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RESEARCH ARTICLE

GENDER RELATED EFFECTS OF YEAST SELENIUM ON WEIGHT FOR AGE Z SCORE OF ASYMPTOMATIC HIV TYPE 1 POSITIVE CHILDREN AT NYAMASARIA IN KISUMU KENYA

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A B S T R A C T

Background: Selenoprotein Iodothyronine 5'Deiodonases activates pro-T3 to 3,3'-5T3(Tri-iodothyronine) which is involved in growth through a gene mediated protein metabolism. Oestradiol (E2) enhances activity of selenoproteins in adult pre-menopausal women taking selenium supliments, however the effect of selenium supplementation on weight change of different gender of asymptomatic HIV positive pre-puberty children is still unknown.

Methods: In this study of 25 Females and 25 Males randomly chosen asymptomatic HIV positive children 3 – 16 years old, 25 of the children were given, a fixed dose of 50µg yeast selenium while a matched control of 25 were put on placebo. Weight of children were taken at 3 months intervals up to 6 months, using electronic personal scale (model 10010), the resultant data was analyzed by Epi Info version 6,and SPSS version 16.

Results: No significant difference in mean weight of children was observed at baseline between the controls and children on test . Children on selenium had weight increase of 2.5Kg at six months .The weight for age Z score increased above -2SDs cut off point at six months amongst the children on selenium, in all age categories, 3-5 years 1.20 ± 2.45, 6-8years 0.19 ± 0.880, 9-15 years 0.97 ± 1.22, while there was a decrease in all the age categories in matched controls to below -2SDs at six months , 3-5 years -2.218 ± 1.46, 6-8 years -2.95. ± 3.10, 9-15 -2.30 ± 1.240. There was a significant WAZ difference between controls and selenium group at six months {F (5,12) = =5.758, P=0.006}. Prevalence of underweight in control was 48% compared to the test group at 9% at six months. Female children on selenium initially had a decrease and then sharp increase in WAZ (Tick Phenomenon), compared to the males who had a steady increase in WAZ.

Conclusion: It can be concluded that intake of yeast Selenium led to significant improvement in weight for age Z score at six months and further that there is gender related differences in weight change between HIV positive asymptomatic female and male children taking selenium as a supplement

INTRODUCTION

HIV infection is accompanied by progressive nutrition alterations and pathological changes, with the critical pediatric HIV patients WAZ cut-off point being -2SDs (Cogill., 2003).This point marks beyond which there is increase in morbidity among the patients, the condition if unchecked likely to develop to fully blown AIDS.

The thyroid gland is one of the body tissues with the highest levels of selenium concentrations (Dickson 1967). The combined deficiency of selenium and iodine leads to myxidematous cretinism (Contmpre *et al.*, 2004) .In the thyroid hormones, selenocystein (SeCy) carries the active sites of the selenoproteins, in the two iso-forms of iodothyronine 5' deiodonases (DIOs).

The weight change is associated with protein synthesis and deposition in the body. Selenium is part of a group of seleno-enzymes Iodothyronine 5' deiodonases which catalyzes activation and deactivation of the thyroid hormone 3 3'-5 Tri-iodothyronine (Korle., 2005), which is largely controlled at target cell level by regulation of intracellular DIO activities (Berry *et al.*,1991). The hormone 3 3'-5 T3 is responsible for protein metabolism including growth through regulation of gene expression and protein metabolism (Korle *et al* ., 2005)

Some studies have shown positive correlation between selenium levels in the body and level of circulating 3,3'-5 T3 (Arthur *et al.*,1988).Low selenium levels in the body have been observed to lead to increased T4 in circulation, but a reduction of 3,3'-5 T3 and Thyrotropin TSH. Various studies have shown the inverse relationship between the level of selenium in the body and level of thyroglobulin and serum

concentration of 3,3'-5 T ,and T4 (Strain *et al*.,1997, Ravaglia *et al*., 2000).While studies by Derumeaux *et al*., 2003 and, Zagrodzki *et al*., 2000 have shown inverse relationship between selenium levels in the human body and thyroid volume, and thyroid tissue damage, in women but not men.

Besides DIOs, the family of Iso-forms of glutathione peroxides (cGPX, pGPX) and Thioredoxine reductases (TRrX) is associated with thyroid gland protection, since the thyroxine biosynthesis by the follicles is highly reactive process which leads to production of reactive oxygen species (ROS), (Ekholm *et al*., 1997) and needs to be mopped out to avoid peroxidation of the thyrocytes (Korle *et al*., 2009). This implies that sufficient intake of selenium is needed to ensure thyroid hormone production and thyroid tissue protection by cGSH-px and TxnrD. Some studies have reported association of multiple thyroid nodule risk, low volume of thyroglobulin in adult women with low serum selenium (Rasmussen *et al*., 2011).

