Analysis of the effect of fluoride on male infertility in regions with reported high level of fluoride presence (endemic fluorosis)

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Abstract: The present research report has looked into the correlation between male infertility and the fluoride level in water, the occurrence of dental and skeletal fluorosis, [the volume and quality of] semen and the amount of fluoride contained therein. Results have shown that fluoride might be a leading cause of male infertility in regions with endemic fluorosis.

Keywords: Fluoride, Endemic Fluorosis, Male Infertility

Fluoride and its damaging effect on human fertility have already been widely reported in various studies, from biological research reports to analyses from endemic fluorosis regions. However, the findings of these reports have not been entirely consistent and the conclusions have often differed. We gathered data on the rate of male infertility in endemic fluorosis regions and nonendemic regions, and our findings are listed below.

Information and Methodology

- 1. Definition of endemic fluorosis region: A region was defined as a high fluoride region where the water fluoride level exceeds 1.0mg/L, the occurrence of dental fluorosis in students aged between 8-15 years is greater than 30%, and individuals are found to have skeletal fluorosis upon X-ray inspections. Regions satisfying these conditions are considered an "endemic fluorosis region." Regions where reported incidents are lower than the rates listed above were not considered to be an endemic fluorosis region.
- 2. Definition of male infertility: Couples living in the studied regions who appeared to be of good health prior to their marriage, and who lived together in harmony for more than 3 years after their marriage, or where an ofage fertile woman has lived in harmony with her spouse for more than 2 years, or couples which had been practicing unprotected sex but had not yet conceived, were all deemed to be suffering from primary infertility or secondary infertility. A person experiencing one or more of the following conditions was considered to be suffering from male infertility or reproductive functional disability: less than 1.0 ml of semen secreted in each ejaculation; density of sperm lower than 600 x 109/ L; a

- rate of sperm abnormality greater than 5%; or an automatic death rate of the sperm greater than 40%.
- 3. Research method: We employed direct electro method to inspect the level of fluoride in drinking water and in semen. We have used spectroscopic methods to test the amount of trace elements such as Zn, Cu, Mo, Fe and As contained in various types of food and vegetable items. We have also performed a census on the occurrence of male infertility in the inspected region. As per results of the medical history, we have asked individuals who appeared to be suffering from male infertility (and who did not appear to be suffering from common symptoms of male infertility) to refrain from having sexual intercourse for 3 days. We then asked them to collect the semen ejaculated in this "first sexual contact" after the period of abstinence, and submit the specimen to medical professionals in order to carry out standard lab tests. These lab tests focused, in particular, on the amount of fluoride contained in the semen specimens.

Results

A. Common Conditions

The surveyed regions with high levels of fluoride and normal fluoride levels are agricultural communities. Inhabitants of these regions are primarily Muslim and do not have any special habits in their daily routine which are out of the ordinary. The Male subjects in the study all share similar livelihoods, cultural and economic backgrounds. We refrained from performing research among different ethnicities. In regions with high levels of fluoride, the occurrence of dental fluorosis in schoolaged children is between 44.12% and 87.55% and

skeletal fluorosis is at 30%. The same rate of occurrence in regions with normalized level of fluoride is 4.80% and 0%, respectively. 57 cases of male infertility have been recorded as per table 1 below.

Table 1 –Details of 57 Cases of Male Infertility						
Item	No. of Occurrences	%				
Regions with endemic fluorosis	40	70.18				
Non-endemic regions	17	29.82				
Individuals in their 1st marriage	46	80.70				
Re-married individuals	11	19.30				
Voluntarily married individuals	47	82.46				
Individuals in arranged marriages	10	17.54				
Individuals with lack of sexual activity	28	28.28				
Individuals with history of masturbation	11	11.11				
Individuals with history of spermatorrhea	23 23.23					
Premature ejaculation	33 33.33					
Impotence	4 4.04					
No. of births and abortions	18	0.31				

B. Results of the Research on Cause(s) of Disease

1. Fluoride content of the drinking water. Inhabitants in both the endemic fluorosis and non-endemic regions consume water from dugout underground wells. Non-endemic regions have been drawing water from a well whose amount of fluoride was measured at 0.46 mg/L, whereas inhabitants from regions lightly/somewhat/

severely affected by endemic fluorosis had fluoride levels in their water of 0.96, 1.25 and 2.0 mg/L, respectively.

- 2. Fluoride content of consumed food items and vegetables. 25 food samples taken from endemic fluorosis regions (millet, beans and wheat) contain, in general, 0.66 +/- 0.20 mg/kg; 25 other food samples (Chinese bok choy, leek, green pepper, etc) contain, in general, 0.63 +/- 0.32 mg/kg. In comparison, 8 food samples (food items and vegetables) taken from the nonepidemic region were found to contain 0.64 +/- 0.18 and 0.52 +/- 0.20 mg/kg (P>0.05), respectively. If we were to assume that each person consumes 3 L of water and 0.5 kg of food and vegetables on a daily basis, then inhabitants of a region not affected by epidemic fluorosis would be consuming 2.15 mg/day from water, food and vegetables daily. Inhabitants of an endemic region would be consuming 3.79-6.91 mg/day (P<0.05 ~ 0.01).
- **3**. *The amount of trace elements being consumed*. Upon calculation, it appears that the consumption of trace elements such as Zn, Cu, Mo, Mn, Fe, L, As are all within normal ranges. (1)

C. Male Infertility

The occurrence of male infertility in non-endemic fluorosis regions was found to be 3.33% (17/451), in comparison to 6.32% in endemic regions (40/633), with P<0.05. Amongst these cases, occurrence of primary male infertility was 2.88% (13/451) in non-endemic regions, versus 5.21% in endemic regions (33/633), with 0.05>P>0.025. Occurrence of secondary male infertility was found to be 0.89% (4/451) and 1.11% (7/633), with P>0.05, respectively. In non-endemic regions, amongst the 17 cases investigated, there was no finding of any occurrence of changes in alignment related to skeletal fluorosis. In comparison, amongst the 40 cases investigated in a region affected by epidemic fluorosis, we have found 12 cases of mild skeletal fluorosis, 14 cases of moderate skeletal fluorosis and 8 cases of severe skeletal fluorosis, bringing the total to 34 clinical cases.

