

Available online at www.sciencedirect.com

ScienceDirect

www.elsevier.com/locate/jes

JES
JOURNAL OF
ENVIRONMENTAL
SCIENCES
www.jesc.ac.cn

Meta-analysis of the effect of low-level occupational benzene exposure on human peripheral blood leukocyte counts in China[☆]

Hao Zhang^{1,2}, Hong Li^{2,*}, Zhijian Peng^{1,*}, Juan Cao², Jiemeng Bao²,
Lei Li^{2,3}, Xuezhong Wang², Yuanyuan Ji^{2,4}, Zhuojiong Chen²

¹ School of Science, China University of Geosciences, Beijing 100083, China

² State Key Laboratory of Environmental Criteria and Risk Assessment, Chinese Research Academy of Environmental Sciences, Beijing 100012, China

³ Academy of Environmental Planning and Design, Co., Ltd., Nanjing University, Nanjing 210093, China

⁴ College of Earth Sciences, Jilin University, Changchun 130061, China

ARTICLE INFO

Article history:

Received 28 May 2021

Revised 10 August 2021

Accepted 11 August 2021

Available online 14 January 2022

Keywords:

Benzene at workplaces

Low-level occupational exposure

Peripheral blood

Leukocyte

Meta-analysis

ABSTRACT

To investigate the effect of low-level occupational benzene exposure on human peripheral blood leukocyte counts of the workers, domestic and foreign published research data on the change of human peripheral blood leukocyte counts under low-level occupational benzene exposure from January 1990 to December 2020 were collected and analyzed. According to the literature inclusion and exclusion criteria, 18 independent studies from 12 publications were selected for meta-analysis to explore the effect of low-level occupational benzene exposure on human peripheral blood leukocyte counts. The results showed that the peripheral blood leukocyte counts abnormal rates of low-level occupational benzene exposure group were higher than those of the control group, and the difference was statistically significant. Low-level occupational benzene exposure could result in a relatively higher abnormal rate of peripheral blood leukocyte counts in the exposed population, indicating that low-level occupational benzene exposure at workplaces specified by the current benzene occupational exposure limit in China would affect the peripheral blood leukocyte counts of the workers, thus benzene with concentrations under the limit in the ambient air of workplace could be still harmful to the health of the exposed workers. The results of this study could provide a scientific basis for future revision of the benzene occupational exposure limit in China, and could also be a reference for the formulation of environmental standard concerning benzene in China in the future.

© 2022 The Research Center for Eco-Environmental Sciences, Chinese Academy of Sciences. Published by Elsevier B.V.

[☆] This article is dedicated to Professor Dianxun Wang.

* Corresponding authors.

E-mails: lihong@caes.org.cn (H. Li), pengzhijian@cugb.edu.cn (Z. Peng).

Introduction

As an important volatile organic compound, benzene has blood toxicity and carcinogenicity (Junaidi et al., 2019; Majumdar et al., 2019; Schnatter et al., 2010). The International Agency for Research on Cancer (IARC) officially classified benzene as a class I carcinogen in 1982; and leukemia induced by benzene was identified as one of the eight occupational tumors in China in 1987 (Huff, 2007; Robert et al., 2010).

In China, the maximum permissible concentration of occupational benzene exposure was 50 mg/m³ in 1956, and it decreased to 40 mg/m³ in 1979 (Xia et al., 2005). In 2002, the permissible concentration time-short term exposure limit (PC-STEL) was revised to 10 mg/m³, the permissible concentration time-weighted average (PC-TWA) was reduced to 6 mg/m³, and the breathing zone air monitoring method was replaced by individual sampling monitoring method (GBZ 2-2002); relevant concentration limits for benzene were not revised in subsequent revisions (GBZ 2.1-2007 and GBZ 2.1-2019) (Xia et al., 2005). The production and use of pure benzene in China are increasing year by year. The production reached 11.45 million tons in 2016. By 2023, the supply is expected to reach around 19.3 million tons, and the total demand will reach 21.95 million tons (Yu, 2017). In recent years, the incidence of occupational acute and chronic benzene poisoning in China has been ranked among the top three reasons for acute and chronic poisoning (Huff, 2007; Cao, 2008). The main occupational health hazards of benzene are acute poisoning caused by inhalation of a large amount of benzene vapor in a short time and chronic poisoning caused by long-term low-level exposure, which can cause great harm to the respiratory system, hematopoietic system and nervous system (Ji et al., 2020; Robert et al., 2010; Smith et al., 2011).

