

EFFECT OF HIGH FLUORIDE WATER ON INTELLIGENCE OF SCHOOL CHILDREN IN INDIA

MH Trivedi,^a RJ Verma,^a NJ Chinoy,^{a†} RS Patel,^b NG Sathawara^c

Ahmedabad, India

SUMMARY: The intelligence quotient (IQ) was measured in 190 school-age children, 12–13 years old, residing in two village areas of India with similar educational and socioeconomic conditions but differing in fluoride (F) concentration in the drinking water. The children in the high F area (drinking water F 5.55 ± 0.41 mg/L) had higher urinary F levels (6.13 ± 0.67 mg/L) than the children in the lower F area (drinking water F 2.01 ± 0.09 mg/L; urinary F levels 2.30 ± 0.28 mg/L). The mean IQ score of the 89 children in the high F area was significantly lower (91.72 ± 1.13), than that of the 101 children in lower F area (104.44 ± 1.23). A significant inverse relationship was also present between IQ and the urinary F level. In agreement with other studies elsewhere, these findings indicate that children drinking high F water are at risk for impaired development of intelligence.

Keywords: Fluoride in drinking water; India school children; Intelligence quotient; Urinary fluoride.

INTRODUCTION

According to current research findings, fluoride (F) produces neuronal dysfunction and synaptic injury by a mechanism that involves free radical production and lipid peroxidation.^{1–4} A recent study revealed that a high F level in drinking water depressed learning-memory ability of brain in Wistar rats,⁵ in agreement with earlier findings of Mullenix et al. showing that F exposure caused a common pattern of sex and dose-specific behavioral deficits in rats.⁶ Brain histology of NaF-intoxicated rabbits revealed loss of molecular layer and glial cell layer, and Purkinje neurons exhibited chromatolysis and acquired a 'ballooned' appearance.⁷ Reduction and even complete loss of Nissl substance was observed in rabbit⁷ and rat⁸ brain.

In recent studies in our laboratory, we found a significant dose-dependent reduction in DNA, RNA, and proteins in the cerebral hemisphere, cerebellum, and medulla oblongata regions of the brain in mice.^{9–10} In related work, Wang and co-workers¹¹ recorded evidence of DNA damage in brain cells of adult rats exposed to high F and low iodine. Effects of F on the thyroid gland and its function have also been studied.^{12–14} Moreover, animal experiments on the effect of high F and low iodine on biochemical indexes and the antioxidant defense of the brain have revealed decreased learning-memory in offspring rats.^{15–16}

An association of high F in drinking water with lower intelligence in children in China has been reported by Li et al.¹⁷ Earlier, Xiang et al.¹⁸ determined a benchmark concentration-response relationship between IQ <80 and the F level in

^aFor Correspondence: RJ Verma, Department of Zoology, University School of Sciences, Gujarat University, Ahmedabad-380 009, Gujarat, India, E-mail: ramtejverma2000@yahoo.com;

^bProfessor and Head, Dean Department of Education, University School of Psychology, Philosophy & Education, Gujarat University, Ahmedabad-380 009, India.

^cAsst. Director, Department of Hygiene, N.I.O.H (National Institute for Occupational Health), Meghani Nagar, Ahmedabad-380 016, India. [†]Deceased May 8, 2006.

drinking water was 2.32 mg F/L, and the lower-bound confidence limit was 1.85 mg F/L. By contrast, Spittle et al.¹⁹ found no trend for IQ to decline in children drinking artificially fluoridated for seven years in an area of South Island, New Zealand. Nevertheless, other studies indicate that exposure to increased levels of F are associated with lower IQ.²⁰⁻²¹ In India, both iodine deficiency disorders and fluorosis due to excessive consumption of F cause two prevalent endemic diseases that coexist in certain regions in the country.²² However, the majority of studies that show a correlation between lower IQ and elevated F intake are from China, and no such studies that we are aware of have been reported from India.

The aim of the present investigation was to examine F exposure of two groups of school children and its impact on their intelligence quotients.