^{*} To draw water from common dugout underground wells, inhabitants dig out vertical wells of relatively even dimensions (height/depth/orientation) on deserted fields or on mountain edges and cliffs. Once the different wells are connected underground, they cover the various openings and only leave one opening as the water source. This water source is usually located near a village or plots of land. The rest of the openings are only open when regular clean-ups (of mud) are required.

Table 2 - Data gathered from semen samples collected from infertile male subjects in non-endemic regions and endemic fluorosis regions

Data found in semen samples	Non- endemic regions	Endemic fluorosis regions	P value			
Cases recorded	17	9				
Density of sperm count 10 ⁹ / L (X +/- SD)	490 +/- 320	220 +/- 180	<0.01			
Abnormally formed sperm count (%)	11	17	>0.05			
Spermatorrhea (%)	24.00	46.51	<0.01			

D. Results of Semen Inspection

Due to cultural reasons and taboo, we have only managed to gather 26 samples of semen from infertile male subjects. Endemic sperm specimens and the amount of fluoride contained therein show dramatic differences in data from regular samples. The correlation between water fluoride and the rate of dental fluorosis, as well as that of water fluoride and the level of fluoride detected in semen, measured at 0.98 and 0.96 respectively (Table 3).

Table 3 displays the water fluoride levels and dental fluorosis rates (r > 0.98) and the relation to fluoride content in semen (r > 0.96), showing a positive correlation (P < 0.05). The fluoride content of semen from infertile males from different endemic fluorosis regions also increases corresponding to an increase in water fluoride concentration ($P > 0.05 \sim P < 0.01$).

Table 3 - A comparison of the amount of fluoride found in semen samples gathered from infertile male subjects with water fluoride level and dental fluorosis rate in non-endemic and endemic fluorosis regions

Item	Non-epidemic region	Endemic fluorosis region			R	Р	
		1	2	3			
Cases recorded	17	11	13	16			
Water fluorosis (mg/L)	0.46	0.96	1.25	2.0			
Dental fluorosis (%)	4.8	44.12	49.30	87.55	0.98	<0.05	
(mg/L) of fluoride in semen samples	0.053 +/- 0.024	0.058 +/- 0.032	0.071 +/- 0.038	0.114 +/- 0.030	0.96	<0.05	
Р		>0.05	>0.05	<0.01			
P1			>0.05	<0.01			
P2				<0.01			

P - comparison between data gathered from non-endemic and endemic fluorosis regions; P1 - comparison between endemic fluorosis region 1 and region 2/3; P2 - comparison between endemic fluorosis region 2 and region 3.

Discussion

Male causes explain about 30-50 % of cases of infertility. The cases of male infertility accounted in this paper have already excluded common medical causes. There are no cases of gonadal damage caused by radiation, no cryptorchidism, no tuberculosis of the reproductive system, no trauma or surgical history, no diseases in the area of endocrinology, and the relevant amount of trace element intake was also within the normal range. Therefore none of these factors could constitute a probable explanation for the difference in male infertility rates between the endemic fluorosis and non-endemic fluorosis regions. In the 57 cases we examined, there were 99 instances of sexual defects; as manifested by loss of libido, masturbation, spermatorrhea, premature ejaculation, impotence - all of which could affect the quality and volume of sperm. The daily intake of fluoride of an adult in endemic fluorosis regions from grains, vegetables and water are respectively 1.8, 2.2, and 3.2 times that of non-endemic fluorosis regions. The fluoride content in semen from infertile males, the rate of oligospermia, the total rate of male infertility and the rate of primary infertility in endemic fluorosis regions are all evidently higher than those in non-endemic fluorosis regions. Concentration of sperm is also lower in comparison with non-endemic fluorosis regions. The relative risk of male infertility in endemic fluorosis regions is 1.83 times that of non-endemic fluorosis regions and the absolute risk is 2.93% higher than nonendemic fluorosis regions.

Krishna's study found [5] that in endemic fluorosis regions (water fluoride 4-8mg/L) there was a decrease in volume and quality of sperm in 70% of married males, and a male fertility rate of only 24%. Мандр observed [6, 7] that cows and pigs who continually consume water that contains 6.5mg/L of fluoride have delayed estrous cycle in seedlings, their fertilization rate and conception rate are low, the periods between labor and fertilization are long; chickens that drank water containing 8.5 - 13.5 mg/L of fluoride had a decrease in quantity and quality in their egg production (5% - 85%). Other research shows [8] that water containing NaF at 1.0 ppm can cause permanent damage to the DNA of male mice, damaging testes and causing abnormality in chromosomes; the longer the exposure the greater the abnormalities, with the chromosomal change low-grade and irreversible. [The research has also shown that] placing small mice in an environment containing 0.025mg/m² in the air for 5 weeks causes testicular lesions and degeneration.

According to our preliminary findings, fluoride could be one of the major factors contributing to the increase in male infertility rates in endemic fluorosis regions. The subject warrants further observation and investigation.

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