NFIS

National Fluoridation Information Service

NFIS Advisory

A review of recent literature on potential effects of CWF programmes on neurological development and IQ attainment

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May 2013

National Fluoridation Information service

The National Fluoridation Information Service (NFIS) is a consortium funded by the Ministry of Health, led by Regional Public Health working in partnership with:

- Hutt Valley DHB Community Dental Services,
- Environmental Science and Research,
- Centre for Public Health Research at Massey University and
- National Poisons Centre.

Our work includes:

- Following public debate and choices on water fluoridation
- Monitoring international research on the usefulness of water fluoridation
- Critically reviewing emerging research
- Working with District Health Boards and Councils to provide accurate and up-to-date information to their communities
- Providing clinical advice to the Ministry of Health
- Monitoring water fluoridation policy
- Providing access to New Zealand oral health data and research
- Sharing information via quarterly e-newsletters and e-briefings and the NFIS website

BACKGROUND

There has been much written on the internet and in commentaries about CWF about possible dangerous effects of CWF interventions on neurodevelopment and IQ attainment in humans. Opponents to CWF frequently cite this discussion as a reason for local body politicians to oppose CWF programmes and as a reason to end the intervention. The argument is generally referenced to international data (largely from China) investigating the effects of drinking water contaminated with high amounts of fluoride. The quality and consistency of the studies are limited and local body politicians (in New Zealand) have expressed finding it hard to know what weight should be given to this research when making decisions about community water fluoridation.

To make sound decisions it is important for local body politicians to be able to compare the validity of this research and any assumed link to CWF with other research on the safety of CWF interventions. The purpose of this advisory is to clarify the validity of this research and any implications for the New Zealand situation.

KEY SCIENTIFIC QUESTION

Is there any evidence that CWF programmes are damaging to the developing brain in humans?

Question framed

What do the current international and national literatures say about the effects of CWF programmes on the developing human brain?

REVIEW OF EVIDENCE

Part 1: Are their known water contaminants which affect neurodevelopment? What are the main known variables which impact on IQ attainment in humans?

There is only limited information on the effects of drinking water contaminants on neurodevelopment in humans. Some data is available on the effects of excess levels of arsenic and lead. Overall, there is sufficient evidence to conclude that some deleterious effects on IQ can occur from these elements. However these studies have not provided precise estimates of effects, due to limitations in study design.

An IQ test is an examination that attempts to measure "how you think," as opposed to your accumulated knowledge, or "what you know." The name "IQ" stands for "intelligence quotient," because the first such tests were scored by a process of mathematical division, and the result of division is known as a quotient. While tests are no longer scored this way, the name has stuck. An IQ is a score derived from one of several standardized tests designed to assess intelligence.

The variables known to affect IQ include both genetic (hereditable) and environmental factors. The latter can include maternal health, nutrition, nurture and parenting, psychological and physical health, stress, sleep problems, drug and alcohol abuse, and head injury.

When modern IQ tests are devised, the mean (average) score within an age group is set to 100 and the standard deviation (SD) almost always to 15. The intention is that approximately 95% of the population scores within two SDs of the mean i.e. have an IQ between 70 and 130. IQ scores are used as predictors of educational achievement, special needs, job performance and income. They are also used to study IQ distributions in populations and the correlations between IQ and other variables.

The average IQ scores for many populations have been rising at an average rate of three points per decade since the early 20th century, a phenomenon called the Flynn effect. It is disputed whether these changes in scores reflect real changes in intellectual abilities.

Part 2: Is there any evidence of negative effects of fluoride on the development of the brain at any concentration?

There is some evidence suggesting a possibility of slight adverse effects on measured IQ at high drinking water concentrations of fluoride, but no good evidence of effects at concentrations found in NZ fluoridated water supplies.

Several studies have involved exploring the relationship between children's estimated levels of fluoride exposure and their intelligence, as estimated by IQ tests. In most cases, exposure has been defined in terms of fluoride concentrations in their drinking water (drinking water

fluoride concentrations; DWFC) and/or urine, with comparison of the IQ profile of a higher DWFC group with that of a lower DWFC group of children. A 2006 Report by the National Research Council of the U.S. National Academies (NRC, 2006)[1] discusses a number of such studies from China.

