinically examined by a physician for issues such as infection, ruptured eardrum, and etcetera. Participants who had severe hearing problems were excluded from the study.

7: Subjective factors assessment

To collect and study demographic characteristics and assess subjective factors, a questionnaire including 30 questions was completed for every worker, and the collected data were analyzed statistically.

8: Psychometric conditions Measurement

Temperature, RH, and air pressure were measured to correct the volume of collected air under standard conditions. A moisture meter (ASMAN model, Sibata co.Japan) was used for RH measurement. Mercury manometer and thermal anemometer (TA2 model, TSI co.USA) were used for air pressure and temperature measurements.

9: Social hearing loss

To determine the percentage of hearing loss or disability, combined hearing impairment was calculated in the frequencies of 500, 1000, and 2000 Hz, and age correction was performed.

Results

For the analysis of data, S-PLUS (TIBCO Software Inc., Palo Alto, CA, USA) and SAS statistical software (SAS Institute, Cary, NC,

USA) were used. To compare RLB and RLA in the three groups, the non-parametric and covariance statistical methods were used. The indices of RLA and RLB were considered as dependent variables and the abovementioned groups as independent variables (treatment). The variables of years of service, age, dose rate, and concentration of toluene in a work shift (TWA) were considered as confounding variables in the analysis of covariance.

The first result showed that both RLA and RLB variables in the three groups were statistically significant ($P < 0.50$). The majority of hearing losses were observed in

group 3 (RLA = -4.27 and RLB = -2.06). In groups 1 and 3, no significant relation was found between service and distraction, but the difference between RLA and RLB was significant ($P < 0.50$) (Table 1). The analysis showed that in group 1, with increase in relative humidity, air velocity, LPeq, and SPL, the RLA and RLB increased and their difference was significant ($P < 0.50$). In group 3, there was a significant difference between RLA and D; with increasing of D%, RLA also increased). Considering the results obtained in groups 1 and 3, RLA has shown a significant difference ($P < 0.50$) (Table 1).

Table 1: Measured parameters in the three occupational groups

	Group 1			Group 2			Group 3		
	x	s	N	x	S	N	x	s	N
Age	41.8	7.56	33	45	8.51	5	39.5	10.76	26
Time served	12.73	5.35	33	17.4	7.09	5	10.65	7.15	26
TWA (ppm)	0	0	0	96.3	6.45	5	10.73	8.87	26
RLA	-3.45	12.8	33	0.02	9.02	5	4.27-	7.5	26
RLB	-0.78	13.51	33	0.33	8.63	5	-2.06	15.8	26
D%	92.64	2.91	33	-	-	5	83.53	4.17	26
LpA (dB)	99.3	10.15	33	-	-	5	83.5	9.11	26
Leq (dB)	95.8	11.05	33	-	-	5	77.6	3.9	26
Air velocity (m/s)	0.89	0.03	33	1.53	2.88	5	0.7	0.21	26
RH	38	3.94	33	19.7	8.72	5	27	2.57	26
Temperature (°C)	30	0.03	33	27.5	1.51	5	28	0.82	26

TWA: Time-weighted average; RLA: hearing loss for right and left ear (air way); RLB: hearing loss for right and left ear (bone way); D %:(absorbed noise percent); LpA: Overall noise level; Leq: Equivalent noise level; RH: Relative humidity

The concentration of toluene in the breathing zone of workers is illustrated in figure 1. The concentration of toluene for group 1 was 0,

and in the breathing zone of group 2 was higher than group 3.