Studies have shown that high-level occupational benzene exposure can result in the human peripheral blood leukocyte counts lower than normal value; however, it is inconclusive about the effect of low-level occupational benzene exposure on leukocyte counts (Robert et al., 2010; Chang, 2009; Swaen et al., 2010). At present, epidemiological investigation and animal experiments are mainly used in domestic and foreign studies on the effects of low-level benzene on workers' health (Li et al., 2012; Tan et al., 2015). Although a large number of epidemiological investigations and animal experiments have been conducted clinically on the effect of benzene on workers' health, there are biases in the conclusions reported in different studies due to factors, such as geographical regions, time, equipment, statistical powers of individual studies and sample sizes. Currently, some meta-analyses have been carried out on the effect of low-level occupational benzene exposure on peripheral blood leukocyte counts of workers in China, and the effects of benzene exposure on leukocyte counts or T lymphocytes have been analyzed (Li et al., 2012; Qu et al., 2020; Tan et al., 2015). However, there are some problems in these meta-analyses, such as incomplete literature collection and inconsistent literature screening and evaluation (Li et al., 2012; Tan et al., 2015; Wen et al., 2018; Zeng et al., 2017). Our team has been engaged in the establishment of an atmospheric environment benchmark system for a long time and carried out studies in this field in 2012 (Li et al., 2012). To

promote the revision of low-level occupational benzene exposure in current occupational health standard in China, epidemiological data on the effect of low-level occupational benzene exposure on human peripheral blood leukocyte counts in China were reviewed based on previous studies and more rigorous and uniform screening in literature inclusion and exclusion criteria were used to ensure that the data obtained are more accurate and representative; and the effect of low-level occupational benzene exposure on human peripheral blood leukocyte counts was explored by meta-analysis. The results of this study could provide a scientific basis for future revision of the benzene occupational exposure limit in China, and could also be a reference for the formulation of environmental standard concerning benzene in China in the future.

1. Materials and methods

1.1. Protocol and registration

This meta-analysis had applied for registration in the PROSPERO international prospective register of systematic review (PROSPERO# CRD42021244248) when we started to search related studies. The meta-analysis was conducted according to the guidelines outlined in the Cochrane Handbook for the Systematic Reviews of Interventions and Preferred Reporting Items for Systematic Review and Meta-Analysis 2020 (PRISMA 2020).

1.2. Literature sources

A total of 102 pieces of domestic and foreign published literature on the changes in human peripheral blood leukocyte counts under low-level occupational benzene exposure in China between January 1990 and December 2020 were collected by searching seven databases of VIP Chinese Science and Technology Journal Database, CNKI (China National Knowledge Infrastructure), Wanfang Digital Journal Database, Scopus, Embase, Web of Science and PubMed with subject terms and keywords of "benzene" and "leukocyte", and search languages of Chinese and English. The last search date is March 23th, 2021. The Newcastle-Ottawa-Scale (NOS) was used to assess the quality of papers (SI).