MATERIALS AND METHODS

Our study was undertaken on 190 school-age children in the 6th and 7th standard (12–13 years old) of the lower F area of Chandlodia, Ahmedabad (101 students), and the high F area of Sachana (89 students), in the Sanand district of Gujarat, India. The children were life-long residents of their respective locations with only one school in each area. The nutritional and middle class socioeconomic status of both areas is very similar and good, but slightly lower in Sachana. Iodized salt is used in both areas.

The intelligence quotient (IQ) was measured in the children of both areas by using a questionnaire prepared by Professor JH Shah, copyrighted by Akash Manomapan Kendra, Ahmedabad, India, and standardized on the Gujarati population with 97% reliability rate in relation to the Stanford-Binet Intelligence Scale.²³ Before the students were allowed to open the questionnaire, the examiners gave a friendly explanation of the important instructions to avoid mental stress for those taking the test. Questions were related to the educational background of the children, and the test had to be completed in 8 min under the supervision of examiners.

Scores were ranked as: mental retardation (IQ <70), borderline (IQ 70–79), dull normal (IQ 80–89), normal (IQ 90–109), bright normal (IQ 110–119), superior (IQ 120–129), and very superior (IQ >129).¹⁸

The drinking water and urine samples of the children of both areas were collected in plastic bottles, stored under refrigeration, and used for the measurement of F using an ion selective electrode (Orion research, USA. Model no 96-09).

Values are expressed as Mean±SEM. Student's t test was used for statistical analysis of the data, and values of $p < 0.05$ were considered significant.

RESULTS

As seen in Table 1, mean urinary F levels were significantly higher in the children living in the area where the F content in drinking water was high compared to the area where it was much lower.

Table 1. Drinking water and urinary F level of children living in lower F Chandlodia and high F Sanacha (Mean ± SEM)

Area	Number of children examined	Level of F in drinking water (mg/L)	Urinary F level (mg/L)
Chandlodia, Ahmedabad District	101	2.01 ± 0.009	2.30 ± 0.28
Sanacha, Sanand District	89	5.55 ± 0.41*	6.13 ± 0.67*

*p<0.001 (Compared to lower F level).

Table 2 shows that the mean IQ of the 89 children in the high F water area of Sachana was 12.2 percent lower than the mean IQ of the 101 children in the lower F area of Chandlodia, which is highly significant. Significant differences between the IQ of male and female children within each of the two areas were also found.

Table 2. IQ scores of school children (numbers in parenthesis) living in lower F Chandlodia and high F Sachana (Mean ± SEM)

Group	Chandlodia, Ahmedabad	Sachana, Sanand
Total		
	104.44 ± 1.23 (101)	91.72 ± 1.13** (89)
According to gender		
Male (Total 6 th /7 th)	104.80 ± 1.47 (62)	90.24 ± 1.58** (56)
Female (Total 6 th /7 th)	103.87 ± 2.21 (39)	94.15 ± 1.35† (33)
According to gender and grade level		
6 th Standard		
Male	105.22 ± 2.45 (31)	96.25 ± 2.73† (20)
Female	105.55 ± 2.95 (18)	93.35 ± 2.23† (14)
7 th Standard		
Male	104.38 ± 1.67 (31)	86.70 ± 1.70** (36)
Female	102.42 ± 3.27 (21)	94.73 ± 1.72* (19)

*p<0.05; †p<0.01; **p<0.001 (compared to higher IQ group).

As seen in Table 3 and illustrated in the Figure, the IQ of nearly half the children in the lower F area of Chandlodia was in the normal range of 90 to 109. The IQ of 38.61% the children in this village area was above the normal range, and only 11.88% were below the normal range. On the other hand, the IQ of a much larger percentage of the children in the high F area of Sachana was in the normal range, and only 2.25% were above that range, with none with an IQ above 119. Moreover, in Sachana the IQ of 28.09% of the children was below the normal range—over twice the percentage found in Chandlodia.

