

PREVALENCE OF NEUROLOGICAL MANIFESTATIONS IN A HUMAN POPULATION EXPOSED TO FLUORIDE IN DRINKING WATER

JD Sharma,^a Deepika Sohu, Parul Jain
Jaipur, India

SUMMARY: A health survey of a human population exposed to low, medium, and high fluoride (F) concentrations in drinking water in villages of Sanganer Tehsil, India, was conducted. A total of 2691 subjects were personally interviewed and classified from low (<1.0 ppm), medium (1.0-1.5 ppm) and high (1.5-6.4 ppm) F villages. Among the subjects were 1145 children aged 12 to 18 years and 1546 adults aged >18 years who were interviewed for various neurological ailments, viz., headache, insomnia, lethargy, polyuria, and polydipsia. There were no neurological manifestations in children in the low and medium F villages, whereas, in the high F villages, 9.48% of the children had headache, 1.21% had insomnia, and 3.23% exhibited lethargy. There were no cases of polyuria or polydipsia among the children in any of the villages. Among adults in the low, medium, and high F villages, 1.56%, 2.51%, and 26.96%, respectively, suffered with headache, while 1.17%, 1.12%, and 24.74% had insomnia, and 2.73%, 3.63%, and 23.70% manifested lethargy. No cases of polyuria or polydipsia were reported in the low and medium F villages, whereas in the high F villages there were 0.74% and 1.19% cases, respectively. The severity of the ailments increased with the increasing F concentration in the drinking water. Although the percentage of headache, insomnia, and lethargy among the adults was fairly small in the low and medium F villages, it was considerable in the high F endemic villages, clearly indicative of a role of fluoride in such neurological outcomes. The data also indicate that the largest number of cases were headache, followed by lethargy and insomnia in the endemic village areas.

Keywords: Endemic fluoride; Fluoride in water; Headache; Insomnia; Lethargy; Neurological manifestations; Sanganer Tehsil, India.

INTRODUCTION

Fluorosis caused by excess intake of fluoride (F) is a slow, progressive degenerative disorder in man and animals that produces deleterious effects on the skeletal system,¹⁻³ dental tissues,³⁻⁶ soft tissues,^{5, 7-8} enzyme activities,^{5, 9} and locomotor behavior.¹⁰⁻¹¹ F has the ability to interfere with brain function,¹² reducing IQ levels in children,¹³⁻¹⁵ cognition and memory,¹⁶ and learning ability.¹⁷ It also impairs the central nervous system functions.¹⁸

The present study was designed to investigate the effect of high fluoride in drinking water on neuro-behavioral patterns of a human population in villages of a F endemic area.

MATERIALS AND METHODS

On the basis of the fluoride concentration in the groundwater, 20 villages of Sanganer Tehsil, India, were divided into two groups with 10 villages in each group: a F non-endemic (low F group having F in drinking water below 1 ppm) or medium F (in the range of 1.0-1.5 ppm) and a F endemic group (drinking water F more than 1.5 ppm).

^aFor correspondence: Dr (Mrs) JD Sharma, Associate Professor, Department of Zoology, University of Rajasthan, Jaipur, Rajasthan, India; E-mail: jaishree_ajay@yahoo.co.in.

A human health survey was conducted in the above-selected villages. A questionnaire was prepared with the help of medical doctors to personally interrogate and to investigate the health problems of the inhabitants of the F-affected villages.

RESULTS

As found here, F ingestion in excess can lead to various neurological manifestations. Inhabitants of certain villages in Sanganer Tehsil were found to be suffering from various neurological disorders due to high levels of F in the groundwater. The main neurological manifestations observed were headache, insomnia (lack of sleep), lethargy (fatigue), depression, polyuria (tendency to urinate frequently), and polydipsia (excessive thirst).

In the low and medium F villages, no child was found to have any of these neurological symptoms. In the high F area, a few children were found to have headache, insomnia, and lethargy, most of them complaining of headache followed by insomnia and lethargy. No child in high fluoride area was found to have polyuria or polydipsia (Table 1).

