EFFECTS OF SODIUM FLUORIDE ON THE ELECTROCARDIOGRAM OF MALE RABBITS

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SUMMARY: Effects of fluoride (F) on electrocardiogram (ECG) values were determined in ten healthy adult male New Zealand white rabbits. After the initial ECG values were measured, the rabbits were administered 20 mg NaF/kg body weight by oral intubation for two months, and the new ECG values were determined. There was a significant ($p<0.001$) decrease in the R-R interval (duration between the peaks of two consecutive R waves of ECG) and P-R interval (duration from the starting of P wave to the starting of QRS complex in ECG), while significant ($p<0.001$) increases in the mean heart rate and corrected QT intervals were observed compared to the initial baseline values. The results indicate that F adversely affects the ECG in male rabbits.

Keywords: Electrocardiogram; ECG in rabbits; Fluoride and ECG; Heart rate; Q-T Interval.

INTRODUCTION

Excess fluoride (F) in the environment adversely affects the health of humans and animals.[1] Chronic fluorosis is commonly found in many regions of the world.[2,3] In recent years many health professionals have realized that F accumulates in and affects not only bones and teeth, but, to a lesser extent, it also concentrates in soft tissues, especially the cardiovascular system.[4] A study of 271 electrocardiograms of dental fluorosis sufferers indicated that 29.5% had abnormal heart rhythms, and 12.8% had reduced myocardial function.[5] High blood F levels have an effect on body calcium. Calcification of the aorta, and other arteries, resulting in arteriosclerosis including coronary arteriosclerosis, has been demonstrated in China.[6,7] The severity of skeletal fluorosis in humans is directly related to the severity of abnormal cardiac function, as demonstrated by the electrocardiograms.[4] Besides these studies on humans, Kilicalp et al. have found that chronic fluorosis causes electrocardiogram abnormalities in dogs.[8]

Although various effects of chronic fluorosis on different body systems have been examined,[6,7,9] studies on the circulatory system are limited. In this investigation our aim was to determine the effects of F exposure on electrocardiogram (ECG) values in male rabbits.

MATERIALS AND METHODS

This research was conducted in the Department of Physiology after approval by the Institutional Animal Ethical Committee.

Animals and housing: Ten healthy, adult New Zealand white male rabbits were used for the study. All the rabbits were of same age group, with weight range of 1.5–2.5 kg. The rabbits were housed in a well-ventilated animal house and caged separately, at a temperature of 29–32ºC and exposed to 10 to 12 hr of daylight.

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Experimental design: Baseline ECG was recorded on a two-channel polygraph instrument (manufacturer RMS, Chandigarh, India). The rabbits received food and water *ad libitum*. Sodium fluoride (Ranbaxy laboratories S.A.S Nagar, India) was given using a feeding tube attached to a hypodermic needle at a dosage of 20 mg NaF/kg body weight/day.[10] After 2 months the ECG was again recorded and compared with the baseline values. The R-R interval was taken between the peaks of two consecutive R waves, P-R interval was taken from starting of P wave to the starting of QRS complex, the Q-T interval was measured from the start of QRS complex to the end of the T wave. The corrected Q-T (QTc) interval was calculated by Bazett's formula: QTc = QT interval/vR-R interval (ms).

Statistical analysis: All readings were taken from the record of fifty cardiac cycles of each rabbit, and the data were combined to calculate the mean and standard deviation (SD) values. Results were compared between the baseline and final values by Paired T-test using Microsoft excel 2007 version and SPSS version 10.

RESULTS

The Table shows there was a significant decrease in the R-R and P-R interval among the rabbits administered NaF for 2 months as compared to baseline values. There was a significant increase in the mean heart rate (HR) and corrected QT interval.

