RBCMS
Revista Brasileira de
Ciências Médicas e da Saúde
Brazilian Journal of Medical Science and Health

REVIEW ARTICLE

Lead Poisoning: A Systematic Review

Intoxicação por Chumbo: Uma Revisão Sistemática

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ABSTRACT

Objective: Review accepted lead limits, risks and diseases generated by exposures below these limits, as well as identify epidemiological data of lead poisoning in Brazil. **Methods:** We have analyzed the studies that has been published in the databases MedLine (National Library of Medicine) and SciELO where the searching strategy used the following **keywords:** “lead poisoning” at MedLine; and “Poisoning” and “Lead” at SciELO. Inclusion and exclusion criteria were applied based on the types of studies. **The outcomes selected were:** lead levels below 10 μg/dL, neurotoxic effects in children, environmental pollution as aggravating lead poisoning. **Results:** Initially, 12664 studies involving lead poisoning were identified. After submitting to the inclusion and exclusion criteria, 5 articles remained, which were part of the scope of this review. **Conclusion:** This review confirms the need for further studies to assess the major sites of lead poisoning risks and which could be the basis for changes in regulatory standards establishing exposure limits.

Keywords: Metals, Heavy; Lead Poisoning; Lead

RESUMO

Objetivo: Revisar os limites de chumbo aceitos, os riscos e doenças gerados em exposições abaixo desses limites, bem como identificar os dados epidemiológicos de intoxicação por chumbo no Brasil. **Método:** Foram analisados os estudos publicados nas bases de dados MedLine (National Library of Medicine) e SciELO onde a estratégia de busca utilizou as seguintes **palavras-chave**: “lead poisoning”, no MedLine; e “Poisoning” e “Lead”, no SciELO. Os critérios de inclusão e exclusão foram aplicados com base nos tipos de estudos. **Os desfechos selecionados foram:** níveis de chumbo abaixo de 10 μg/dL, efeitos neurotóxicos em crianças, poluição ambiental como agravante nas intoxicações por chumbo. **Resultados:** Foram identificados inicialmente 12664 estudos envolvendo intoxicação por chumbo. Após submeter aos critérios de inclusão e exclusão, permaneceram 5 artigos, que fizeram parte do escopo dessa revisão. **Conclusão:** Esta revisão confirma a necessidade de novos estudos que avaliem os principais locais de riscos de intoxicação por chumbo e que possam ser base para alteração nas normas regulamentadoras que estabelecem os limites de exposição.

Palavras-chave: Metais Pesados; Intoxicação por Chumbo; Metais.

INTRODUCTION

Heavy metals are chemical elements with a density greater than 7 g/cm^3 and are considered ubiquitous in the environment, having as sources natural means, as in the case of volcanic activities and rock decomposition, and anthropogenic sources, as in the case of mining, agriculture, and industrial activities[1-3]. They are classified according to their toxicity as essential and non-essential, the former have human physiological functions in certain concentrations, such as zinc, iron, and manganese; while non-essentials have no physiological function, being considered toxic and raising concerns according to their concentrations, such as, for example, mercury, arsenic, cadmium, chromium, and lead[4,5].

Lead has been used by humanity for thousands of years and for different purposes, such as the production of electric accumulators, ammunition, the production of paints, glass, plastics, and ceramics (1). Its toxicity has records that lead it to the era before Christ, being considered one of the oldest and most studied toxic agents of occupational importance and responsible for diseases of environmental origin more common worldwide[1,6,7]. This metal is responsible for causing systemic intoxication, inducing damage to multiple organs, even at lower levels of exposure[1].

Despite efforts to reduce the sources of exposure to lead in recent decades, this metal remains a major cause of environmental health problems. Few studies in Brazil raise epidemiological data for the entire population and information on diseases and conditions caused by exposure to lead has not yet been fully quantified in Brazil[8,9].