The authors of this report considered that the significance of these studies was uncertain. They noted most of the papers were brief reports and omitted important procedural details; for example most did not indicate whether or not the IQ tests were administered in a "blinded" manner (with the examiner being unaware of which fluoride group any child was from); which is an essential requirement to control the risk of observer bias.

Other uncertainties exist with these studies. For example the IQ results show erratic, patterns with small changes in age, casting some doubt on the validity[i] of the IQ measurements. Also, there is potential for bias, due to insufficient control for confounding factors[ii]. It is generally recognised that many extraneous factors can have significant influences on a child's IQ, including the educational level of their parents, and family income.[2, 3, 4] In some of the studies, there were clear inequalities between the different groups with respect to these factors.

The Chinese study reports also contain equivocal findings and questionable statistical analyses. In one of the better known studies (Xiang et al)[5] for example, there was far from a clear (negative) linear correlation between drinking water or urinary fluoride levels and mean IQ. (This is supported by the estimated Pearson correlation coefficient[iii] (R) value, which measures the degree of linear relationship between two variables. An R value can range between – 1 and + 1, and a value near zero means there is a random, nonlinear relationship between the two variables.

The obtained value of – 0.164 indicates that there was little in the way of a meaningful negative correlation between urinary fluoride levels and children's IQ).

This means that the process of extrapolation from a known high to a theoretical low urine or drinking water fluoride concentration, involving "reading off" the IQ value corresponding to the low concentration on the basis of such a straight line, is flawed. Therefore, there are uncertainties regarding the relevance of these studies to the New Zealand situation. This is because the high exposure (eg DWFCs) groups had DWFCs substantially higher than the

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[i] The internal validity of a study is the degree to which the results of its observations are correct.

[ii] A confounding factor is one which has an independent effect on the study outcome (eg IQ) and also occurs to an unequal degree in the different study groups. (eg in high versus low fluoride groups).

[iii] The Pearson product moment correlation coefficient (R), as employed by Xiang et al, measures the degree of linear relationship between two variables. If there is a perfect linear correlation between two variables (eg X and Y), all the observed values lie on a straight line on a graph, and R equals either 1.0 or – 1.0 (perfect positive or negative correlation respectively). For values of R between 0.16 and 0.29, correlation is weak to low, and for values of R below 0.16, correlation is too low to be meaningful.

levels in NZ fluoridated supplies, the latter, ranging between 0.7 to 1ppm, are closer to the levels found in the low DWFC ("control") groups in the Chinese studies.

Similar inconsistencies apply to a 2011 Study by Ding et al,[6] which divided subjects into five groups, on the basis of urinary fluoride concentrations. The highest mean IQ occurred in the second highest of the five urinary fluoride groups (not in the lowest urinary F group[iv]), and the highest urinary F group had the middle value IQ (not the lowest). A similar inconsistent pattern was noted when subjects were divided into ten groups on the basis of urinary fluoride concentrations. The highest urinary F group had the middle value IQ, not the lowest IQ. The highest IQ was found in the fourth, not the lowest urinary fluoride group, the IQ of the eighth (third highest) fluoride group was the same or very similar to that of the second fluoride group, and the lowest mean IQ was in the seventh group, not the tenth. The IQ findings therefore did not show consistent linear trends in relation to fluoride level.

In 2012, researchers published a review and meta-analysis of studies investigating fluoride neurotoxicity by means of epidemiological studies in children.[7] They initially identified 39 studies published between 1980 and 2011; however subsequent exclusions revealed 27 eligible studies with high exposure and reference groups, and end points of IQ scores or related cognitive function measures. Among these, 25 were from China and 2 from Iran. Two cohorts were exposed to fluoride from coal burning; otherwise exposure was via fluoride in drinking water. The Combined Raven's Test-Rural edition in China (CRT-RC) was used to measure the children's intelligence in 16 of these 27 studies. Other measures used were the Weschler Intelligence test (3 studies), Binet IQ test (2 studies), Raven's test (2 studies), Japan IQ test (2 studies), Chinese comparative test (1 study) and the mental work capacity index (1 study).