1.3. Literature inclusion and exclusion criteria

Studies which meet the following criteria were included: (1) independent occupational epidemiological investigations published at home and abroad from January 1990 to December 2020; (2) the benzene exposure concentrations of subjects in each group met the values as stipulated in China's national occupational health criteria Occupational Exposure Limits for Hazardous Agents in the Workplace - Part 1: Chemical Hazardous Agents (PC-STEL 10 mg/m³, PC-TWA 6 mg/m³) (GBZ 2.1-2019); (3) all selected publications referred to prospective cohort studies; (4) abnormal peripheral blood leukocyte counts of subjects in each group were determined by the leukocyte counts lower than $4.0 \times 10^9 \text{ L}^{-1}$ as stipulated in Diagnosis of Occupational Benzene Poisoning (GBZ 68-2013); (5) subjects of each group were comparable in age, working year,

working duration, and so on; (6) except benzene exposure, the subjects of each group were not exposed to other obvious occupational harmful factors; (7) there were at least two groups (exposed group and control group); (8) aged 18 to 60 years, with working lengths over 6 months and without other underlying disease. The included pieces of literature were assessed strictly. There were no statistically significant differences in age, sex, working years, smoking status between the exposed groups and control groups (Li et al., 2012).

Meanwhile, studies will be excluded if one of the following conditions is met: (1) that do not specify the research method used; (2) that do not specify the type of benzene exposure concentration data; (3) the occupational benzene exposure information of each group was not available or the data could not be extracted; (4) published in languages other than Chinese and English; (5) not individual study publications, such as meta-analysis, review, comments, lecture, repeated report and non-original study report; (6) the concentrations of benzene and its homologs were over the standard values at the workplaces.

In this study, independent occupational epidemiological investigations published at home and abroad from January 1990 to December 2020 were strictly screened per the pre-specified literature inclusion and exclusion criteria. Titles, abstracts and the related data of the citations retrieved by the literature search were screened independently for inclusion/exclusion by more than 2 review authors. Any disagreement was resolved by a third reviewer. Finally, 12 original publications were selected and a total of 18 independent studies were included in the 12 publications.

1.4. Statistical analysis

A meta-analysis was performed on the literature that met the inclusion criteria using Stata 12.0 software, which was developed by the US Computer Resource Center and is now a product of STATA company. It is small, flexible, easy to operate, integrated with complete statistical analysis methods and with powerful functions, and is well received by beginners and advanced users (Bai et al., 2007; Wang et al., 2008). The non-heterogeneous data in the literature were combined by the fixed-effects model, while the heterogeneous data were combined by the random-effects model. The effects of each study were weighted and combined based on the test results, the combined values were calculated by odds ratio (OR) which can be affected by different factors, e.g. geographical regions, time, equipment, statistical powers of individual studies and sample sizes, and the combined effect was estimated by 95% confidence interval (95% CI). Heterogeneity across studies was determined by the *P* value and *I*-square (I^2) statistics. Additionally, the statistical significance of the pooled standardized mean difference was examined by the *Z* value. A cumulative meta-analysis was conducted on the selected literature, i.e., a meta-analysis was conducted after the completion of each study, so that the dynamic change trend of the research conclusion could be clearly defined and the impact of each study on the comprehensive conclusion could be reflected (Zhao et al., 2002; Liao et al., 2003; Zhang and Zhong, 2012). The sensitivities of the selected studies were analyzed by removing the maximum weight literature, and bias was deter-

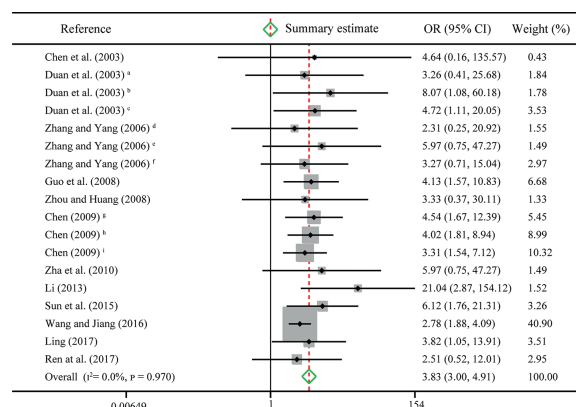


Fig. 1 – Meta-analysis forest plot of the effect of low-level occupational benzene exposure on human peripheral blood leukocyte counts.

mined by Begg and Egger tests as *Z* value and *t* value, separately (Zhang, 2016; Xu et al., 2009).