HIV incorporates selenium into its viral proteins at expense of its host and thus takes control of selenium supply (Foster., 2002). This leads to deficiency of seleno-proteins and its' components (cystein, glutamine and tryptophan). This study was designed to study the effect of yeast selenium supplementation on weight change in asymptomatic HIV positive children of different gender.

Objectives of the Study

The objective of this study was to determine the effect of yeast selenium intake on change of Weight of different gender of asymptomatic HIV positive children 3-16 years old in Nyamasaria.

RESEARCH METHODS

Study Area

The average HIV prevalence rates in the site is 18.2% is well above the national prevalence which is 6.9% (KAIS., 2012), the most vulnerable being young men and women 20-35years (FAO/IFAD., 2002).The impact can be clearly perceived by the prevalence rates, there has been marked increase in number of widows and orphans in the county in the last two decades. Nyamasaria the site of the study is located in Kisumu peri-urban community. Three factors are considered to contribute to a much high prevalence in the site;-its closeness to lake hence is fishing community with high HIV prevalence, the cultural practices including sexual rituals which tend to predispose this community to high HIV prevalence and being near major transport corridor to and from Uganda and beyond, which leads to availability of casual and transactional sex along the routes. (Buvea *et al*., 1999).

Study Design

This was a clinical prospective study involving 3-16 year old HIV positive orphan children enrolled at orphan children in Nyamasaria in Kisumu Town. The study was nested in a bigger study 'The effects of yeast selenium on pathogenesis of HIV positive children in Nyamasaria in Kisumu"

Sampling Criteria

Fifty children were recruited to the study from Nyamasaria in Kisumu County. The children were enrolled into the study if they were between from age 3 and 16 years and the consent given by their guardians, and those who were HIV positive in WHO stage three and below. They were excluded if they were below three years and above 16 years didn't have guardian consent and were in HIV WHO stage four. Computer generated random numbers was used to select the required number after consultation with authorities at the centre.

Sample Size Determination

The sample size was determined by Epi Info version 6 for cohort studies in which the required minimum sample size at 95% Confidence interval and precision/power of 80%, and prevalence of HIV amongst the study subjects 15%(KAIS, 2007), Relative Risk of 5% the number in test group is given as 13 while for the controls at 13 the minimum sample size being 26.

Ethical Consideration

Approval to conduct the study was given by Kenyatta National Hospital Ethics Research and Standard committee. All patients who met the criteria were given equal chance to be enrolled in the study. Informed consent was given by the guardians/parents and the information collected was kept confidential.

Administering of Selenium to the children

The participants on test were assigned to, and received 50µg selenium (yeast) for up to 6 months. The dose was about a half of tolerable upper limit for children which are 100µg (yeast selenium) per day hence considered safe. Every week an evaluation of the intervention was done and replenishment of the selenium stock to monitor the compliance with the treatment. At 3 months intervals, the research assistants collected data on Weight to the nearest 0.1kg.

Data Collection

Interview of Guardians

At baseline, an interview of Childrens' guardians were done by trained research assistants who collected data of children's' socioeconomic status and those of their guardians using structured questionnaire.

Measuring Childrens'Weight

The weight of the children was collected by electronic personal scale (model 1001) as suggested by Cogill (2003). The scale was put on a flat surface and the reading adjusted to zero. Each child was told to stand on the scale evenly with barefoot wearing minimum clothing. The reading was taken

to the nearest two decimal points in Kilograms for each child and recorded.

Statistical Analysis.

Compliance with the study regime was calculated as number of tablets absent from the bottles supplied divided by tablets supplied-Score was calculated to asses any improvement on the children anthropometry. P-value presented is two sided statistical significance of 0.05 or below. Analysis was carried out using SPSS version 16.00(SPSS, Inc.Chicago, IL, USA).While means are values + or – SD unless stated.

RESULTS

Effect of Selenium Administration on Weight Gain

The mean weight gain at six months compared to baseline was observed in all the four age categories of the test group. The mean weight increased from 18±10.9 to 22.4±12.2 an increase of 2.75 kilograms (3-5 years old), 20.30±3.00 to 22.6±2.50 an increase of 2.30 kilograms (6-8years old) and 27.20±3.80 to 31.4±3.50 an increase of 3.25 kilograms (9-11 years old) and 3.0 kilograms (12-15 years old) for the test group.