Due to the lack of data, Brazilian legislation was based on studies performed in other countries to determine its lead poisoning parameters. Through Regulatory Norm NR-7, Ordinance No. 24, of the Secretariat for Safety and Health at Work - SSST, of December 29, 1994, the upper limit of legal normality (parameters for biological control of occupational exposure to lead) was established) of 40 µg/dL, and the Maximum Allowable Biological Index (IBPM), 60 µg/dl. These indexes do not take into account criteria that interfere in the levels of intoxication, such as socioeconomic, clinical, nutritional differences and even the norms and working hours of the Brazilian population[5,10,11]. These indexes also cannot be used in evaluations of the non-occupational population, mainly because some studies have shown associations between low levels of lead in the blood (<10 µg/dL) and adverse health effects, mainly related to the neurotoxicity of this metal, and the same studies, as well as those performed by the Centers for Disease Control and Prevention (CDC), concluded that there is no safety margin in lead exposures, especially for children[12-14].

There are rules in the country that regulate the allowed levels of lead in food, RDC No. 42, of 29 August 2013[15], in air pollution in the workplace, NR 15 - Unhealthy Activities and Operations[16], in lead-based outdoor paints and child and school use paints, varnishes, and surface coating materials, Law No. 11,762 of August 1, 2008[17]; and since the 90s, lead is no longer allowed in automotive gasoline, and specifications for the sale of automotive gasoline have been established through ANP Ordinance No. 309, of December 27, 2001[18]. However, without inspections and research, it is not possible to state that the Brazilian exposure to lead is being reduced.

In view of this brief exposure, the aim of the present study was to review the allowed lead limits, the risks and diseases generated under exposures below these limits, as well as to identify the epidemiological data of lead poisoning in Brazil.

METHODS

Research Strategies

Studies published in the MedLine (National Library of Medicine) and SciELO databases were analyzed. The continued search was used to complement the summary of the studies with other articles and data from official websites such as the Ministry of Health, Ministry of Labor and the Centers for Disease Control and Prevention (CDC).

The search strategy used the following keywords: "lead poisoning", in MedLine; and "Poisoning" and "Lead", in SciELO. The inclusion and exclusion criteria were applied based on the types of studies.

Inclusion, Exclusion and Outcome Criteria

Clinical, randomized, observational and clinical studies in humans were selected, according to the criteria presented in Chart 1.

RESULTS

Initially, 62 studies were identified in SciElo and 12602 in MedLine involving the descriptor "lead poisoning". Using the MedLine filter, through the inclusion and exclusion criteria, 21 articles were selected. The same criteria were used in SciElo, by reading the abstracts, selecting 36 articles. The titles and abstracts of the 57 articles were read to select the works that were used in the review, excluding those that did not match the purpose of the review. Finally, 5 studies were selected. Below is the flowchart (Figure 1) that shows the selection of articles in stages and Table 1 showing the summary of the studies and their main results.

DISCUSSION

In Brazil, there are few data on lead poisoning in the general population, both in occupational exposure and in the unexposed. Some studies indicate that in Brazil there are many sources of lead contamination that vary from the pollution of the work environment

Chart 1. Inclusion and exclusion criteria applied in the selection of studies

Inclusion criteria - Medline	
Outline	• Clinical trials, randomized trials, observational trials, clinical trials
Species	• Humans
Text availability	• Full text
Exclusion Criterion - Medline and SciELO	
Outline	• Review articles
Form of publication	• Only in summary
Main outcomes	
• Levels below 10µ/dL and neurotoxic effects in children	
• Environmental pollution as an aggravating factor in lead poisoning	

to domestic dust. A study performed by Roscoe et al., in 1999, in the United States, and another performed by Olympio et al., in 2010, in Bauru, SP, pointed out that living in or around lead-contaminated areas and having lived with people who work in battery, paint, or ceramic factories that use lead are risk factors for exposure to this metal in homes, as particles of this element can be carried to the home environment on the skin and clothing of workers, if it is not carried out the proper hygiene[19.20].

There are laws that define the limits of lead allowed in water, food and that prohibit the use in gasoline and paints and the NR7 legislation that defines the limits for occupational exposure; however, there are no laws that determine the allowed limits for lead in the blood of the non-occupationally exposed population, nor studies that show the reality of the population's exposure in the country. It is worth noting that the NR7 itself is based on studies performed in North America, which does not represent the reality in Brazil, since factors such as ethnicity, nutrition, and even exposure level interfere with absorption and, consequently, lead poisoning[5]. Not only about the inadequate transposition of values, there are still concerns about the fact that these values are not updated even after studies have shown health hazards in concentrations below the established limits.[19.21]