2. Results

2.1. Literature description

A total of 102 publications with relevant subject terms and keywords were retrieved. The obtained publications were screened according to the inclusion and exclusion criteria in Section 1.3. A total of 12 publications were included in the meta-analysis, including 18 independent research cases and the quality of the included studies been assessed by the NOS before further study (Table S1). There were several studies published in the recent 5 years, but these studies did not meet the inclusion criteria of this study, therefore we did not include them in our study. The diagnostic criteria in the included publications were clearly described. All regions involved in the publications were coastal cities in China, and the industries involved were mainly suitcase enterprises, spraying and printing industries and petrochemical industries. The data extracted from the 18 selected independent studies are shown in Table 1.

2.2. Data analysis

The heterogeneities of the 18 independent studies included in the meta-analysis were tested. And the results showed that there was no heterogeneity among studies ($P = 0.970$; $I^2 = 0.0\%$) (Fig. 1). Based on the heterogeneity results, the fixed-effect model was used for analysis. The combined OR value of the effect of occupational benzene exposure on leukocyte counts decrease of workers was 3.83 (95% CI: 3.00 - 4.91), assuming test $Z = 10.69$ and $P < 0.01$, indicating that the risk of leukocyte counts decrease of workers exposed to occupational benzene was 3.83 times that of the control group.

Table 1 – Data extracted from nine selected independent studies.

Selected literature	Published year	Study region	Benzene exposure level (mg/m ³)	Exposed		Non-Exposed		Odds ratio (OR)	95% Confidence interval (CI)
				Population number	Abnormal rate (%)	Population number	Abnormal rate (%)		
Chen et al. (2003)	2003	Guangzhou	0.88 ^T	6	16.7%	8	0.0%	4.64	0.16–135.57
Duan et al. (2003) ^a	2003	Zhengzhou	0.4–5.8 ^S	467	2.1%	150	0.7%	3.26	0.41–25.68
Duan et al. (2003) ^b	2003			467	5.1%	150	0.7%	8.07	1.08–60.18
Duan et al. (2003) ^c	2003			467	6.0%	150	1.3%	4.72	1.11–20.05
Zhang and Yang (2006) ^d	2006	Longyan	0.4–5.8 ^S	186	2.2%	106	0.9%	2.31	0.26–20.92
Zhang and Yang (2006) ^e	2006			186	5.4%	106	0.9%	5.97	0.75–47.27
Zhang and Yang (2006) ^f	2006			186	5.9%	106	1.9%	3.27	0.71–15.04
Guo et al. (2008)	2008	Guangzhou	< 6 ^T ; <10 ^S	1049	2.4%	841	0.6%	4.13	1.57–10.83
Zhou and Huang (2008)	2008	Haikou	2.46 ^T	183	2.2%	150	0.7%	3.33	0.37–30.11
Chen (2009) ^g	2009	Changshu	0.7–1.6 ^S	155	13.5%	150	3.3%	4.55	1.67–12.39
Chen (2009) ^h	2009			264	11.7%	250	3.2%	4.03	1.81–8.94
Chen (2009) ⁱ	2009			312	9.3%	300	3.0%	3.31	1.54–7.12
Zha et al. (2010)	2010	Zhangzhou	2.1–2.2 ^S	186	5.4%	106	0.9%	5.97	0.75–47.27
Li (2013)	2013	Jingmen	0.15 ^S	458	8.5%	227	0.4%	21.04	2.87–154.12
Sun et al. (2015)	2015	Beijing	2.75–8.95 ^S	333	4.5%	392	0.8%	6.12	1.76–21.31
Wang and Jiang (2016)	2016	Chengdu	2.62–6.85 ^S	1160	7.7%	1307	2.9%	2.78	1.88–4.09
Ling (2017)	2017	Shenzhen	4.12±0.72 ^S	200	5.5%	200	1.5%	3.82	1.05–13.91
Ren et al. (2017)	2017	Pingdingshan	0.07–0.27 ^T	201	4.0%	123	1.6%	2.51	0.52–12.01

^{a b c} the year of study, 1996, 1998 and 2000, respectively.^{d e f} the year of study, 2001, 2003 and 2005, respectively.^{g h i} the year of study, 2006, 2007 and 2008, respectively.^S STEL, the permissible concentration time-short term exposure limit (PC-STEL) is 10 mg/m³.^T TWA, the permissible concentration time-weighted average (PC-TWA) is 6 mg/m³.

