FLUORIDE

Quarterly Journal of The International Society for Fluoride Research Inc.

The Pros and Cons of Water Fluoridation Remain a Highly Controversial Issue: Prevention of Dental Caries and the Possible Risk of Intellectual Decline in Children

Unique digital address (Digital object identifier [DOI] equivalent): https://www.fluorideresearch.online/epub/files/352.pdf

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Submitted: 2025 May 14
Accepted: 2025 June 07
Published as e352: 2025 Jun 08

ABSTRACT

In many countries around the world (especially developed ones), fluoride addition to drinking water has achieved relatively obvious effects in improving oral health and preventing dental caries. However, while implementing water fluoridation, as the additional fluoride continuously enters the body over a long period, adverse effects on the body have also been discovered, especially the obstruction to children's intellectual development, which has attracted the attention of the international community. This paper mainly collects and analyzes the review literature and research reports on the impact of fluoride content in drinking water on children's intelligence since 2020. Although most papers published affirm that higher fluoride content in drinking water is closely related to the occurrence of mental retardation in children, many studies suggest that the range of fluoride concentration in drinking water stipulated by the World Health Organization has no significant impact on children's intelligence. Some studies also suggest that the articles on intellectual disabilities in children caused by high fluoride mainly come from underdeveloped countries with certain deficiencies in the advancement of their research methods and the design of the research topics. Importantly, in recent years, these research teams from Sweden, the United States, Canada and Denmark have discovered the impact of fluoride on children's intelligence by using more advanced methods, providing strong evidence for the relationship between fluoride content and children's intellectual disability.

Keywords: *Fluoride; Water fluoridation; Intelligence; Children; Dental caries*

The utilization of fluoride should take into account both the prevention of dental caries and the influence on intelligence in children. It is an academic and clinical application issue that is both contradictory and full of philosophy.

The role of water fluoridation in preventing dental caries

Fluoride can enhance the enamel's resistance to acid erosion, inhibit the metabolism of oral bacteria, and reduce the risk of tooth decay.[1] Studies show that the rational use of fluoride can obviously reduce the incidence of dental caries in children, especially for those with a high-sugar diet or poor oral hygiene.[2] In many countries around the world, the rate of dental caries among children is reduced by adding fluoride to drinking water (0.5-1.5 ppm), recommended by the World Health Organization (WHO), fluoride toothpaste or professional fluoride coating on the surface of teeth.[3] The Centers for Disease Control and Prevention of the United States has listed community water fluoridation (CWF) as one of the top ten public health

achievements of the 20th century because it has contributed to preventing tooth decay and improving oral health over the past 70 years.[4] CWF has been recognized by more than 90 countries around the world, international governments and health organizations.

Potential risks of excessive fluoride exposure on intelligence quotient (IQ) of children

Long-term excessive intake of fluoride (especially before the age of six) can lead to abnormal mineralization of tooth enamel, resulting in dental fluorosis, which is manifested as white spots or brown streaks on the tooth surface.[5] Extremely high doses of fluoride exposure may cause bone lesions and lead to skeletal fluorosis, which is a relatively serious symptom in endemic fluorosis areas.[6] In addition, chronic fluorosis can cause damage to multiple systems of the body.[7] People have expressed concerns about the potential harmful side effects of water fluoridation on human health, including dental fluorosis, bone abnormalities, cancer induction, reproductive dysfunction, thyroid function changes, neurodevelopmental and cognitive decline, etc. [4]

Damage to the central nervous system and decline in children's cognitive function have been confirmed in endemic fluorosis areas.[8] However, whether long-term use of water fluoridation leads to decline of intelligence in children has been a highly controversial issue for many years.