A "standardized weighted mean difference" (SMD)[v] was computed. Among the 27 studies, all but one showed random-effect SMD estimates that indicated an inverse association, ranging from -0.95 to -0.10. However information on the child's gender and parental education were not reported in more than 80% of the studies, and parental income was not reported in 93%; so that these variables (some potential confounding factors) were not included in the models used to compute the standardized weighted mean.

[iv] As would be expected if the relationship were linear

[v] Standardised weighted mean difference. The mean difference is the average difference between the "experimental" and "control" group across studies. Use of a weighted mean difference means the results of some of the studies make a greater contribution to the average than others. Studies with more precise estimates for their results (narrower confidence intervals) are given more weight. The Standardised Weighted Mean Difference is *a* weighted mean difference standardised across studies giving *the* average difference in standard deviations for the measures of that outcome.

The relative risk (RR)[vi] of a low/marginal score on the CRT-RC among children with high fluoride exposure compared to those with low exposure was 1.93 (95% CI 1.46 - 2.55). When the model was restricted to those 9 studies using the CRT-RC tests and drinking water fluoride only exposures, the RR was 1.75 (95% CI 1.16 - 2.65). However, while increasing fluoride exposure showed an inverse association with IQ test scores, the available exposure information did not allow a formal dose-response analysis because individual exposures (or urinary fluoride levels) were not usually known. This is a significant limitation of the analysis.

In conclusion, there is limited evidence of a possible negative effect of fluoride on development of the brain, as assessed by IQ, at high fluoride exposures. There are some mechanistic hypotheses for these possible effects. For example, fluoride can interfere with several enzyme systems, including cholinesterase and enzymes involved in glycolysis; this may result in general central nervous system depression.[8]

However the human data is inconsistent, and cannot be reliably extrapolated to levels of exposure associated with DWFCs of ~ 0.7 to 1.0 mg/L in fluoridated water supplies. The same difficulty applies to animal studies, where generally very high DWFCs have been used for the experimental groups, as opposed to levels nearer 1 mg/L.

Part 3: Is the research in this area robust enough to draw general conclusions about any such relationship? Are any potential mechanisms for proposed effects understood?

The available evidence raises the possibility that high levels of fluoride in drinking water may have subtle effects on children's IQ. However all of these studies have limitations in design and analysis, a clear dose-response relationship between DWFCs and assessed IQ are often not evident. The study authors are frequently very cautious in their comments, and several noted that any indicated negative effect applied only to high DWFCs. An hypothesis of fluoride neurotoxicity would also be supported by some experimental animal studies, however the great majority of these have only considered high fluoride intakes.

However collectively the data described are not robust enough to draw a firm conclusion that high fluoride levels in drinking water supplies contribute to retarded development of children's brains. Also there is no clear evidence to suggest an adverse effect on IQ at lower fluoride intakes such as that likely to occur in New Zealand, where fluoridated water supplies contain fluoride in the 0.7 to 1.0 mg/L range.

Thus the balance of current scientific evidence does not suggest any risk for the development of full IQ potential for New Zealand Children from current community water fluoridation initiatives, where maximum DWFCs are 1 mg/L.

[vi] The relative risk is the ratio of the risk of finding an occurrence (eg low IQ) among the "exposed" group relative to such a risk in the "unexposed" group. (eg high versus low DWFC groups)

IMPLICATIONS FOR NEW ZEALAND

What implications, if any, can be concluded from the evidence for

a. the MoH's current CWF policy

Due to the high DWFCs occurring in the Chinese and some other studies, they are not very relevant to the New Zealand situation. Due to the inconsistent results and questionable analyses in these studies, they cannot be reliably extrapolated to the DWFCs found in New Zealand fluoridated water supplies.

However consideration should be given to following the recent U.S. example to limit DWFCs to 0.7ppm, rather than permit a range of 0.7 to 1ppm. This is not because levels of 1mg/L are considered hazardous; rather that allowance should be made for exposures from other sources of fluoride.

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