Table 1. Neurological manifestations among children in low, medium, and high F villages of Sanganer Tehsil

Village area	Sex ^a	Total no of children surveyed	Neurological manifestations				
			Headache	Insomnia	Lethargy	Polyuria	Polydipsia
Low F (<1.0ppm)	M	186	0	0	0	0	0
	F	186	0	0	0	0	0
Medium F (1.0-1.5ppm)	M	180	0	0	0	0	0
	F	175	0	0	0	0	0
High F (>1.5ppm)		418	47 (11.24) ^b	16 (3.83)	6 (1.44)	0	0
	M	213	29 (13.62)	13 (6.10)	4 (1.88)	0	0
	F	205	18 (8.78)	3 (1.46)	2 (0.98)	0	0

^aM = Male, F = Female. ^bValues in parenthesis are percentages of each group.

In the low F villages, a small number of adults suffered from neurological manifestations, the most common of which was lethargy followed by headache and insomnia. No case of polyuria or polydipsia was observed among adults in the low F villages (Table 2).

Table 2. Neurological manifestations among adults in low, medium, and high F vil lages of Sangner Tehsil

Village area	Sex ^a	Total no of adults surveyed	Neurological manifestations				
			Headache	Insomnia	Lethargy	Polyuria	Polydipsia
Low F (<1.0 ppm)	M	513	8 (1.56) ^b	6 (1.17)	14 (2.73)	0	0
		259	5 (1.93)	3 (1.16)	9 (3.47)	0	0
		254	3 (1.18)	3 (1.18)	5 (1.97)	0	0
Medium F (1.0-1.5 ppm)	M	477	12 (2.51)	7 (1.47)	22 (4.61)	0	0
		242	8 (3.30)	4 (1.66)	13 (5.37)	0	0
		235	4 (1.70)	3 (1.28)	9 (3.83)	0	0
High F (>1.5 ppm)	M	566	179 (32.19)	151 (27.16)	164 (29.50)	5 (0.90)	8 (1.44)
		292	96 (32.88)	80 (27.40)	109 (37.33)	3 (1.03)	5 (1.71)
		274	83 (31.44)	71 (26.89)	55 (20.83)	2 (0.76)	3 (1.14)

^aM = Male, F = Female. ^bValues in parenthesis are percentages in each group.

In the medium F villages a considerable number of adults suffered from lethargy followed by headache and insomnia. As in the low F villages, no subject was found to be suffering from polyuria or polydipsia (Table 2). Males were more prone to the neurological manifestations than females.

In the high F villages the percentage of adult inhabitants suffering from headache, insomnia, lethargy, polyuria, and polydipsia was high compared to the low and medium F villages. The most frequent neurological manifestation among adults was headache again followed by insomnia and lethargy. A few cases of polyuria and polydipsia were also reported among adults in the high F villages (Table 2).

The results revealed that in the study villages, the most prevalent neurological manifestation was headache in both children and adults, followed by lethargy and insomnia. However, there were a few cases of polyuria and polydipsia among adults, but not children, especially in the high F villages (Table 3). Again, males were found to be more prone to fluorosis than females. The most vulnerable age group for all the neurological manifestations was 40-60 years followed by 18-40 years (Table 3).

Table 3. Neurological manifestations in inhabitants of different age groups and sex of villages of Sanganer Tehsil