The references of review articles involving the topic concerning fluoride exposure and intelligence of children here are mostly selected from these databases such as BIOSIS, Embase, PsycInfo, PubMed, Scopus, Web of Science, ScienceDirect, Embase, Cochrane, as well as CNKI and Wan-Fang (Chinese databases). A latest review included 74 studies, most of which were conducted in China (n=45), India (n=12), Iran (n=4), Mexico (n=4), Canada (n=3), Pakistan (n=2), Denmark (n=1), New Zealand (n=1), and Spain (n=1).[9] Among them, 64 studies reported the negative correlation between fluoride exposure and children's intelligence quotient; 31 studies concerned the measurement of fluoride in drinking water and a dose-response association was found between the fluoride exposure group and the reference group ($P < 0.001$). When the exposure group was restricted to less than 4 ppm of fluoride, the correlation was inversely proportional. However, when it was lower than 1.5 ppm, this association is zero. Analysis of 13 individual-level measurement studies found that the IQ score decreased by 1.63 points for each increase of 1 ppm of urinary fluoride ($P<0.001$). Whereas, when fluoride exposure was lower than 1.5 ppm in drinking water, the data on the dose-response relationship between fluoride exposure and children's IQ were limited and uncertain. An evaluation report in 2016 released by the National Toxicology Program (NTP) of the United States pointed out that low to moderate level of evidence indicated a learning and memory deficits in non-human mammals exposed to fluoride.[10] This systematic review identified studies that evaluated and estimated the relationship between fluoride exposure and the cognitive or neurodevelopmental effects in adults and children, and evaluated them respectively. Among 53 low-quality studies on children, 46 found evidence that fluoride exposure was negatively correlated with children's IQ. This review found that with a certain degree of credibility, higher estimates of fluoride exposure, in which when the fluoride concentration in drinking water exceeded the 1.5 ppm stipulated in the WHO's "Drinking Water Quality Guidelines", was always associated with lower IQs in children. Recent epidemiological results support the view that an increase in fluoride intake in the early stage of development may lead to considerable IQ deficits.[11]

Many people believe that more research is needed to fully understand the impact of low fluoride exposure on children's IQ. A review excluding non-Latin published papers indicated that among the 39 health outcomes reviewed, four causal relationships were further evaluated.[12] Strong evidence for the causal relationship between dental fluorosis and the decline in children's IQ scores had been reported. However, the biological mechanism of its effect has not yet been clarified, and the dose-response curve at lower concentrations is also unclear. In studies with a high risk of bias, the negative correlation between fluoride exposure and IQ was particularly evident, while in the study only determined to have a low risk of bias, no adverse effects occurred.[13] Overall, most studies have shown that exposure to fluoride has an adverse effect on children's IQ, however, since the main role of residual confounding cannot be ruled out, other prospective studies are needed with low risk of bias and new epidemiological investigations to ultimately evaluate the relationship between fluoride exposure and cognitive neurodevelopment.[14] The 2019 Canadian Agency for Drugs and Technologies in Health (CADTH) Rapid Response Report reviewed a prospective cohort study conducted in Canada, in which the authors concluded that exposure to higher levels of fluoride during pregnancy was associated with lower overall IQ scores in children aged 3 to 4, but this effect was significant only when the analysis was limited to boys.[4]

Some authors conducted a systematic review of the literature on whether fluoride exposure increases the risk of low IQ in China (from 1988 to 2008), including 16 case-control studies, which evaluated the development of low IQ in children exposed to fluoride at an early stage.[15] It was found that there was a consistent and strong link between exposure to fluoride and low IQ. The probability of developing low IQ of children living in fluorosis areas is five times higher than that of children living in non-fluorosis areas or areas with mild fluorosis. A review analyzed the effect of the

prevention and control program for fluorosis implemented in China for over 40 years, as well as the impact of fluorosis on children's health.[16] Among the 70 included studies, 38 reported the effects of improving water quality for the reduce of fluoride due to high level of this ion in the water, the incidence of dental fluorosis in children and urinary fluoride levels, and 32 reported children's IQ and health status. After adopting the strategy of improving water quality, the fluoride content in drinking water, and the levels of urinary fluoride and dental fluorosis in children decreased significantly. Given that the results show that the IQ of children in the high-fluoride area is significantly lower than that of children in the low-fluoride area, reducing the fluoride content in drinking water and monitoring water quality are important strategies for the prevention and treatment.