The main concern with lead rates is the fact that many studies, as well as the CDC, have concluded that there is no safe level for lead poisoning in children - even values below 10 µg/dL, previously considered as a limit value, they are considered neurotoxic. Since 2012, the CDC considers this value only as a reference to identify exposure and initiate protocols to control poisoning and contamination[7,22]. Some studies mention the possibility of the occurrence of a "silent pandemic" of neurodevelopmental disorders arising from exposure to this metal in children when it is continuous, even at low concentrations[23]. Silent because it does not present symptoms in most cases and when symptoms do exist, it is generally confused with other diseases, and the possibility of poisoning by this heavy metal is not investigated (23).

Lead poisoning pathways are mainly respiratory and gastrointestinal, after the lead is absorbed into the bloodstream where it binds to erythrocytes and is transported to soft tissues, especially to the brain, kidneys, liver, heart among others[7.24]. Most of the lead, around 95% in adults and 70% in children, is deposited on bones and teeth, where they remain for years, having a half-life of approximately 30 years in this tissue[7,24]. This deposition in the bones and long half-life have serious consequences for the organism, since this lead can be released again into the bloodstream, gradually or even acutely in cases of fractures; which represents a greater risk for children and pregnant women who have active bone remodeling. In addition to the long half-life period, it is still a bioaccumulative element, that is, even if low doses do or do not cause health problems acutely, a period of prolonged exposure to these concentrations may contribute to future diseases and serious health problems for the individual.

Lead affects all organs and systems of the human body, it is responsible for causing hypochromic microcytic anemia with increased reticulocytes, interfering with heme synthesis and destroying erythrocytes[2,6,7]. It is absorptive and when in low doses can increase the risk of spontaneous abortions, premature births or underweight newborns. Lead poisoning also interferes with the transformation of vitamin D, decreasing its absorption; in kidney function, it causes tubular damage; in addition to directly or indirectly affect other organs. The main toxic effect of lead is on the nervous system because it ranges from behavioral changes, such as motor dysfunction, hyperactivity, and decreased IQ, peripheral neuropathies, which can even cause acute encephalopathies[2,6,7,23].

The neurotoxic phenomena of lead are mainly due to its ability to replace calcium, which allows it to cross the blood-brain barrier and its interference in the release of neurotransmitters from presynaptic nerve endings, a fundamental role of calcium in the body[2,25,26]. In particular, in the developing nervous system, the continuous release of quantities below the neurotransmitter threshold in the synaptic cleft influences the maintenance of the efficiency of a synaptic