Change in Weight for Age Z -score

There was progressive increase in weight for age Z score among the children on test in all age groups 3-5years (1.20± 2.45), 6-8years (0.19±0.88) and age groups 9-15 years (-0.97±1.22) was observed suggesting growth, while in the matched controls there was a decrease in weight for age Z score in all different age groups 6-8years (-2.949±3.01) and 9-15 years (-2.30±1.24) at six months compared to baseline s

WAZ SCORES OF TEST AND CONTROLS		
	Se Group (WAZ±SE)	Control Grp (WAZ ±SE)
Three Months		
3-5 years	0.15± 1.110	-2.01 ± 0.160
6-8 years	0.006 ± 1.22	-1.63± 0.051
9-16 years	0.19± 0.880	-2.95 ± 3.010
Six Months		
3-5 years	1.10 ±0.890	-2.95±0.160
6-8 years	-0.63±0.76	-2.76±1.150
9-16 years	0.97± 1.22	-2.30 ±1.240

ANOVA Weight for age Z score between test and Controls

Further analysis shows significant difference in weight for age Z Score (WAZ) between the test group and the controls was significant {F (df 5, 12) = 5.758, p= 0.006} as shown in table 11 below. Weight for age Z scores among different gender of the test group increased compared to the baseline with girls score having slightly more increase compared to boys.

Table 1 ANOVA WAZ between Test and Controls

	Ss	df	ms	f	p
Between gps	80.496	5	16.099	5.758	0.006
Within gps	33.549	12	2.769		
Total	114.044	17			

Change of Mean Weight for Age Z Scores by Gender

Weight for age Z scores among different gender of the group on Se increased compared to the baseline with girls score having slightly more increase compared to boys. WAZ for girls increased from -0.343 to 0.314, and for boys from -0.491 to 0.201. Among the controls the WAZ scores did not show much change among all gender categories. The WAZ for girl from -2.536 to -0.440 and boys from -2.047 to -2.039 at six months.

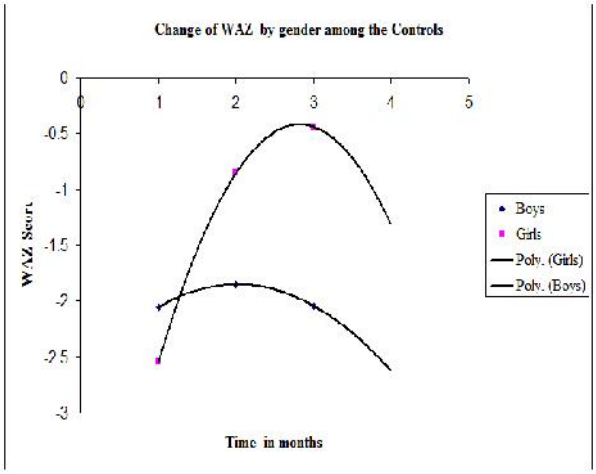

Figure 1 Change of WAZ among the controls

Figure 2 shows change in mean WAZ among the children on selenium. Weight for age Z scores among different gender of the test group increased compared to the baseline with girls score having higher increase compared to boys shown in figure 4.5. WAZ for girls increased from -0.343 to 0.314 and for boys from -0.491 to 0.201.

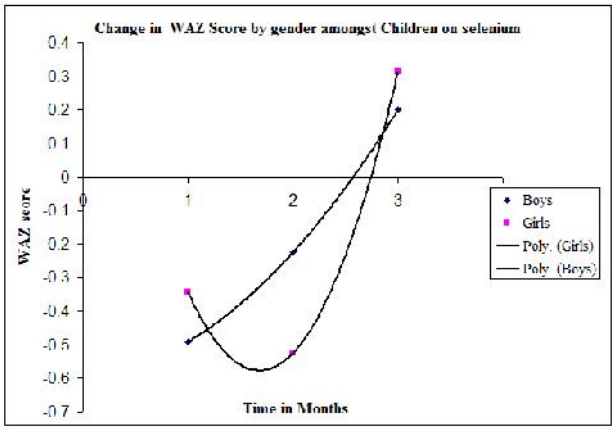

Figure 2 Change of WAZ amongst children on test

Change in Weight for Age Z score By Gender and Age for Children on Selenium

Weight for age Z score by age and gender. The Weight for Age Z Score for boys on selenium had slight increase or remained the same at six months. The boys' age group of 3-5 years had an increase from -1.93 to 2.09 at six months, while 9-15 years had a slight decrease from -0.995 to -1.478. All age categories of boys were above cut-off point of -2.0SDs at six months. Among the girls on selenium there was slight decrease among the age group 3-5 years from 0.539 to -0.274 at six months. There was an increase from 0.119 to 0.312 in age group 6-8 years and from -1.678 to -0.904 in age groups 9-15 years. Girls in all age categories were above WAZ score cut-off point at six months.