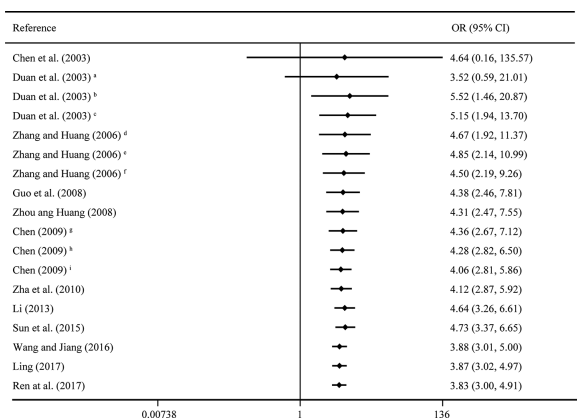


Fig. 2 – Cumulative meta-analysis forest plot of the effect of low-level occupational benzene exposure on human peripheral blood leukocyte counts.

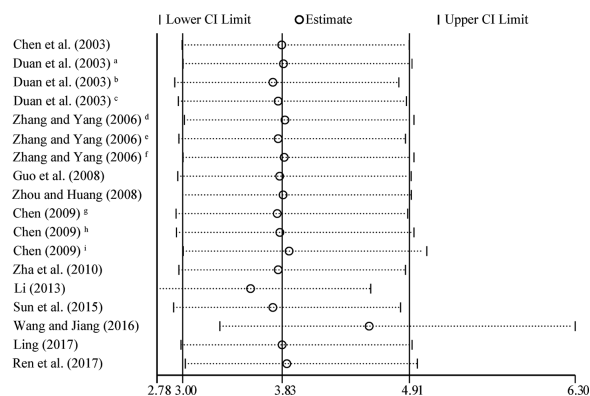


Fig. 3 – Meta-analysis estimates, given named study is omitted.

2.3. Cumulative meta-analysis

Cumulative meta-analysis showed that the OR (95% CI) value tended to be stable with the increase of the sample size with a good trend of change. The analysis showed that, although the newly added study had a certain influence on the combined OR value, it tended to be stable as a whole and was statistically significant (Fig. 2).

2.4. Analysis of literature sensitivity and bias

In this study, its impact on the combined effect size and the reliability of meta-analysis were evaluated by removing a single study. After removing a single study, the combined OR value was similar to that without removing the single study (Figs. 3 and S1).

Begg test showed $Z = 0.27$, $P = 0.01$; and Egger test showed $t = 2.87$, $P = 0.01$ (95% CI: 0.8 - 1.21) (Figs. 4 and S2), indicating that there was no obvious bias in the analysis.

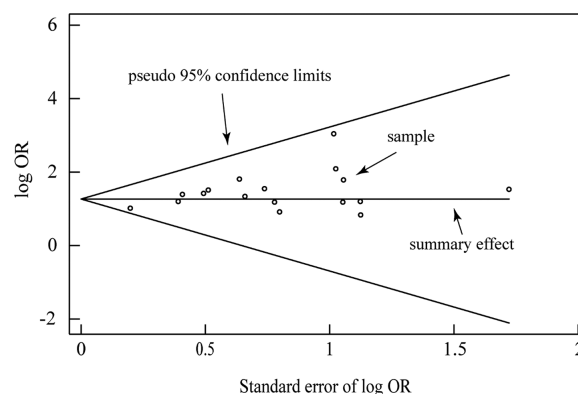


Fig. 4 – Begg's funnel plot with pseudo 95% confidence limits.