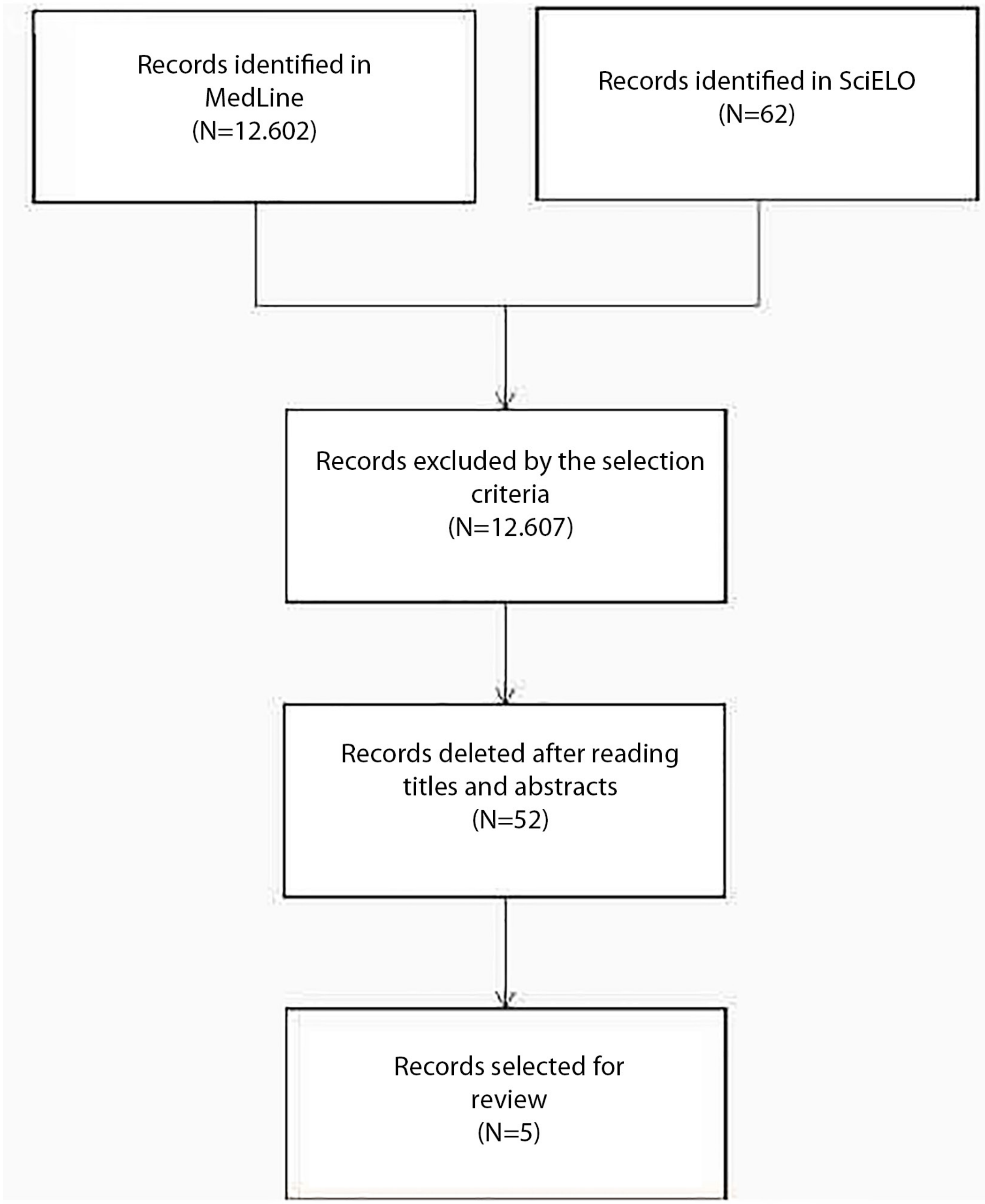

Figure 1 . Flowchart of the selection of studies included in the review

connection and the survival of the postsynaptic cell[25]. Cognitive and neuropsychological development is also compromised due to anemia and low iron absorption that are consequences of lead poisoning, even at low concentrations[2,26].

A study performed by Dr. Lanphear in 2000, concluded that concentrations below 10 µg/dL interfere with cognitive and academic skills[22]. Another study performed in 2003 by Dr. Canfield with children concluded that children's intellectual functioning is inversely associated with blood lead concentrations, even at levels below the limit defined by the CDC[27].

Lead exposure occurs mainly in battery production industries, recycling plants, and mining areas, but this metal can be present in several other places, from the environment to homes, such as painting walls, old pipes, in some food and even colorful toys and magazines, as well as in the dust of houses that are close to sources of lead emission or that have a resident who works in these places and does not manage the proper hygiene of the body and clothes[23,28,29]. Children are more susceptible to environmental lead poisoning because the contact and ingestion of lead particles present in household dust, in the splinters of wall paints and in the

Table 1. Summary of studies and their main results involving lead poisoning.

AUTOR/ANO	AMOSTRA	MÉTODO/INTERVENÇÃO	RESULTADOS
Ferron et al. (2012)	97 children, 0 to 5 years, Porto Alegre/RS	BE: Atomic absorption spectrometry in a graphite furnace Q: sociodemographic information, recycling, and housing. EA: dispersive energy X-ray fluorescence spectrometer	BAR: Pb-S ≥ 10.0µg/dL = 16.5% EAR: Soil: high levels Atmospheric: low levels.
Olympio et al. (2010)	160 teenagers 14 to 18 years Bauru/S	DEA: Pb = Atomic absorption spectrometry with graphite furnace P = Optical absorption spectrometry with inductively coupled plasma. Q: prior lead exposure	DEA PB: 134.8 µg/dl - exposed DEA PB: 76.25 µg/dl - not exposed QR: Lead exposures at home
Padula et al. (2006)	857 children 0 to 12 years Bauru/SP	Q: factors of exposure to lead at the site; possible sources of exposure not related to the area	BAR: Pb-S ≥ 10µg/dl = 314 children
Mattos et al. (2009)	64 children 0 to 16 years Rio de Janeiro - RJ	BE: Pb-S = Atomic absorption spectrometer EA: electrothermal atomic absorption spectrometer	BAR: Mean Pb-S = 5.6µg/dL Pb-S ≥6µg/dL = 40%
Canfield et al. (2003)	172 children 6, 12, 18, 24, 36, 48, and 60 months	BE: Atomic absorption spectrometry IQ: Stanford-Binet Intelligence Scale - 3 to 5 years.	BAR: 6 months = 3.4µg/dL 2 years = 9.7µg/dL 5 years = 6.0µg/dL IQ: linear + 10 µg/dL Pb, - 4.6 points in QI Non-linear 1 to 10 µg/dL, - 7.4 QI points

