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Short Term Effect Of Zinc On Major Blood Electrolytes In Wistar Rat

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Abstract : Zinc (Zn2) is an essential micronutrient of human body and Zn2 deficiency has been found to be associated with many diseases. It is also a potential therapeutic agent for a number of diseases. Studies have shown that some relationship exists between Zn2 levels and the major electrolyte concentration in blood, but the short term effect of Zn2 administration on major electrolytes has not been studied. This study aimed at finding the short term effect of parenteral Zn2 administration on blood levels of Sodium, Potassium and ionized Calcium. Towards this, 6 anaesthetized rats received single dose intraperitoneal Zn2 in the test group and 6 rats received Normal saline in the control group in a randomized way. Blood levels of these electrolytes at base line (zero hour) and after one, two and three hours post-intervention were compared between test and control group. The statistical analysis was done using Mann Whitney U test. Inter-group analysis of the electrolytes at zero, first, second and third hour did not show any significant difference between test and control group. We conclude that parenteral administration of Zn2 has no effect on the blood levels of major electrolytes and hence does not cause any electrolyte imbalance.

Keyword : Zinc, Electrolytes, Sodium, Potassium, Calcium, Rat blood

Introduction:

Zinc (Zn2+) is an essential micronutrient of human body and is an important cofactor for many enzymes (1). Zn2+ deficiency has been associated with many diseases. Acrodermatitis enteropathica is a very severe form of Zn2+ deficiency and hence Zn2+ is the treatment of choice (2,3). Zn2+ is being extensively used in the treatment of other various types of illnesses as well. Treatment of diarrhoea with Zn2+ is an established mode of management (4). It may even be useful in diarrhoea associated with HIV infection (5). Wilson disease is treated by Zn2+ (6). There are also evidences that Zn2+ can be useful in the management of Pneumonia along with other medications (7). Zn2+ at 0.5mM concentration is also a non-specific blocker of voltage gated H+ channel *in vitro* (8,9). In patch clamp studies Zn2+ has been found to block proton channels in Neutrophils (10). With the increasing use of Zn2+, the *in vivo* short term effect of Zn2+ on different physiological parameters has to be understood. The short term effects of Zn2+ administration on blood electrolyte levels has not been studied. Studies have shown that there is circadian variation of blood Zn2+ level in the body. There is also a positive correlation between the Zn2+ and ionized calcium (iCa2+). However, the blood total calcium does not show good correlation (11). It has been found that Zn2+ can normalize the serum Sodium (Na+) level which goes down in ethanol-fed rats (12). It has also been found that Zn2+ in diet can influence body Sodium and Potassium (K+) levels (13). Na+ transport from the small and large intestine is decreased in Zn2+ deficiency where as there is no such effect for K+ (14). The Na+, K+, iCa2+ are some of the major blood electrolytes essential for body functions. We studied the short term effect of parenteral Zn2+ on these blood electrolytes.

Materials And Methods:

The study was approved by the Institutional Review Board and Institutional Animal Ethics Committee.

Fig.1: Rat Carotid artery cannulated

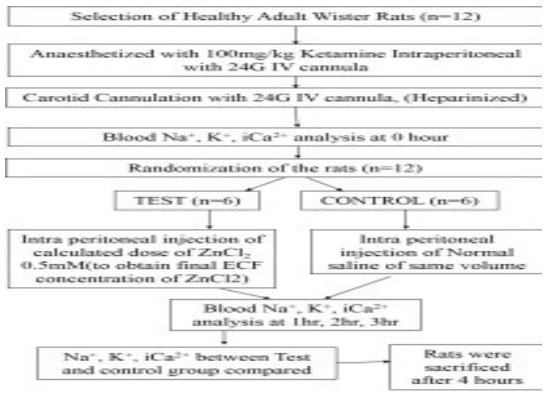

Fig.2: Detailed diagrammatic algorithm of study method

Twelve adult Wistar rats (6 tests and 6 controls) weighing between 240 to 300 grams were used in the experiments. Computer generated randomization numbers were used to randomize the rats in the two groups. Commercially available Zinc chloride dissolved in minimal volume of normal saline were used in the intervention group and normal saline of equal volume was used for control group. The dose was calculated such that the final concentration of Zinc chloride (ZnCl2) in rat ECF becomes 0.5mM ZnCl2 which is the concentration of ZnCl2 that can block proton channels in *in vitro*. Ketamine (100 mg/Kg body weight of the rat) was given intra peritoneally to anaesthetize the rats. An intraperitoneal line with 24G scalp IV set was fixed for administration of top up doses of anaesthesia whenever required. Carotid artery was cannulated using 24G IV cannula and was heparinised (Fig.1). After initial stabilization for few minutes, the first arterial blood sample was taken at 0 hour, before administering ZnCl2 or Normal saline intra-peritoneally. The test rats were given an intraperitoneal injection of calculated dose of ZnCl2 (final concentration of 0.5mM in ECF) dissolved in Normal saline. Dose was calculated as per the body weight of the rat. Control rats were given comparable volumes of Normal saline only. Then the blood samples were collected at 1hour, 2hour and 3hour post-intervention and electrolytes were measured using an analyzer (Abbott i-stat portable clinical analyzer). Animals were monitored for 4 hours after which they were sacrificed with high dose of anaesthesia. Details of experimental algorithm is given in Fig.2.

Statistical Analysis: Data was expressed as Median and Inter-quartile range. Na+, K+, iCa2+ values at 0hr, 1hr and 3hr were compared between intervention and control groups by Mann Whitney U test.

