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Research progress on the correlation between environmental factors and childhood leukemia

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Abstract. Among the malignant diseases that pose a significant risk to children's health and wellbeing is leukemia. As the incidence, diagnosis rate, and mortality rate of leukemia continue to rise, researchers and academics have conducted in-depth investigations into the factors that contribute to the development of this disease in young people. Some of the causes of childhood leukemia can be traced back to the outside world. In this study, we will examine what has been learned so far about how external environmental pollution factors are linked to childhood leukemia.

Keywords: environmental factors, leukemia, risk factors.

1. Introduction

Acute leukemia (AL), the most frequent pediatric cancer, has increased over the past few decades, jeopardizing children's physical and mental health. Since the 21st century, with the deepening and application of new technologies in basic medicine and experimental research and the improvement of epidemiological research methods, some scholars have noticed that the increase in childhood leukemia incidence and mortality is closely related to external environmental factors, especially environmental pollution. Numerous research has shown that environmental exposure, such as radiation, air pollution, chemical exposure, home renovation, traffic smoke, cigarettes, viral infections, etc., increases childhood leukemia [1-2]. This article will focus on the risk factors for environmental pollution in the external environment related to the occurrence of childhood leukemia.

2. External physical and chemical environmental risk factors

2.1 Ionizing radiation

According to the results of the relationship between survivors of the atomic bombing and fetuses who received low-dose X-ray radiation in utero and leukemia, there is no doubt that ionizing radiation causes leukemia. Ionizing radiation includes parental occupational exposure, parental diagnostic exposure, and children's exposure. In a German case-control study, maternal workplace exposure to ionizing radiation raised the risk of lymphoma in kids, while father's occupational exposure significantly increased the risk of leukemia (OR=1.80, 95%CI=0.71~4.58). The risk of leukemia in offspring of parents exposed to diagnostic X-ray radiation before birth is OR=1.33, 95%CI=1.10~1.61. [3]. Infante-Rivard et al. [4] found that the risk of leukemia after birth irradiation X-ray (diagnostic) was 1.04 (95% CI=0.72~1.49),

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and the risk of leukemia in two or more irradiators was significantly higher than that of the control group that had never been irradiated (OR=1.6l, 95%CI=1.13~2.28). The study also found that the risk of leukemia increased correspondingly with radiation volume. In a Shanghai investigation of environmental risk factors for acute leukemia in children [5], children with a history of X-ray exposure had a higher risk of leukemia (OR=3.2, 95%CI=1.6~6.1). Some studies have suggested that ionizing radiation works by inducing DNA damage and affecting DNA repair mechanisms (altering DNA repair processes, inhibition of DNA topoisomerase or cell-specific immune processes), ultimately leading to leukemia [6].

2.2 Electromagnetic radiation

With the rapid development of the national economy and technology, wireless communication networks and a large number of electronic and mechanical equipment have also been produced and updated year by year. Electromagnetic radiation is a non-ionizing radiation that is produced by everyday devices like mobile phones, home appliances (like TVs, tablets, microwave ovens, refrigerators), and FM radio stations, among others. When people are exposed to high levels of electromagnetic radiation for an extended period of time, they may experience symptoms like dizziness, fatigue, memory loss, and other negative effects. However, studies have shown that people exposed to a certain dose of electromagnetic radiation experience no adverse effects. Pregnant women who have been exposed to radiation are at increased risk of childhood leukemia [8]. How to effectively avoid electromagnetic radiation pollution from dangerous groups such as children and pregnant women is an urgent issue to be considered while bringing convenience to the progress and development of social science and technology.

2.3 Air pollution

Air pollution from parents' secondhand smoke, traffic pollutants, interior decorating, and furniture coatings overexposes leukemia patients [9]. At the same time, due to the different stages of children's physiological development, most children are accustomed to breathing through the mouth, bypassing the filtration system of the nasal cavity, which allows more harmful substances to enter the respiratory system [10]. Based on epidemiological and laboratory evidence, air pollution, particularly caused by traffic exhaust, is associated with acute leukemia in children [11]. Diesel and petrol exhaust are human carcinogens according to the International Agency for Research on Cancer. Traffic exhaust gases, especially benzene, are thought to be hematotoxic and leukemia-causing and can induce DNA double-strand breaks, to which children are more susceptible.

Studies have shown [12] that leukemia mortality is directly and significantly correlated with NO_2 and CO concentrations in the air ($P<0.05$), and increased PM10 content in the air is also a risk factor for leukemia. Therefore, we should properly solve the problem of external air pollution, pay attention to the sources of these pollutants, start from the source, gradually replace fossil fuels with clean energy through scientific and technological means, better plan urban transportation, and improve public transportation services, and then reduce the adverse effects of external air pollution on children's health.

2.4 Chemical contamination

Acute leukemia in children is caused by benzene in paints and coatings, a carcinogen of leukemia and lymphoma that damages DNA and induces leukemia-specific chromosomal ectopia. Pesticides and insecticides, which can cause acute leukemia, have also garnered attention. Relevant studies have shown [13-16] that women exposed to pesticides (insecticides) during pregnancy have an increased risk of leukemia in their children, and long-term exposure may be associated with offspring leukemia. Exposure of children to mosquito killers increases the risk of leukemia and is associated with greater exposure over time. There are several forms of leukemia caused by pollution of household chemicals such as pesticides and insecticides [17]: (1) Alkylation of alkyl groups in organophosphorus and DNA or proteins in such chemicals, so that cross-linking occurs within and between DNA strands, between chains or between DNA and proteins, and DNA strands are not easy to repair or are prone to error repair, resulting in increased mutation rate, or chromosome or chromatid breakage, resulting in severe

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mutations; (2) Cause oxidative stress leading to nucleic acid molecular base damage, DNA-protein cross-linking and DNA chain breakage, generating lipid peroxidized free radicals and alkyl free radicals, aggravating DNA damage or changing gene expression; Interfere with cellular mitosis, induce micronuclei, or chromosomal aberrations.