3. Discussion

The results of this study showed that the incidence of peripheral leukocyte counts abnormality in the low-level occupational benzene exposure group was 3.83 times that of the control group, indicating that low-level occupational benzene exposure can affect workers' peripheral blood leukocyte counts and the current national occupational health standard in China could not well protect the health of benzene exposed workers. The result of this meta-analysis is consistent with other studies that have also found a reduction in human peripheral blood leukocyte counts based on benzene exposure levels under the current benzene occupational exposure limit in China (Li et al., 2012; Qu et al., 2020; Tan et al., 2015). Currently, the United States and European Union have adopted stricter benzene occupational exposure limits, that is, 8-hr time-weighted average permissible concentration (TWA) of 3.25 mg/m³ (Capleton et al., 2005; Khalade et al., 2010; Li et al., 2012). In order to better protect the safety of workers exposed to benzene, the occupational exposure limit of benzene under the current national occupational health standard should be revised. Therefore, more in-depth occupational epidemiological investigations should be carried out in this field to formulate a reasonable professional standard that could truly protect the health of workers in benzene-related enterprises. In the meantime, it is recommended that benzene-related enterprises should actively upgrade the production processes while implementing the current national occupational health standard, so as to effectively protect the health of benzene exposed workers from the sources. At the same time, the self-protection awareness of benzene exposed workers should be strengthened, and occupational health monitoring should be provided for the early detection, diagnosis and treatment of benzene poisoning.

Relevant studies have found that the concentration of benzene in ambient air in China is at a relatively higher level compared with other VOCs in ambient air, and the resulting environmental pollution and potential harm to human health are also attracting increasing attention (Ji et al., 2020). At present, studies on VOCs benchmark in the ambient air in China is still at the early stage, the determination of the hu-

man health benchmarks of benzene in ambient air needs to be based on a large number of research data analyses on toxicology, epidemiology, environmental concentration, population exposure and health risk assessment, and occupational exposure (especially low-level occupational exposure) (Li et al., 2012). For this reason, the results of this study could not only provide a basis for a future revision of the benzene occupational exposure limit in China but also have a certain reference value for determining the human health benchmark values of benzene in ambient air in China in the future (Li et al., 2012).

Although the pieces of literature were carefully screened in this study, the results may be affected by some unknown factors due to the different quality of the pieces of literature. In addition, small amounts of toluene, ethylbenzene, or xylene may exist in workplaces where benzene is involved, which may also have an impact on the health of workers exposed to benzene.

4. Conclusions

The effect of low-level occupational benzene exposure on human peripheral blood leukocyte counts was investigated by using meta-analysis. The results showed that the incidence of peripheral blood leukocyte counts abnormality in the low-level occupational benzene exposure population was 3.83 times that of the control group. Sensitivity analysis showed that the results of this study have good stability, and the bias of the 12 selected publications was excluded by Begg and Egger tests. The benzene exposure concentration specified in the current national occupational health standard in China could still lead to the workers' peripheral blood leukocyte counts abnormality. At present, the corresponding benzene exposure values are slightly higher than those used in the developed countries in Europe and the United States. It is recommended that benzene-related enterprises should take the initiative to protect the health of the exposed workers under the premise of implementing the national occupational health standard present; In the meantime, in order to better protect the health of the exposed workers, relevant national authorities in China need to formulate stricter benzene occupational exposure limit based on a large number of studies involving toxicology, epidemiology, environmental concentration, population exposure and health risk assessment, occupational exposure studies, especially low-concentration exposure studies, etc. This study could provide a scientific basis for the revision of the benzene occupational exposure limit and could also be a reference for the formulation of environmental standard concerning benzene in China in the future.

Acknowledgments

This work is financially supported by the programs from the Beijing Municipal Science and Technology Commission (No. Z181100005418015), the Special Research Project for the National Environmental Protection Public Welfare Industry of China (No. 201009032) and the Finance Allocation Project of Ministry of Ecology and Environment of China (No. 2110105).

Appendix A Supplementary data

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.jes.2021.08.035.