Legend: BE: Biological Evaluation; Q: Questionnaire; EA: Environmental Assessment; Pb-B: Blood-Pb Levels; DEA Dental Enamel Analysis; Pb: Lead; P: Phosphorus; BAR: Biological Analysis Result; QR: Questionnaire Result; EAR: Environmental Analysis Result; IQ: Intelligence quotient.

toys and magazines becomes greater due to the relationship of the child habit of “hand-mouth” and “mouth-object”. In addition to this factor, the level of absorption by the children’s organism is higher and the immaturity of the organism itself, which is in formation and has blood-brain barriers still under development[2,28,30].

In Brazil there are studies in specific areas of environmental accidents involving metals, such as the cases of Adrianópolis, PR, and Santo Amaro,BA,[31] and areas around industries that involve lead in their processes, as an example the research performed in Bauru,SP,[30]. In this study, data were collected on children living within a radius of up to 1000m in an accumulator industry, which produces automotive lead-acid batteries. Among the 857 children examined, 314 presented values greater than 10 µg/dL, a limit defined by the CDC, some of which were higher than 25 µg/dL. In both cases neuropediatric examinations were necessary and in some cases even hospitalization for treatment[30].

Two studies, one performed in Rio de Janeiro, in the Parque João Goulard community, and the other performed in Vila Dique, in Porto Alegre, RS, investigated and identified a high prevalence of lead contamination in children, and in both cases the areas surveyed had no previous reports of contamination by environmental lead, but were located close to industrial facilities and informal garbage dumps[28,32]. The study performed by Mattos, included 64 children, resulting in 5% of these with more than 10 µg/dL of lead and 40% with values between 6 µg/dL to 10 µg/dL[32], while the study by Ferrom, performed with 97 children, found 16.5% of children with a lead level above 10 µg/dL[28]. These studies show that lead poisoning goes well beyond occupational exposure and needs to be monitored even in environments where there is no detection of a specific source of lead emission, especially in children, as some studies point to the existence of damage even at the lowest doses[28,32].

Another aggravating factor with lead poisoning is the lack of knowledge and information by the population about the risks to which they are exposed. A 2010 study performed in Bauru, SP, pointed to the lack of information from the population on the forms of contamination, prevention, symptoms, and care in relation to lead, although many have already heard about lead being a toxic metal[23]. Given the above, it is observed that the danger represented by lead is greater than society understands. There are risks of environmental exposures unknown to most of the Brazilian population, and that the dangers to health have an alarming proportion.

All the abovementioned makes it essential that revisions of the NR7 are performed and the establishment of parameters for the Brazilian population in general, especially children and pregnant women, in addition to studies that show the true levels of exposure and contamination in the country, which in recent years has suffered from very serious environmental disasters as in the cases of Mariana and Brumadinho, oil spills in the oceans, in addition to having many small battery recycling plants and facilities of secondary smelters, many without due safety criteria and some even clandestine that emit pollutants to their workers and to the neighboring population.

CONCLUSION

The evident scarcity of epidemiological data involving lead poisoning in Brazil makes it difficult to assess the country's real situation, since the few existing studies have demonstrated the existence of exposure and poisoning by this metal in the country. This review confirms the need for new studies that assess the main risk sites and that can be the basis for changes in regulatory standards that establish exposure limits, especially in the face of international studies that show that many diseases occur below these limits.

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