Table 3. IQ distribution in children in lower F Chandlodia and high F Sachana

IQ	Chandlodia				Sachana			
	Male	Female	Total	%	Male	Female	Total	%
≥130	2	0	2	1.98	0	0	0	0
120–129	2	1	3	2.97	0	0	0	0
110–119	22	12	34	33.66	2	0	2	2.25
90–109	31	19	50	49.50	35	27	62	69.66
80–89	5	4	9	8.91	10	4	14	15.73
70–79	0	2	2	1.98	6	2	8	8.99
≤69	0	1	1	0.99	3	0	3	3.37
Total	62	39	101	100	56	33	89	100

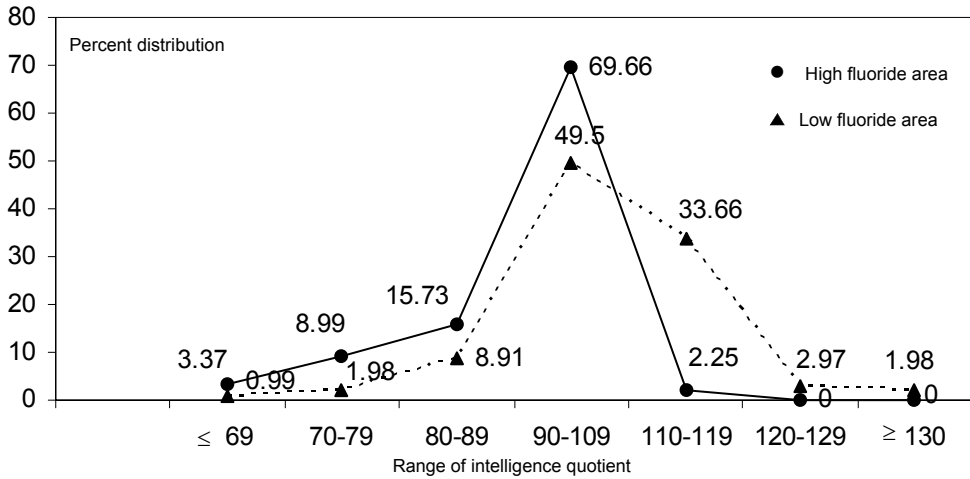


Figure. IQ score distribution of children in the high and lower F areas.

DISCUSSION

This study indicated that the mean IQ level of students exposed to high F drinking water was significantly lower than that of the students exposed to a lower F level drinking water. Because the kidney is the principal organ for the excretion of F, the rate or degree of exposure to F was checked by analyzing the urinary F level.²² In high F Sachana, more children had IQ scores below the normal 90–109 range than in lower F Chandlodia, where more children scored above the normal level. It thus appears that elevated F exposure depressed higher levels of intelligence even more than it affected normal and below normal intelligence of the children. Overall, the difference in mean IQ between the two groups was 12.2%, which, statistically, is highly significant. The normal IQ range for these areas is 100–110.²³

The biomechanism of the action of F in reducing IQ is not clear. However, there is evidence that it may involve in alteration of membrane lipid and reduction in cholinesterase activity in the brain. Guan et al.²⁵ demonstrated that the contents of phospholipids and ubiquinone are altered in the brain of rats affected by chronic fluorosis, and therefore changes in membrane lipids could be involved in the pathogenesis of this disorder. F is also known to have adverse effects on cholinesterase activity involved in the hydrolysis of esters of choline.²⁶ This toxic effect may lead to altered utilization of acetylcholine, thus affecting the transmission of nerve impulses in brain tissue.²⁷⁻²⁹ Recently, NaF has been found to alter the levels of dopamine, serotonin, 5-hydroxyindoleacetic acid, homovanillic acid, norepinephrine, and epinephrine in the hippocampus and neocortex regions of the rat brain.³⁰ Earlier, Yu et al.³¹ demonstrated changes in neurotransmitters and their receptors in human fetal brain from an endemic fluorosis area.

It is also well established that F can pass through the placenta to the fetus, and with subsequent continuous exposure to F during childhood, it may have adverse

effects on the developing brain, thereby causing decreased IQ in children.³²⁻³⁴ The greater reduction in IQ of children exposed to high F in our study compared to previous studies might reflect the magnitude of the difference in F concentration in the drinking water of the two areas, the modified version of the IQ test, and/or environmental, genetic, and cultural variations. The difference in F concentration in the drinking water between the two areas is 3.54 mg/L, which is higher in comparison to the studies done by Lu et al.²⁰ (2.78 mg/L), Xiang et al.¹⁸ (2.11 mg/L), and Seraj et al.³⁵ (2.1 mg/L).

