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University of Zimbabwe

The serum concentrations of zinc, copper and selenium in children with inflammatory bowel disease

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Abstract

Objective: To estimate the levels of trace elements in children with inflammatory bowel disease (IBD).

Design: Prospective cross sectional study

Setting: Gastroenterology Unit, Great Ormond Street Children's Hospital, London, UK.

Subjects: Seventy four children with inflammatory bowel disease confirmed endoscopically and histologically (38 ulcerative colitis and 36 Crohn's disease) and 40 age matched controls had their serum zinc, copper and selenium assayed at presentation.

Main outcome measure: Serum levels of zinc, copper and selenium in children with inflammatory bowel disease and age matched controls.

Results: Seventy four children with inflammatory bowel disease confirmed endoscopically and histologically (38 ulcerative colitis and 36 Crohn's disease) and 40 age matched controls had their serum zinc, copper and selenium assayed at presentation. The serum levels of selenium were significantly lower in cases of ulcerative colitis 0.63 ± 0.25 mmol/L and Crohn's disease 0.69 ± 0.25 mmol/L than in the controls 0.84 ± 0.13 mmol/L ($p < 0.01$). The serum copper concentration was significantly higher in those with Crohn's disease 22.7 ± 5.49 mmol/L than in those with ulcerative colitis 17.6 ± 5.15 mmol/L and the controls 20.76 ± 4.06 mmol/L ($p < 0.01$). Children with Crohn's disease had a lower serum zinc level 11.01 ± 2.49 mmol/L compared to the control level of 13.6 ± 1.63 mmol/L ($p < 0.05$), but the levels were not significantly different in the controls and ulcerative colitis ($p > 0.10$). Children with inflammatory bowel disease have abnormal levels of the trace elements which is more marked in those with Crohn's disease.

Conclusion: Children with IBD in this study show abnormalities of the trace elements which is probably a result of inadequate intake, reduced absorption, increased intestinal loss due to impairment of the absorption as a result of the inflammatory process. The reduced free radical scavenging action of zinc and selenium as a result of their deficiency may contribute to the continued inflammatory process of IBD. The recommendation of the supplementation of these trace elements in IBD is further supported by the findings of this study in children.

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Introduction

Inflammatory bowel diseases (IBD) are a group of chronic inflammatory process of the bowel whose aetiology is unknown and are seen commonly in Caucasians and Jews, but rarely in blacks.^{1,2} These conditions are characterised by recurrent bloody diarrhoea, abdominal pain, tenesmus, malaise, perianal abscess and anaemia resulting in malabsorption and increased loss of nutrients.³

Zinc and selenium have been reported to be low in adults with IBD^{4,5} and children with allergic colitis.⁶ Zinc deficiency leads to a decreased natural killer cell activity.^{7,8} There are conflicting reports of the copper status of adults with IBD.^{9,10} Oxygen free radicals mediate tissue injuries and a high level of free radicals has been observed in IBD.⁹ Antioxidant agents of which selenium and zinc are important mop up these free radicals.

The available literature on the trace element status of children with inflammatory bowel disease is limited. Since trace elements are scavengers of free radicals, and since free radicals are high in IBD, this study aims at estimating the levels of the trace elements in children with IBD.

Materials and Methods

Seventy four children with histologically confirmed IBD and 40 healthy controls had their serum zinc, copper and selenium levels assayed before the commencement of therapy at the Great Ormond Street Children's Hospital, London over a nine months period. All the patients had endoscopies with biopsies done and were grouped based on endoscopic and histological findings.

Anti-endomysial, antireticulin and antigliadin antibodies were negative in all the patients studied, including the controls, to exclude those with Gluten Induced Enteropathy.

Histological Diagnostic Criteria.

Crohn's disease — transmural inflammatory; focal inflammatory cell aggregation with non caseating epithelioid granuloma formation.

Ulcerative colitis — diffuse mucosal inflammatory cell infiltration, with crypt architectural distortion, loss of goblet cells and paneth cell metaplasia.

Blood samples were obtained at presentation before the commencement of therapy.

Zinc was analysed by flame atomic absorption photometry, selenium by hydride atomic absorption spectrometry and copper by furnace electrothermal atomization absorption spectrometry. Quality assurance was ascertained using a commercially prepared reference.

The values were expressed as the mean and standard deviation and the values in the three groups were compared using the two-tailed Student's t-test, Pearson correlation coefficient to test correlation where applicable.

Results

Seventy four children with IBD (36 with Crohn's disease and 38 with ulcerative colitis) had endoscopic and histological assessment of the gastro-intestinal tract done

in this study. The pathological findings were more marked in the terminal ileum and proximal large bowel in Crohn's disease, (63.9%) and the distal large bowel and rectosigmoid colon in ulcerative colitis (60.5%), (Table I).

Table I: The part of the gastro-intestinal tract involved in the disease process during endoscopic examination in Crohn's disease and ulcerative colitis.

	Crohn's disease n = 36	Ulcerative colitis n = 38
Terminal ileum	15 (41.7%)	2 (5.3%)
Proximal large bowel	8 (22.2%)	5 (13.2%)
Descending colon	3 (8.3%)	8 (21.1%)
Recto sigmoid colon	2 (5.6%)	17 (44.7%)
Combined	8 (22.2%)	6 (15.8%)

Table II shows that the mean age of the controls and the children with IBD were comparable in this study ($p > 0.10$). The mean serum level of copper 22.7 ± 5.49 mmol/L was significantly higher in Crohn's disease than in ulcerative colitis 17.59 ± 5.17 mmol/L, and controls ($p < 0.01$). Both ulcerative colitis (0.63 ± 0.1 mmol/L) and Crohn's disease (0.69 ± 0.25 mmol/L) patients had significantly lower levels of selenium than the controls (0.84 ± 0.13 mmol/L), $p < 0.001$. There is a significantly lower zinc level in Crohn's disease than in the controls ($p < 0.05$), but the levels were comparable in ulcerative colitis and the controls ($p < 0.05$).