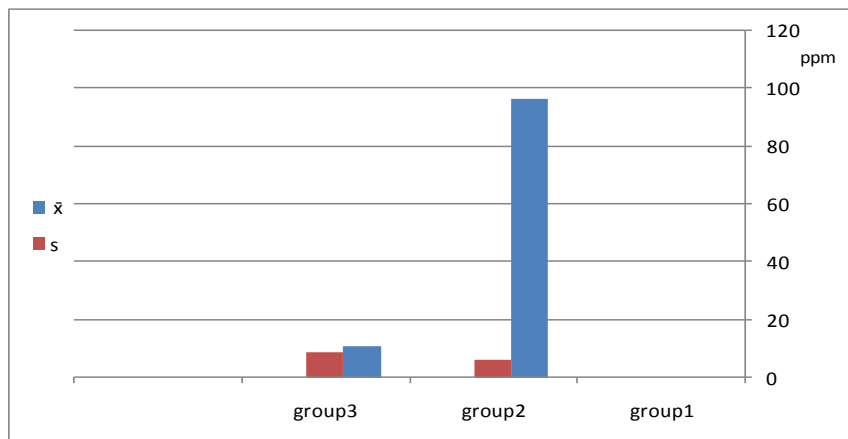


Figure 1: The concentration of toluene in the breathing zone of workers

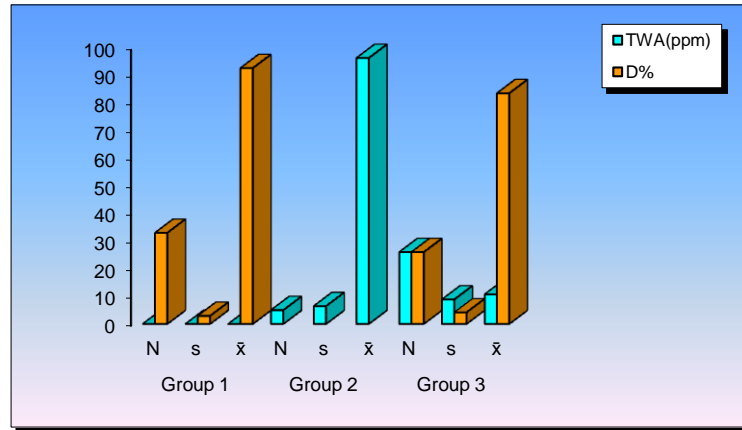


Figure 2: Time weight average of toluene and sound adsorption percentage in the three occupational groups

According to figure 2, in group 1, mean noise level was higher than group 3 (92.64 ± 2.9 dB) and group 2 had higher absorption rate of toluene compared to group 3 (Figure 2).

In group 3, the highest mean SPL, mean TWA, and D% were observed in workers with 1-5 years of experience, 10-15 years of experience, and 5-10 years of experience, respectively. Moreover, data analysis showed that in group 1, with increase in the rate of wind, SPL, and Leq, RLA also increased, and this difference was significant.

Discussion

Previous human studies on the ototoxic effect of occupational exposure to toluene are not conclusive. Since the ototraumatic interaction between solvent and noise exposure was suggested by Barregard and Axelsson (1984) (12), the effects were assumed to be dependent on the exposure dose and period. A series of animal studies provided clear evidence of ototoxic effects with a very high level of toluene exposure over a short period of time (Johnson et al. 1990; Lataye and Campo 1997; Lataye et al. 1999; McWilliams et al. 2000) (19). In humans, limited studies have been conducted on this type of ototoxic effect in occupational settings (Abbate et al. 1993; Morata et al. 1993, 1995, 1997; Schaper et al. 2003) (19). With simultaneous exposure to toluene and noise, the risk for hearing loss at 25 dB and higher was also much greater in the

present study than in the study of Morata et al. (1993) (19). In comparison to the study by Morata et al., our study participants were older (41.8 vs. 32.5 years on average) and had a longer work history (12.3 vs. 8.1 years on average). Many of our study participants had a longer employment history. This may explain why the rate of hearing loss was also profoundly higher in the noise-exposed group (19).

This study shows that the risk of hearing loss due to simultaneous exposure to toluene and noise is greater than the risk caused by noise or toluene alone.

The other unique finding in this study is that the magnitudes of ototoxic effect were different for various tested pure-tone frequencies among workers exposed to toluene plus noise, and noise or toluene alone. This finding has not been reported previously for toluene. It is noteworthy that the patterns of hearing impairment, measured by pure-tone frequencies, associated with toluene plus noise exposure are similar to those associated with simultaneous exposure to carbon disulfide and noise (Chang et al. 2003) (20).

Both toluene and carbon disulfide have greater impact on speech frequencies than noise alone, with the largest gap at the frequency of 500 Hz. Therefore, the toluene plus noise group had poorer thresholds than did the noise-only group at 1000 Hz frequencies, but not necessarily at high frequencies. This was

similar to the mean hearing threshold pattern found for the ototoxicity of styrene by Morata and et al. 2002. We suspect that other types of ototoxic solvents may have other types of effects on hearing measured by pure-tone frequency (19).