Factors influencing the assessment of water fluoridation

Since a number of published studies have shown that a higher fluoride content in drinking water may be associated with low IQ in children, some people believe that these studies were conducted in rural and endemic fluorosis areas as well as areas with lower socioeconomic status in countries such as China, India, Iran or Mexico, in which the level of fluoride in natural water and fluoride salts is many times higher than the current level in developed countries.[4] In these studies, various methodological limitations were also discovered, including insufficient control of important confounding factors and low-quality research designs.

On the other hand, although health authorities have declared over the past 75 years that fluorination of community water is safe and has affected more than 400 million people worldwide, a study in Canada reported that higher fluoride exposure among pregnant women was associated with lower IQ scores in young children.[17] However, the study was criticized for its methods and the significance of the results. It has been indicated by Till and Green that the tendency to ignore new evidence that is inconsistent with the common view hinders the response to the early warning of fluoride as a potential developmental neurotoxin. In addition, they suggest that the evolving evidence should encourage scientists and health authorities to reevaluate the safety of water fluoridation for children's IQ.

The latest research results

A latest study by Professor Kippler's team from the Department of Environmental Medicine at Karolinska Institute in Sweden exhibited that they conducted a follow-up investigation on 500 mother-child pairs in rural areas of Bangladesh, where drinking water naturally contains fluoride.[18] In the follow-up of 10-year-old children, the fluoride concentration in household drinking water ranged from 0.04 to 0.74 ppm (98% came from private wells), which was lower than the existing threshold of 1.5 ppm for fluoride content in drinking water stipulated by the WHO and the European Union. The research team found that maternal urinary fluoride concentrations were inversely associated with full-scale raw scores at 5 and 10 years of children, respectively. In cross-sectional analysis at 10 years, child urinary fluoride was inversely associated with full-scale raw scores. The authors concluded that urinary fluoride concentrations measured prenatally and during childhood were associated with lower cognitive abilities, especially perceptual reasoning and verbal abilities in Bangladeshi children. Since Karolinska Institute is an internationally leading medical university, we believe the research level and laboratory conditions should be quite advanced. The research results support the persistence of the related defects caused by fluoride exposure and address previous concerns about the reliability of cognitive tests for young children.[19]

Recently, a prospective cohort study was conducted mainly among Hispanic women and children residing in Los Angeles, California.[20] The study adopted the Preschool Child Behavior Checklist (CBCL) to quantify neurobehavior, including the comprehensive scores for total problems, and internalized and externalized problems, and conducted linear and logistic regression model adjusted for covariates. It was found that prenatal fluoride exposure was associated with increased neurobehavioral problems, which suggests that there may be a need to establish recommendations for limiting fluoride exposure during the prenatal period.

A study combined new data from the prospective Odense Children's Cohort (OCC) with the results of two previous birth cohort studies from Mexico and Canada, and examined creatinine-adjusted urinary fluoride concentrations in urine samples from pregnant women and IQ of the children in 837 mother-child pairs.[21] The results showed that the combined analysis of all three cohorts demonstrated a statistically significant association between urinary fluoride and IQ, indicating that pregnant women and children may need protection to prevent fluoride toxicity. For this significant discovery, the journal, Fluoride, published a special commentary on it.[22]

CONCLUSION

Based on that a considerable number of studies involved in the damage to health caused by a certain amount of fluoride in water, when considering water fluoridation for the prevention of dental caries in public communities, its safety and effectiveness should be fully evaluated. Special attention should be paid to the impact of long-term excessive fluoride intake on children's intelligence. The total amount of fluoride

intake by children should be fully considered, and the intake routes of fluoride from sources such as drinking water, toothpaste and food should be comprehensively taken into account. It is important to strengthen the research on the local application of fluoride in the oral cavity to effectively prevent dental caries.

ACKNOWLEDGEMENTS

The study was financially supported majorly by the National Natural Science Foundation of China (grant number: 82404317, 82360672)

CONFLICT OF INTERESTS

The authors declare that they have no conflict of interest for the study.

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