Table II: The serum concentration of zinc, copper, selenium and albumin in Crohn's disease, ulcerative colitis and the controls.

	Crohn's disease n = 36	Controls n = 40	Ulcerative colitis n = 38
Age (months)	94.18 \pm 42.56	85.38 \pm 47.56	81.38 \pm 22.04
Zinc (mmol/L)	11.01 \pm 2.49**	13.6 \pm 1.63	12.39 \pm 3.0**
Copper (mmol/L)	22.7 \pm 5.49**	20.76 \pm 4.01	17.59 \pm 5.17**
Selenium (mmol/L)	0.69 \pm 0.25**	0.84 \pm 0.13	0.63 \pm 0.1**
Albumin (Gm/L)	36.95 \pm 6.15**	42.2 \pm 4.06	38.0 \pm 6.14**

p value for above table.

	Zinc	Copper	Selenium	Albumin	Age
Crohn's disease vs Control	<0.005	<0.025	<0.005	<0.001	>0.25
Ulcerative colitis vs Control	<0.05	<0.001	<0.001	<0.005	>0.10

** Indicates that statistical comparison is significant.

Table III: The correlation between the age and the serum concentrations of zinc, copper and selenium in children with Crohn's disease and ulcerative colitis.

	Crohn's disease (n = 36)			Ulcerative colitis (n = 38)		
	Copper mmol/L	Zinc mmol/L	Selenium mmol/L	Copper mmol/L	Zinc mmol/L	Selenium mmol/L
0-5 yrs n=7	24.8	11.3	0.63	n=8 18.2	12.1	0.59
5-10 yrs n=11	22.9	10.9	0.72	n=8 17.5	12.5	0.63
> 10 yrs n=16	21.8	11.3	0.69	n=22 17.3	12.3	0.63
"r"	-0.29	0.05	0.23	-0.15	0.02	0.28
p	<0.001	*NS	<0.001	<0.05	*NS	<0.001

*NS is not significant.

The albumin levels were significantly lower in ulcerative colitis and Crohn's disease compared to the controls ($p < 0.005$).

There is a low positive correlation between the age and selenium levels in both Crohn's disease and ulcerative colitis ($r = 0.22$ and 0.28 , $p < 0.005$ respectively), but there is a negative correlation between the age and copper in Crohn's disease ($r = -0.28$, $p < 0.001$) which is more marked than in ulcerative colitis ($r = -0.15$, $p < 0.05$).

Children below the age of five years tend to have a more marked derangement of the trace elements compared to the older children. Children with an extensive involvement of the bowel had significantly higher copper and lower selenium and albumin levels than those with distal large bowel involvement only ($p < 0.025$).

Discussion

Children with ulcerative colitis and Crohn's disease in this study have low serum concentrations of selenium, which is similar to the findings in the adults with early stage Crohn's disease and ulcerative colitis.^{10,11} Those children with Crohn's disease had very significantly lower levels of zinc when compared to the controls, a finding that is in consonance with previous reports in adults¹¹ but in contrast with that of some other workers.¹⁰

Increased natural killer cell activity has been linked to zinc deficiency.^{13,14} The low zinc and selenium levels in IBD in children could be as a result of reduced intake, reduced absorption or increased mobilisation for mop up free radicals which contribute to tissue injury in these conditions.^{4,14} The positive correlation between zinc and albumin is well recognised,¹⁴ and patients with IBD have low albumin levels probably due to malabsorption or reduced intake. Whether the low zinc level is as a result of hypoalbuminaemia or increased utilisation for free radical mop up is not clear.

In this study, there was a significantly increased copper level in children with Crohn's disease but not in those with ulcerative colitis, a finding that is similar to that seen in the adults.^{10,11} Copper level is known to be elevated under inflammatory conditions and this has been attributed to increased ceruloplasmin.¹¹

The possible role of excess copper catalysing free radical formation and increased mucosal oxidative stress in IBD is plausible.

The trace elements are more deranged in children with Crohn's disease than in ulcerative colitis in this study. Previous workers have shown that there is no correlation between the part of the intestine involved and the disease process.¹⁰ We did not observe any correlation between the sex and the trace element levels in children with IBD, which is contrary to the observation in adult Crohn's disease and ulcerative colitis.¹⁰ There is a positive correlation between selenium levels and age, but a negative correlation between copper levels and age in both Crohn's disease and ulcerative colitis in this study. This will tend to suggest a cumulative effect of increased copper and decreased

selenium levels, which will favour further tissue injury and inflammation.

The linkage between zinc and natural killer cell activity has prompted a recommendation of zinc supplementation in patients with mild to moderately active IBD^{3,15} and allergic colitis.⁶

Children with IBD in this study show abnormalities of the trace elements which is probably a result of inadequate intake, reduced absorption, increased intestinal loss due to impairment of the absorption as a result of the inflammatory process. The reduced free radical scavenging action of zinc and selenium as a result of their deficiency may contribute to the continued inflammatory process of IBD. The recommendation of the supplementation of these trace elements in IBD is further supported by the findings of this study in children.

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