REFERENCES

- Bai, J., Zhong, W., Zheng, M., Chen, F., 2007. Meta-analysis in. *Stata. J. Evid.-Based Med.* 7, 363–368.
- Cao, X., 2008. The poisoning and its prevention of benzene (in Chinese). *Occup. Health* 3, 96–97.
- Capleton, A.C., Levy, L.S., 2005. An overview of occupational benzene exposures and occupational exposure limits in Europe and North America. *Chem. Biol. Interact.* 153–154, 43–53.
- Chang, J., Xu, D., Dong, X., Wang, Q., Wang, G., Tang, Z., et al., 2009. Correlation between blood indexes and GSTT1, GSTM1 genotypes in environmental exposure to low level benzene. *J. Environ. Health* 26, 423–425.
- Chen, J., Liu, W., Huang, Z., Wu, J., Chen, S., Yang, L., et al., 2003. Gene polymorphism of peripheral blood TCR V β subfamily in benzene-exposed workers. *Chin. J. Ind. Med.* 16, 148–151.
- Chen, L., 2009. Analysis of peripheral hemogram of benzene exposed workers in some township enterprises of bag manufacturing in Changshu city during 2006–2008. *Occup. Health* 25, 2154–2155.
- Duan, X., Yu, S., Yang, J., Guo, J., 2003. Investigation on the health effects of long-term exposure to low concentrations of benzene, toluene and xylene on workers (in Chinese). *Ind. Health Occup. Dis.* 29, 45–47.
- Guo, J., Liang, X., Deng, C., 2008. Change of blood white cell of workers exposed to benzene. *Occup. Health Emerg. Rescue.* 26, 149–150.
- Huff, J., 2007. Benzene-induced cancers: abridged history and occupational health impact. *Int. J. Occup. Environ. Health* 13, 213–221.
- Ji, Y., Gao, F., Wu, Z., Li, L., Li, D., Zhang, H., et al., 2020. A review of atmospheric benzene homologues in China: characterization, health risk assessment, source identification and countermeasures. *J. Environ. Sci.* 95, 225–239.
- Junaidi, E.S., Jalaludin, J., Tualeka, A.R., 2019. A review on the exposure to benzene among children in schools, preschools and daycare centres. *Asian J. Atmos. Environ.* 13, 151–160.
- Khalade, A., Jaakkola, M.S., Pukkala, E., Jaakkola, J.J., 2010. Exposure to benzene at work and the risk of leukemia: a systematic review and meta-analysis. *Environ. Health* 9, 31.
- Li, L., Li, H., Wang, L., Zhang, X., Xu, L., 2012. Influence of low-level occupational benzene exposure on human peripheral blood leukocyte counts: a meta-analysis. *J. Environ. Health* 29, 637–639.
- Li, M., 2013. Investigation on the effect of low-concentration mixed benzene exposure on peripheral blood picture of workers (in Chinese). *J. Pub. Health Prev. Med.* 24, 92–93.
- Liao, R., Wu, Y., Yang, X., Yang, H., Zhong, W., 2003. Cumulate meta-analysis of the effect of platinum-based adjuvant chemotherapy for completely resected non-small cell lung cancer. *J. Evid.-Based Med.* 3, 196–203.
- Ling, J., 2017. Analysis of the effect of low-level benzene exposure on workers' peripheral blood routine and urine benzene metabolites (in Chinese). *J. Qiqihar Univ. Med.* 38, 72–74.
- Majumdar, D., Bhanarkar, A., Gavane, A.G., Rao, C., 2019. Measurements on stationary source emissions and assessing impact on ambient air quality around two Indian refineries. *Asian J. Atmos. Environ.* 13, 73–87.