The average air concentrations of toluene at work sites in group 2 was higher than group 3, but the results showed that the rate of hearing loss was higher in group 3. Furthermore, the average D% of noise at work sites in group 1 was higher than group 3, but the rate of hearing loss in group 3 was higher than group 1. Therefore the impact of toluene and noise on hearing loss can be additive.

Based on this study, hearing loss mostly occurs at midrange frequencies than other ranges. Therefore, these results are comparable to those of studies by some researchers such as Bushnell et al. (20). They found that toluene decreases the response rate in the auditory system (20). This finding was confirmed by Liu-Y et al. in 1997 (22). They proved the effect of toluene on the cochlea in vivo; thus, we can deduce that toluene is involved in hearing loss through affecting the auditory system (21). They found that toluene is effective on hearing loss in midrange frequencies. This finding is consistent with the findings of Johnson-AC 1993 and 1994 on rats and mice (23).

Lataye and Campo conducted a survey on the effects of simultaneous exposure to noise and toluene on hearing function of rats (24). They showed that the auditory deficit induced by the combined exposure exceeded the summated losses caused by toluene and noise within the range of 2-32 kHz of test frequencies alone (24). These results are in accordance with our results.

Our results showed that there was an elevated hearing impairment in workers exposed to toluene plus noise compared with those exposed to noise alone. The impact was greater for speech frequencies than higher frequencies. These data suggest that the current work site and concentration of 96.3 ppm of toluene does not protect workers

against hearing loss in the simultaneous presence of noise and toluene at the work site. Therefore, our results are in accordance with those of Unlu I et al. (17).

Conclusion

This study showed that the risk of hearing loss due to simultaneous exposure to toluene and noise was greater than the risk caused by noise or toluene alone. It is noteworthy that the patterns of hearing impairment, measured by pure-tone frequencies, associated with toluene plus noise exposure are similar to those associated with simultaneous exposure to carbon disulfide and noise. Recent studies suggest that several substances present in the industrial environment can synergically interact with noise or potentiate noise-induced hearing loss. However, in the majority of cases where synergy or potentiation were proposed, it cannot be clearly decided whether there is interaction or not, due to a lack of toxicological data.

The weakness or lack of data on noise and chemical exposure in several studies was the main difficulty in arriving at a conclusion. In an occupational environment, since the workers are usually exposed to mixtures of substances, it is not easy to evaluate the effects associated with exposure to a specific chemical. In addition, from one study to the next, different thresholds are used to distinguish the groups exposed to noise from those that are not. Effective intervention is needed to improve industrial safety of individuals experiencing ototoxic effects of solvents. The findings of this study and studies on other solvents can help policymakers establish threshold limit values for solvents and implement such interventions.

This study has made the following recommendations which may serve as a general guideline for industrial hygienists:

- Occupational health professionals and the workforce should be made aware of the risks posed by ototoxic substances. Employers and workers should be advised accordingly.

- Ototoxicity should be incorporated in occupational health-screening activities.

- Appropriate tools should be developed for early diagnosis of chemically-induced hearing impairment.

- Suitable scientific investigations, such as longitudinal epidemiological studies, into ototoxic properties should be encouraged.

Future researches should focus on quantifying the combined effects of ototoxic substances and noise. However, statistics on occupational diseases and their prevalent causes clearly indicate that ototoxic substances should not divert risk managers' attention from the fundamental requirements in combating noise-induced hearing loss at the workplace that still has priority over chemically-induced hearing impairment.