Thyroid hormones play an important role in development of brain and thus might also affect IQ level. As noted in the Introduction, important aspects of F/iodine interactions on thyroid function are now being explored,¹²⁻¹⁴ and Susheela et al.²² have found that elevated F intake may cause iodine deficiency in fluorotic individuals, even when they reside in non-iodine deficient areas.

Clearly, for the benefit of future generations, urgent attention needs to be directed to improving our understanding of and correcting adverse effects of F on intelligence.

ACKNOWLEDGEMENTS

We take this opportunity to express our gratitude to Ms Yasheshvini A Trivedi and Twinkle N Tiwari for their kind assistance in conducting the IQ test. We also thank the technical staff of the National Institute of Occupational Health, Mr Pradeep Arya and Mr Idrish Shaikh, for their kind help with the analysis of urine and water samples.

REFERENCES

- 1 Guo XY, Sun GF, Sun YC. Oxidative stress from fluoride-induced hepatotoxicity in rats. *Fluoride* 2003;36:25-9.
- 2 Shivarajashankara YM, Shivashankara AR, Rao SH, Bhar PG. Oxidative stress in children with endemic skeletal fluorosis. *Fluoride* 2001;34:103-7.
- 3 Shivarajashankara YM, Shivashankara AR, Bhat PG, Rao SH. Effect of fluoride intoxication on lipid peroxidation and antioxidant systems in rats. *Fluoride* 2001;34:108-13.
- 4 Rzeuski R, Chlubek D, Machoy Z. Interactions between fluoride and biological free radical reactions. *Fluoride* 1998;31:43-5.
- 5 Wu C, Gu X, Ge Y, Zhang J, Wang J. Effects of fluoride and arsenic on brain biochemical indexes and learning-memory in rats. *Fluoride* 2006;39:274-79.
- 6 Mullenix PJ, Denbesten PK, Schunior A, Kernan WJ. Neurotoxicity of sodium fluoride in rats. *Neurotoxicol Teratol* 1995;17:169-77.
- 7 Shashi A. Histopathological investigation of fluoride-induced neurotoxicity in rabbits. *Fluoride* 2003;36:95-05.
- 8 Shivarajashankara YM, Shivashankara AR, Bhat PG, Rao SM, Rao SH. Histological changes in the brain of young fluoride-intoxicated rats. *Fluoride* 2002;35:12-21.
- 9 Verma RJ, Trivedi MH, Chinoy NJ. Black tea amelioration of sodium fluoride-induced alterations of DNA, RNA, and protein contents in the cerebral hemisphere, cerebellum, and medulla oblongata regions of mouse brain. *Fluoride* 2007;40:7-12.
- 10 Trivedi MH, Verma RJ, Chinoy NJ. Amelioration by black tea of sodium fluoride-induced changes in protein content of cerebral hemisphere, cerebellum, and medulla oblongata in brain region of mice. *Acta Pol Pharma-Drug Res* 2007;64:221-25.
- 11 Ge Y, Ning H, Wang S, Wang J. Comet assay of DNA damage in brain cells of adult rats exposed to high fluoride and low iodine. *Fluoride* 2005;38:209-14.