- Qu, W., Wu, J., 2020. A meta - analysis of the influence of occupational benzene exposure on peripheral blood leukocytes in workers. *Chin. J. Health Lab. Tec.* 15, 1899–1904.
- Ren, C., Tian, J., Hai, M., 2017. Results of blood routine examination of benzene-exposed workers within a plant. *Occup. Health Emerg. Rescue* 35, 126–127.
- Robert, S.A., Kerzic, P.J., Zhou, Y., Chen, M., Nicolich, M.J., Lavelle, K., et al., 2010. Peripheral blood effects in benzene-exposed workers. *Chem. Biol. Interact.* 184, 174–181.
- Schnatter, A.R., Kerzic, P.J., Zhou, Y., Chen, M., Nicolich, M.J., Thomas, W.K.L., et al., 2010. Peripheral blood effects in benzene-exposed workers. *Chem. Biol. Interact.* 184, 174–181.
- Smith, M.T., Zhang, L., McHale, C.M., Skibola, C.F., Rappaport, S.M., 2011. Benzene, the exposome and future investigations of leukemia etiology. *Chem. Biol. Interact.* 192, 155–159.
- Sun, Y., Su, D., Zhao, X., 2015. Influence of low concentration benzene series on peripheral hemogram of exposed workers. *Occup. Health* 31, 1120–1122.
- Swaen, G.M., Amelsvoort, L., Twisk, J.J., Verstraeten, E., Slootweg, R., Collins, J.J., et al., 2010. Low level occupational benzene exposure and hematological parameters. *Chem. Biol. Interact.* 184, 94–100.
- Tan, Q., Gu, C., Guo, Y., Huo, S., Luo, C., Chen, G., et al., 2015. Meta-analysis of the effects of occupational benzene exposure on workers' peripheral blood leukopenia (in Chinese). *Chin. J. Ind. Med.* 28, 229–231.
- Wang, J., Jiang, G., 2016. Analysis of the effect of exposure to low-concentration benzene on the blood routine of workers (in Chinese). *Ind. Health Occup. Dis.* 42, 58–62.
- Wang, J., Mo, C., Chen, Q., Xu, Z., Fan, Y., Chai, H., et al., 2008. Application of meta-analysis in Stata on medical researches quantitative assessment. *Chin. Arch. Tradit. Chin. Med.* 26, 947–949.
- Wen, C., Li, R., Xu, H., Liu, M., Su, S., Wen, X., 2018. Meta regression analysis on evaluation of occupational benzene exposure. *J. Environ. Occup. Med.* 35, 750–755.
- Xia, Z., Sun, P., Zhang, Z., Jin, X., 2005. Review and prospect of research on occupational health hazards of benzene (in Chinese). *Chin. J. Ind. Hyg. Occup. Dis.* 23, 241–243.
- Xu, T., Li, X., Wang, W., Hu, P., Du, F., 2009. Detection of publication bias in meta-analysis of dichotomous variable egger test and begg test. *J. Evid.-Based Med.* 9, 181–184.
- Yu, H., 2017. Development situation of pure benzene production and down-stream industrial chain in China. *China Synth. Fibres.* 40, 45.
- Zeng, S., Gao, C., Zhang, B., Li, J., Xiao, Y., Chen, W., 2017. Effect of benzene exposure on blood routine indexes: a meta-analysis. *J. Environ. Health* 34, 128–134.
- Zha, J., Lin, H., Zhang, Q., Fu, X., Lv, Y., 2010. Effect of benzene series at low concentration on health of exposed workers. *Occup. Health* 26, 1828–1829.
- Zhang, S., 2016. Subgroup analysis and sensitive analysis should be set up reasonably in meta-analysis. *China J. Contemp. Neurol. Neurosurg.* 16, 1–2.
- Zhang, T., Zhong, W., 2012. *Applied Methodology for Evidence - Based Medicine* (2nd ed.). Cent. South Univ. Press, p. 40 2nd Edition.
- Zhang, X., Yang, L., 2006. Effects of long-term exposure to low-concentration mixed benzene on the health of workers (in Chinese). *Occup. Health* 22, 1447–1448.
- Zhao, J., 2002. Cumulate meta-analysis method and its application in research of clinical medicine. *J. Evid.-Based Med.* 2, 167–171.
- Zhou, H., Huang, X., 2008. Investigation on effects of adhesive to hematological system of workers. *Chin. Occup. Med.* 35, 445–447.