Results:

Intergroup comparison of baseline (pre-intervention) values at 0hr showed no statistically significant difference for Na+ (P=0.394), K+ (P=0.818) and iCa2+ (P=0.132). (Table 1, Fig.3, Fig.4, Fig.5)

Table 1: Comparison of the baseline values of parameters between Intervention group and control group

Variable	Intervention Group (Zinc chloride) [Median (IQR)] (N=6)	Control Group (Normal saline) [Median (IQR)] (N=6)	P value
Blood Na^+ at 0 hour	142 (140.75, 143.50)	143 (141.75, 144.25)	0.394
Blood K^+ at 0 hour	3.9 (3.575, 4.5)	3.75 (3.25, 4.45)	0.818
Blood iCa^{2+} at 0 hour	1.485 (1.435, 1.55)	1.415 (1.3475, 1.4825)	0.132

Intergroup comparison of blood Na+ values had shown no statistically significant difference between intervention and control group in all 1hr (P=0.589), 2hr (P=0.589) and 3hr (P=0.126) post-intervention samples. (Table2, Fig.3) Intergroup comparison of blood K+ values had shown no significant difference between intervention and control group in all 1hr (P=0.699), 2hr (P=0.937) and 3hr (P=0.931) post-intervention samples. (Table2, Fig.4) Intergroup comparison of blood iCa+ values had also shown no statistically significant difference between intervention and control group in all 1hr (P=0.589), 2hr (P=0.310) and 3hr (P=0.126) post-intervention samples. (Table2, Fig.5)

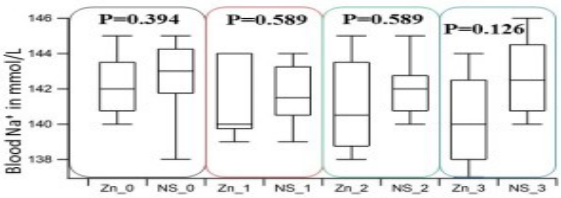

Fig.3: Inter-group comparison of blood Na+ (Zn: Zinc chloride; NS: Normal saline; 0,1,2 and 3: 0,1,2 and 3 hour respectively)

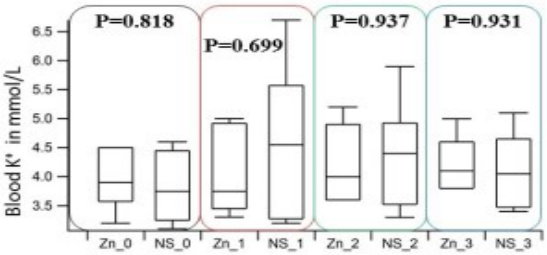

Fig.4: Inter-group comparison of blood K+ (Zn: Zinc chloride; NS: Normal saline; 0,1,2 and 3: 0,1,2 and 3 hour respectively)

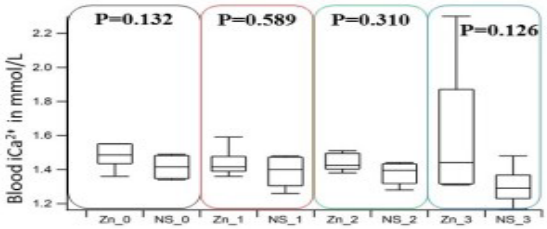

Fig.5: Inter-group comparison of blood iCa2+ (Zn: Zinc chloride; NS: Normal saline; 0,1,2 and 3: 0,1,2 and 3 hour respectively)

Table 2: Post-intervention comparison of the blood levels of Na^+, K^+, iCa^{2+} between Intervention group and control group

Variable	Intervention Group (Zinc chloride) [Median (IQR)] (N=6)	Control Group (Normal saline) [Median (IQR)] (N=6)	P value
Blood Na^+			
1 hour	140 (139.75, 144)	141.5 (140.5, 143.25)	0.589
2 hour	140.5 (138.75, 143.50)	142 (140.75, 142.75)	0.589
3 hour	140 (138.00, 142.50)	142.5 (140.75, 144.5)	0.126
Blood K^+			
1 hour	3.75 (3.45, 4.93)	4.55 (3.28, 5.58)	0.699
2 hour	4 (3.6, 4.9)	4.4 (3.525, 4.925)	0.937
3 hour	4.1 (3.8, 4.6)	4.05 (3.475, 4.65)	0.931
Blood iCa^{2+}			
1 hour	1.415 (1.39, 1.4775)	1.4 (1.305, 1.4725)	0.589
2 hour	1.425 (1.4025, 1.495)	1.395 (1.3175, 1.4325)	0.310
3 hour	1.44 (1.315, 1.87)	1.29 (1.23, 1.3675)	0.126

Discussion:

Zinc did not not cause any electrolyte imbalance in Wistar rats. Intra-peritoneal Zn2+ administration (0.5mM) did not affect Na+, K+, iCa2+ levels in the short-term. Zn2+ being a therapeutic agent used in various diseases, it can be used without much apprehension with regard to its effect on major blood electrolytes. However, effect of Zn2+ on other physiological processes cannot be ruled out on the basis of our results. Although studies showed changes in blood Na+ and K+ concentration in Zn2+ deficiency (12,13), an increase in Zn2+ concentration up to 0.5mM does not produce a significant change. The positive correlation between iCa2+ and zinc reported by Markowitz ME et al (11), studied using the diurnal variation of zinc levels may not be due to the effect of Zn2+ on

iCa2+ but could be some other factors playing on both of them. We conclude that parenteral Zn2+ may not be toxic to the body and does not cause alteration in the major blood electrolyte levels.

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