Table. Comparison of different ECG parameters between baseline and 2-month exposure to NaF in male rabbits

Parameters[a]	Initial value (Mean ± SD)	After 2 months of NaF administration exposure (Mean ± SD)	p value
R-R interval (ms)	244.4 ± 23.89	210.73 ± 22.01	<0.001
Mean HR (bpm)	247.7 ± 22.97	287.69 ± 28.35	<0.001
P-R interval (ms)	79.93 ± 6.75	67.8 ± 4.52	<0.001
QT interval (ms)	158.67 ± 18.18	158.73 ± 23.94	NS
QTc interval (ms)	321.93 ± 31.06	344.49 ± 34.16	<0.001

[a]HR = heart rate; bpm = beats per minute; ms = milliseconds.

DISCUSSION

In our work there was a significant decrease in the R-R and P-R interval on exposure of the rabbits to NaF for 2 months and a significant increase in heart rate, contrary to the findings of Donmez et al., who observed prolongation of the P-R interval and sinus bradycardia (slower heart beat rate) in sheep with fluorosis.[11] In another study there was also a prolongation of the P-R interval in goats exposed to fluoride for 30 days.[12] Likewise, Kilicalp et al. also found a prolongation in the P-R interval and a significant bradycardia in 2-to-3 year-old dogs with chronic fluorosis living in an endemic F area.[8] The increase in heart rate observed in our study may be the result of differences in F dosage, animal species, and length of F exposure compared with these other studies. Nevertheless, the present investigation clearly indicates that F interferes with myocardial metabolism, as observed by Iwase et al., who demonstrated histochemically that F caused

degenerative changes in the myocardium of rabbits administered 10–30 mg of NaF/kg body weight/day orally for 15–169 days, followed by changes in the localisation of glycogen.[13] In humans, Okushi et al. found a higher incidence of myocardial damage electrocardiographically and cardiac dilatation roentgenocardiacally in inhabitants of a high-F zone in Japan, where the drinking water contained 6–13 ppm fluoride.[14] In residents of a Japanese village, where the water F levels ranged between 0.5 and 6.2 ppm, Takamori et al. reported myocardial damage and dilatation of the cardiac muscle and established a direct relationship between increased myocardial damage and mottled enamel by means of electrocardiograms.[15] Rabbits treated with 20 mg of NaF/kg/day showed cloudy swellings of cardiac muscle fibers, fibrous necrosis, fibrinolysis, sarcoplasmic vacuolisation, and dissolution of nuclei occurred in the myocardium.[16] The isovolumic relaxation time (IVRT) and deceleration time (DT) were significantly higher in fluorosis subjects than in controls. Recently, Varol et al. have shown that chronic fluorosis patients had left ventricular diastolic and global dysfunctions.[17]

The development of ventricular arrhythmias has been produced experimentally in dogs given NaF,[18] and repetitive ventricular fibrillation unresponsive to electrical defibrillation has been reported in some cases of acute human F poisoning.[19,20]

In our study, as seen in the Table, there was no significant change caused by NaF in the Q-T interval, but a significant prolongation in the QTc interval was observed. Similar findings have been reported earlier in humans[21] and goats.[12] Hyperkalemia, which may be delayed in onset, has also been proposed as an etiology of F-associated ventricular dysrrhythmias.[20,22-27] Hyperkalemia has been documented in a number of cases of human poisoning with F[27,28] and in dog studies of F poisoning.[24, 25] In addition to direct binding and precipitation of free ionized calcium, potassium abnormalities have been described with NaF toxicity. These abnormalities are postulated to result from at least two other cellular actions of the F anion: 1) F-mediated inactivation of the Na^+/K^+ ATPase, contributing to the accumulation of intracellular sodium and extracellular potassium; and 2) activation of a Na^+/Ca^{2+} ion exchanger that results in the intracellular accumulation of calcium, triggering a calcium dependent potassium channel that in turn mediates potassium efflux.[22,26]

CONCLUSION

We conclude that F definitely has an adverse affect on the mammalian conducting system as observed here by the ECG of male rabbits. Our findings thus provide further support for the need to lower the F content of drinking water in areas of endemic fluorosis.

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