Age range (years)	Sex ^a	Total no of people surveyed	Neurological manifestations				
			Headache	Insomnia	Lethargy	Polyuria	Polydipsia
<6	Total	146	0	0	0	0	0
	M	75	0	0	0	0	0
	F	71	0	0	0	0	0
6-12	Total	277	0	0	0	0	0
	M	133	0	0	0	0	0
	F	144	0	0	0	0	0
12-18	Total	722	47 (6.51)	16 (2.22)	6 (0.83)	0	0
	M	371	29 (7.82)	13 (3.50)	4 (1.08)	0	0
	F	351	18 (5.13)	3 (0.85)	2 (0.57)	0	0
18-40	Total	816	106 (12.99)	82 (10.05)	120 (14.71)	1 (0.12)	2 (0.25)
	M	418	57 (13.64)	45 (10.77)	65 (15.55)	1 (0.24)	2 (0.48)
	F	398	49 (12.31)	37 (9.30)	55 (13.82)	0	0
40-60	Total	541	75 (13.86)	60 (11.09)	91 (16.82)	3 (0.55)	4 (0.74)
	M	280	41 (14.64)	31 (11.07)	52 (18.57)	2 (0.71)	2 (0.71)
	F	261	34 (13.03)	29 (11.11)	39 (14.94)	1 (0.96)	2 (0.77)
>60	Total	199	18 (9.05)	22 (11.06)	27 (13.57)	2 (1.01)	2 (1.01)
	M	95	11 (11.58)	11 (11.58)	14 (14.74)	1 (1.05)	1 (1.05)
	F	104	7 (6.73)	11 (10.58)	13 (12.50)	1 (0.96)	1 (0.96)
Children	Total	1145	47 (4.10)	16 (1.40)	6 (0.52)	0	0
	M	579	29 (5.01)	13 (2.25)	4 (0.69)	0	0
	F	566	18 (3.18) ^b	3 (0.53)	2 (0.35)	0	0
Adults	Total	1556	199 (12.79)	164 (10.54)	238 (15.30)	6 (0.39)	8 (0.51)
	M	793	109 (13.75)	87 (10.97)	131 (16.52)	4 (0.50)	5 (0.63)
	F	763	90 (11.80)	77 (10.09)	107 (14.02)	2 (0.26)	3 (0.39)
Grand Total	Total	2701	246 (9.11)	180 (6.66)	244 (9.03)	6 (0.22)	8 (0.30)
	M	1372	138 (10.06)	100 (7.29)	135 (9.84)	4 (0.29)	5 (0.36)
	F	1329	108 (8.13)	80 (6.02)	109 (8.20)	2 (0.15)	3 (0.23)

^a M = Male, F= Female. ^bValues in parenthesis are percentages in each group.

DISCUSSION

Among neurological ailments caused by F are neurological manifestations such as headache, paralysis, quadriplegia, lethargy, insomnia, etc., but no individual usually suffers to a great extent from any one symptom. Although the blood-brain barrier is relatively impermeable to F, it does not pose an absolute barrier, and F has the ability to enter the brain, where it can disrupt the activity of normally functioning hormones. For example, F can reduce levels of melatonin, the sleep hormone, in the body, causing chronic insomnia.¹⁹

Spittle¹⁰ has recorded cases of severe headache, lethargy, depression, and paralysis in adult subjects exposed to medium-level F in their drinking water. Possible mechanisms whereby F could affect brain function include influencing calcium currents, altering enzyme configuration by forming strong hydrogen bonds with amide groups, inhibiting cortical adenylyl cyclase activity, and increasing phosphoinositide hydrolysis.¹⁰ Shashi²⁰ also has suggested that there is a direct action of F on nerve tissue in the brain that is responsible for central nervous system problems such as tremors, seizures, and paralysis

In the present study, some individuals complained of polydipsia and polyuria. F adversely affects various parts of the brain, affecting behavioral patterns controlled by those parts. Furthermore, F inhibits anti-diuretic hormone production in the brain, and consequently the kidneys (the target organ for the hormone action) are unable to function normally for elimination of sufficient urine and re-absorption of water by the tubules. Srikantia and Siddiqui²¹ emphasized polydipsia and polyuria in endemic skeletal fluorosis in an endemic F area in India.

CONCLUSION

F may cause various neurological manifestations among subjects residing in endemic areas that may be due, at least in part, to the adverse action of F on the brain and various organs such as the kidney controlled by the brain through various hormones.

ACKNOWLEDGEMENTS

The authors are grateful for support from the Ground Water Department, Government of Rajasthan, and the Head, Department of Zoology, University of Rajasthan, Jaipur, Rajasthan (India). This work was presented at the XXVIIIth Conference of the International Society for Fluoride Research, 7-11 August 2008, Toronto, Canada.