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Reference

- Morata TC, Dunn DE, Sieber WK. Occupational exposure to noise and ototoxic organic solvents. *Arch Environ Health* 1994; 49(5):359-65.
- Morata TC, Nylen P, Johnson AC, Dunn DE. Auditory and vestibular functions after single or combined exposure to toluene: a review. *Arch Toxicol* 1995; 69(7):432-43.
- Odkvist LM, Arlinger SD, Edling C, Larsby B, Bergholtz LM. Audiological and vestibulo-oculomotor findings in workers exposed to solvents and jet fuel. *Scand Audiol* 1987; **16(2)**:75-81.
- Abbate C, Giorgianni C, Munao F, Brecciaroli R. Neurotoxicity induced by exposure to toluene, An electrophysiologic study. *Int Arch Occup Environ Health* 1993; 64(6):389-92.
- Vrca A, Karacic V, Bozicevic D, Bozikov V, Malinar M. Brainstem auditory evoked potentials in individuals exposed to long-term low concentrations of toluene. *Am J Ind Med* 1996; 30(1):62-6.
- Morton AJ, Hickey MA, Dean LC. Methamphetamine toxicity in mice is potentiated by exposure to loud music. *Neuroreport* 2001; 12(15):3277-81.
- Dorsey AS, Donohue JM. Toxicological Problem for Toluene. Quick Reference for Health Care Providers. United States: Department of Health and Human Services, Public Health; 1994.
- Morata TC. Study of the effects of simultaneous exposure to noise and carbon disulfide on workers' hearing. *Scand Audiol* 1989; 18(1):53-8.
- Morata TC, Fiorini AC, Fischer FM, Colacioppo S, Wallingford KM, Krieg EF, et al. Toluene-induced hearing loss among rotogravure printing workers. *Scand J Work Environ Health* 1997; 23(4):289-98.
- Berenguer P, Soulage ChO, Fautrel A, Pequignot JM, Abraini JH. Behavioral and neurochemical effects induced by subchronic combined exposure to toluene at 40 ppm and noise at 80 dB-A in rats. *Physiol Behav* 2004; 81(3):527-34.
- Nies E. Ototoxic substance at the workplace: a brief update. *Arch Hig Rada Toksikol* 2012; 63(2):147-52.
- Barregård L, Axelsson A. Is there an ototraumatic interaction between noise and solvents? *Scand Audiol* 1984; 13(3):151-5.
- Loukzadeh Z, Shojaoddiny-Ardekani A, Mehrparvar AH, Yazdi Z, Mollasadeghi A. Effect of exposure to a mixture of organic solvents on hearing thresholds in petrochemical industry workers. *Iran J Otorhinolaryngol* 2014; 26(77):235-43.
- Johnson AC, Juntunen L, Nylén P, Borg E, Höglund G. Effect of interaction between noise and toluene on auditory function in the rat. *Acta Otolaryngol* 1988; 105(1-2):56-63.
- Muijser H, Lammers JH, Kulig BM. Effects of exposure to trichloroethylene and noise on hearing in rats. *Noise Health* 2000; 2(6):57-66.
- Lataye R, Campo P, Loquet G. Combined effects of noise and styrene exposure on hearing function in the rat. *Hear Res* 2000; 139(1-2):86-96.
- Unlu I, Kesici GG, Basturk A, Kos M, Yılmaz OH. A comparison of the effects of solvent and noise exposure on hearing, together and separately. *Noise Health* 2014; 16(73):410-5.
- Unlu I, Kesici GG, Basturk A, Kos M, Yılmaz OH. A comparison of the effects of solvent and noise exposure on hearing, together and separately. *Noise Health* 2014; 16(73):410-5.
- Metwally FM, Aziz HM, Mahdy-Abdallah H, ElGelil KS, El-Tahlawy EM. Effect of combined occupational exposure to noise and

- organic solvents on hearing. *Toxicol Ind Health* 2012; 28(10):901-7.
20. Chang SJ, Chen CJ, Lien CH, Sung FC. Hearing loss in workers exposed to toluene and noise. *Environ Health Perspect* 2006; 114(8):1283-6.
 21. Vrca A, Karacic V, Bozicevic D, Bozikov V, Malinar M. Brainstem auditory evoked potentials in individuals exposed to long-term low concentrations of toluene. *Am J Ind Med* 1996; 30(1):62-6.
 22. Liu Y, Rao D, Fechter LD. Correspondence between middle frequency auditory loss in vivo and outer cell shortening in vitro. *Hear Res* 1997; 12(1-2); 134-40.
 23. Johnson AC. The ototoxic effect of toluene and the influence of noise, acetyl salicylic or genotype, A study in rats and mice. *Scand Audiol Suppl* 1993; 39:1-40.
 24. Lataye R, Campo P. Combined effects of a simultaneous exposure to noise and toluene on hearing function. *Neurotoxicol Teratol* 1997; 19(5):373-82.