- 12 Zhan X, Li J, Wang M, Xu Z. Effects of fluoride on growth and thyroid function in young pigs. *Fluoride* 2006;39:95-100.
- 13 Trabelsi M, Guermazi F, Zeghal N. Effect of fluoride on thyroid function and cerebellar development in mice. *Fluoride* 2001;34:165-73.
- 14 Ge Y, Ning H, Wang S, Wang J. DNA damage in thyroid gland cells of rats exposed to long-term intake of high fluoride and low iodine. *Fluoride* 2005;38:318-23.
- 15 Wang J, Ge Y, Ning H, Wang S. Effects of high fluoride and low iodine on biochemical indexes of the brain and learning-memory of offspring rats. *Fluoride* 2004;37:201-08.
- 16 Wang J, Ge Y, Ning H, Wang S. Effects of high fluoride and low iodine on oxidative stress and antioxidant defense of the brain in offspring rats. *Fluoride* 2004;37:264-70.
- 17 Li XS, Zhil JL, Gao RO. Effect of fluoride on intelligence in children. *Fluoride* 1995;28:189-92.
- 18 Xiang Q, Liang Y, Chen L, Wang C, Chen B, Chen X, Zhou M. Effect of fluoride in drinking water on children's intelligence. *Fluoride* 2003;36:84-94.
- 19 Spittle B, Ferguson D, Bouwer C. Intelligence and fluoride exposure in New Zealand children [abstract]. *Fluoride* 1998;31:S13.
- 20 Lu Y, Sun ZR, Wu LN, Wang X, Lu W, Liu SS. Effect of high-fluoride water on intelligence in children. *Fluoride* 2000;33:74-8.
- 21 Zhao LB, Liang GH, Zhang DN, Wu XR. Effect of a high fluoride water supply on children's intelligence. *Fluoride* 1996;29:190-92.
- 22 Susheela AK, Bhatnagar M, Vig K, Mondal NK. Excess fluoride ingestion and thyroid hormone derangements in children living in Delhi, India. *Fluoride* 2005;38:98-08.
- 23 Desai K, Desai H. *Psychological Measurement*, Gujarat University Press, Gujarat State;India;1989. [in Gujarati].
- 24 Szymaczek JO, Borysewicz-Lewicka M. Urinary fluoride levels for assessment of fluoride exposure of pregnant women in Poznan, Poland. *Fluoride* 2005;38:312-17.
- 25 Guan ZZ, Wang YN, Xiao KQ, Dai DY, Chen YH, Liu JL, Sindelar P, Dallner G. Influence of chronic fluorosis on membrane lipids in rat brain. *Neurotoxicol Teratol* 1999;20:537-42.
- 26 Vani LM, Reddy KP. Effects of fluoride accumulation on some enzymes of brain and gastrocnemius muscle of mice. *Fluoride* 2000;33:17-26.
- 27 Marks DB, Marks AD, Smith CM. *Basic Medical Biochemistry: A Clinical Approach*. Baltimore, MD, USA: Lippincott, Williams & Wilkins; 1996.
- 28 Blaylock RL. Excitotoxicity: A possible central mechanism in fluoride neurotoxicity. *Fluoride* 2004;37:301-14.
- 29 Blaylock RL. Fluoride neurotoxicity and excitotoxicity/microglial activation: Critical need for more research. *Fluoride* 2007;40:89-92.
- 30 Chirumari K, Reddy PK. Dose-dependent effects of fluoride on neurochemical milieu in the hippocampus and neocortex of rat brain. *Fluoride* 2007;40:101-10.
- 31 Yu Y, Wang W, Dong Z. Changes in neurotransmitters and their receptors in human foetal brain from an endemic fluorosis area. *Chang Hua Liu Hsing Ping Hsueh Tsa Chih* 1996;15:257-59.
- 32 Verma RJ, Guna Sherlin, DM. Sodium fluoride-induced hypoproteinemia and hypoglycemia in parental and F₁-generation rats and amelioration by vitamins. *Food Chem Toxicol* 2002;40:1781-88.
- 33 Maduska AL, Ahokas RA, Anderson GD, Liphshitz J, Morrison JC. Placental transfer of intravenous fluoride in pregnant dams. *Am J Obstet* 1980;136:84-86.
- 34 Teotia M, Teotia SPS, Singh RK. Metabolism of fluoride in pregnant women residing in endemic fluorosis areas. *Fluoride* 1979;12:58-64.
- 35 Seraj B, Shahrabi M, Falahzade M, Falahzade F, Akhondi N. Effect of fluoride concentration in drinking water on children's intelligence. *J Dent Tehran Univ Med Sci* 2006;19:80-86. [abstract in this issue of *Fluoride*, p. 200-1].