3. Household environmental pollution factors

3.1 Renovation pollution

In recent years, with the improvement of people's living standards year by year, people's lifestyles have also undergone some changes, home decoration has become increasingly complex, so the problem of indoor air pollution caused by decoration has gradually become prominent, and the relationship between home decoration and children's AL has also attracted the attention of many scholars. Formaldehyde can cause cell mutations, chromosomal abnormalities, and leukaemia by cross-linking DNA proteins. Many kinds of literature [18] shows that the earlier one moves in after renovation, the higher the risk of leukemia, and volatile substances such as benzene, toluene and xylene in home decoration pollution are significantly reduced after 5 months; After 6 months, the excess rate of formaldehyde was significantly reduced [19], and the higher the room temperature and the more air circulation, the faster formaldehyde volatilization [20]. According to studies [21], decoration materials and furniture contain formaldehyde, which releases over 3–5 years and cannot be entirely volatilized within 1–2 years after interior decoration, resulting in indoor dangerous gases surpassing the standard. Usually, the release cycle of benzene is short, about 6 months after decoration can volatilize completely, and the release cycle of formaldehyde is as long as 3~5 years, these volatile molecules in the air benzene, after skin or respiratory absorption, metabolized into phenolic substances in the body. Phenol must be re-detoxified by bone marrow, and the detoxification process can directly cause bone marrow cell damage and changes in the nucleic acid structure of hematopoietic stem progenitor cells, and then cause acute leukemia, aplastic anemia, etc.

3.2 Smoking Environment

Tobacco smoke contains about 4800 compounds, of which more than 60 are known human or animal carcinogens. Evidence suggests that paternal smoking may trigger carcinogenesis in offspring through genotoxic effects on sperm; Maternal exposure to tobacco smoke during pregnancy can have genotoxic effects on the fetus through the uterus; Children exposed to smoke can also experience genetic damage. A case-control research [22] reported a higher risk of AL in children whose dads smoked before, during, and/or after pregnancy and a slightly increased risk in children whose mothers smoked throughout pregnancy. Costa Rica has one of the highest rates of childhood leukemia.

4. Biological environmental pollution factors

With industrialization and urbanization, air pollution, global warming, permafrost melting, and ozone layer hole formation have threatened the external biological environment inhabited by humans, and some pathogenic factors in the natural environment have been activated and bred with external environmental pollution, which is linked to leukemia. HTLV-I infection can cause TL [23]. However, the mechanism of hematological tumors caused by HTLV-I remains unclear. Wu Wencai et al. [24] believe that HBZ (HTLV-1bZIP factor) is the only viral gene that is continuously and stably expressed in all AL patient samples, and HBZ can still maintain cell survival after knocking out Tax, indicating that HBZ protein plays an important role in the oncogenic mechanism of HTLV-I. In addition, Sun Chang et al. [25] believe that hepatitis B virus (HBV) has a certain relationship with the pathogenesis of leukemia, HBV can infect hematopoietic stem cells in the bone marrow and integrate viral genes with human chromosomes so that proto-oncogenes such as N-Ras are activated, and tumor suppressor genes such as p53 are mutated, which in turn leads to the occurrence of leukemia. In addition, Epstein-Barr virus (EBV) is generally susceptible in the population, and EBV is closely related to a variety of diseases of hematologic and non-hematologic origin, including acute leukemia (AL), Burkitt lymphoma, elderly

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EBV(+) diffuse large B-cell lymphoma, post-transplantation lymphoproliferative diseases, nasopharyngeal carcinoma, breast and gastric cancer, E-BV infection is associated with acute leukemia incidence, and EBV in B-AL. EBV-positive leukemia patients have a poor prognosis [26,27]. In recent years, the relationship between EBV infection and leukemia has become a research hotspot. Miao Hongxia et al. [28] found that AL patients had a 40.9% EBV infection rate, much higher than the control group, suggesting that EBV infection may be linked to the occurrence, development, and prognosis of AL. The objective factors of various biological pathogenic factors inducing leukemia in external environmental pollution should be paid attention to.

During the COVID-19 epidemic, millions of children were protected from childhood illnesses. The global COVID-19 pandemic response may boost childhood leukemia rates in the following years. This phenomenon will provide large-scale real-world proof if seen. In the next years, monitoring children leukemia incidence in different nations will help us understand the association between age, infection type, and molecular characteristics. This idea could direct future research on preventing pre-leukemia to leukemia.

5. Conclusion

Environment and childhood leukemia research is growing. Aetiological research are behind, therefore case-control studies provide much of the evidence. This paper introduces the risk factors for childhood leukemia from three perspectives: external physical and chemical environmental pollution, household environmental pollution, and biological environmental pollution. It helps us understand the impact of current environmental pollution on the incidence of childhood leukemia and has greater significance for the prevention and treatment of targeted causes. Genetic factors are also important risk factors for the onset of childhood leukemia, while the joint correlation study of environmental factors and genetic factors has less research data on the pathogenesis of childhood leukemia. In the future, more reliance will be placed on the early identification of childhood leukemia clusters through cancer registry surveillance, prospective, population-based biological sample archiving, and ultimately accurate environmental factor studies. Prevention based on environmental factors is a very important part of the prevention and treatment of childhood leukemia.

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