REFERENCES

- 1 Botha CJ, Nande TW, Mannaar PP, Van-Amstel SR, Jansevan-Rensberg SD. Two outbreaks of fluorosis in cattle and sheep. *J S Afr Vet Assoc* 1993;64:165.
- 2 Gupta SK, Gambhir S, Mithal A, Das BK. Skeletal scintigraphic findings in endemic skeletal fluorosis. *Nucl Med Commun* 1993;14:384.
- 3 Choubisa SL. Some observations on endemic fluorosis in domestic animals in southern Rajasthan (India). *Vet Res Commun* 1999;23:457.
- 4 Boulton IC, Cooke JA, Johnson MS. Fluoride accumulation and toxicity in laboratory population of wild small mammals and white mice. *J Appl Toxicol* 1995;15:423.

- 5 Michael M, Barot VV, Chinoy NJ. Investigation of soft tissue functions in fluorotic individual of North Gujarat. *Fluoride* 1996;29:63.
- 6 Hicks MJ, Flaitz CM. Enamel caries formation and lesion progression with a fluoride dentifrice and a calcium-phosphate containing fluoride dentifrice: a polarized light microscopic study. *ASDC J Dent Child* 2000;67:21.
- 7 Chinoy NJ, Pradeep PK, Sequeira E. Effects of fluoride ingestion on the physiology of reproductive organs of male rats. *J Environ Biol* 1991;13:55.
- 8 Purohit SD, Gupta RC, Mathur AK, Gupta N, Jeswani ID, Choudhary VK, Purohit SK. Experimental pulmonary fluorosis. *Indian J Chest Dis Allied Sci* 1999;41:27.
- 9 Suketa Y, Mikami E. Changes in urinary excretion and related renal enzyme activities in fluoride treated rats. *Toxicol Appl Pharmacol* 1977;40:551-9.
- 10 Spittle B. Psychopharmacology of fluoride: a review. *Int Clin Psychopharmacol* 1994;9:79-82.
- 11 Paul V, Ekambaram P, Jayakumar AR. Effects of sodium fluoride on locomotor behavior and a few biochemical parameters in rats. *Environ Toxicol Pharmacol* 1998;6:187-91.
- 12 National Research Council. Fluoride in drinking water: a scientific review of EPA standards. Washington, DC: National Academies Press; 2006. p. 187.
- 13 Trivedi MH, Verma RJ, Chinoy NJ, Patel RS, Sathawara NG. Effect of high fluoride water on intelligence of school children in India. *Fluoride* 2007;40(3):178-83.
- 14 Wang SX, Wang ZH, Cheng XT, Li J, Sang ZP, Zhang XD, et al. Arsenic and fluoride exposure in drinking water: children's IQ and growth in Shanyin Country, Shanxi Province, China. *Environ Health Perspec* 2007;115(4):643-7.
- 15 Rocha-Amador D, Navarro ME, Carrizales L, Morales R, Calderon J. Decreased intelligence in children and exposure to fluoride and arsenic in drinking water. *Cadernos de Saude Publica* 2007;23(Suppl 4):S579-87.
- 16 Calvert GM, Mueller CA, Fajen JM, Chrislip DW, Russo J, Briggie T, et al. Health effects associated with sulfuric acid and methyl bromide exposure among structural fumigation workers. *American J Public Health* 1998;88:1774-80.
- 17 Chioca LR, Raupp IM, Da Cunha C, Losso EM, Andreatini R. Subchronic fluoride intake induces impairment in habituation and active avoidance tasks in rats. *Eur J Pharmacol* 2008;579(1-3):196-201.
- 18 Guo Z, et al. Study on neurobehavioral function of workers occupationally exposed to fluoride. *Ind Health Occup Dis* 2001;27:346-348.
- 19 Heliman B. Fluoridation of Water: Questions about health risks and benefits remain after more than 40 years. *Chemical and Engineering News* 1998;26-42.
- 20 Shashi A. Histopathological investigation of fluoride-induced neurotoxicity in rabbits. *Fluoride* 2003;36:95-105.
- 21 Srikantia SG, Siddiqui AH. Metabolic studies in skeletal fluorosis. *Clin Sci* 1965;28:477-485.