Table 2 WAZ for Children on control at Baseline

Sex	Age	Baseline weight (kg)	Z scores
M	5	15	-1.735
F	3	11	-2.106
F	4	36	
M	4	10	-3.240
F	4	14	-1.153
M	8	17	-2.670
F	6	15	-2.007
F	8	15	-2.837
M	6	14	-3.851
F	8	17	-3.380
F	6	18	-0.667
F	8	22	-0.813
F	7	18	-1.395
F	8	18	-1.968
M	7	20	-1.081
M	6	17	-1.579
M	12	27	-1.968
M	12	24	-2.430
M	9	20	-2.185
F	12	32	-1.353
M	10	18	-2.812
M	13	15	-3.533
M	10	21	-2.297
F	10	10	-4.241
F	13	26	-1.910

Table 3 Weight for Age Z score of selenium at Baseline

Gender	Age	Weight(kg)	Weight for Age Z score
M	4	14	-1.945
F	4	15	-0.514
M	5	17	-0.790
M	5	16	-1.263
M	5	18	-0.318
M	5	16	-1.263
F	4	15	-0.564
M	4.5	14	-1.831
M	7	21	-0.702
F	7	22	0.038
M	7	30	1.946
F	7	26	0.996
M	6	19	-0.721
F	6	18	-0.677
M	12	40	0.022
M	11	23	-2.205
F	16	40	-1.981
M	11	27	-1.488
F	11	25	-1.915
F	11	30	-1.113
M	10	30	-0.310
F	14	36	-1.781
F	9	27	-0.335
F	9	29	0.079

Weight for Age Z score by gender and Age for children on Control

There was little or no change in weight for age Z score for children in control for all age in all age categories of boys. The boys in age categories of 9-15 years had a decrease of WAZ from -1.37 to -2.08. For the 3-5 years old and 9-15 years old boys the WAZ remained below the cut-off point(-2.00SDs) at 6 months. For the girls on control there was a slight increase of WAZ score in age categories 6-8 years from -1.87 to -1.32 and in age groups 9-15 years from -2.50 to 0.001 at six months.

Prevalence of underweight (< -2SDs) by age and gender at six Months

As shown in Figure 4.5 the prevalence of underweight (< -2SDs) was 64% among the boys and 38% among the girls at six months among the children on control. Among the children on selenium 15% of the boys and no girl showed wasting at six months. Over all prevalence of underweight was 48% of all children on control and 9% among those on selenium at six months.

Table 4 Weight for Age Z score of Children on Control at 3 and 6 months

Gender	Age	3 Months		6 Months	
		Weight(kg)	WAZ	Weight(kg)	WAZ
M	8	12	-4.290	13	-3.968
F	6	25	1.639	26	1.939
F	8	10	-4.629	11	-3.981
M	6	20	-0.293	24	1.129
F	8	29	0.770	28	0.588
F	6	18	-0.677	14	-2.451
F	8	21	-1.105	21	-1.106
F	7	20	-0.669	14	-2.841
F	8	19	-1.609	20	-1.393
M	7	20	-1.081	16	-2.601
M	6	35	-4.872	36	5.212
M	12	18	-3.354	17	-3.508
M	12	17	-3.538	18	-3.354
M	9	24	-1.090	24	-1.090
F	12	20	-3.053	21	-3.055
M	10	20	-2.462	14	-2.452
M	13	23	-1.816	24	-3.753
M	10	55	3.231	32	-0.102
F	10	32	-0.102	20	-3.053
F	13	27	-1.756	-	-

Table 5 Weight for Age Z Score for children on Selenium

Gender	Age	3 Months		6 Months	
		Weight(kg)	WAZ	Weight(kg)	WAZ
M	4	16	-0.365	16	-0.365
F	4	16	0.017	16	0.017
M	5	20	0.551	18	-0.318
M	5	16	-1.263	26	3.042
M	5	21	0.966	23	1.797
M	5	21	0.966	34	6.363
F	4	15	-0.564	15	-0.564
M	4.5	15	-1.335	17	-0341
M	7	24	0.314	26	0.858
F	7	22	0.638	25	0.757
M	7	18	-1.841	19	-1.461
F	7	29	1.714	22	0.038
M	6	23	0.789	23	0.789
F	6	18	0.677	20	0.142
M	12	22	0.221	17	-3.508
M	11	31	-0.771	23	-2.205
F	16	44	-1.482	43	-1.607
M	11	31	-0.771	33	-0.412
F	11	33	-0.633	35	-0.312
F	11	27	-1.594	32	-0.793
M	10	32	0.076	33	0.214
F	14	39	-1.407	41	-1.158
F	9	33	0.666	33	0.666
F	9	26	-0.564	26	-0.564

Table 6 Change on WAZ by Gender and Age Category among the children on Selenium

	Weight for Age Z Score of Boys on Selenium			Weight for Age Z Score of Girls on selenium		
	Base line	3 Months	6 Months	Baseline	3 Months	6 Months
3-5years	-1.93	-0.112	2.019	0.539	-0.274	-0.274
6-8 years	0.665	-0.246	0.062	0.119	1.01	0.312
9-16 years	-0.995	-0.311	-1.478	-1.678	-1.240	-0.904

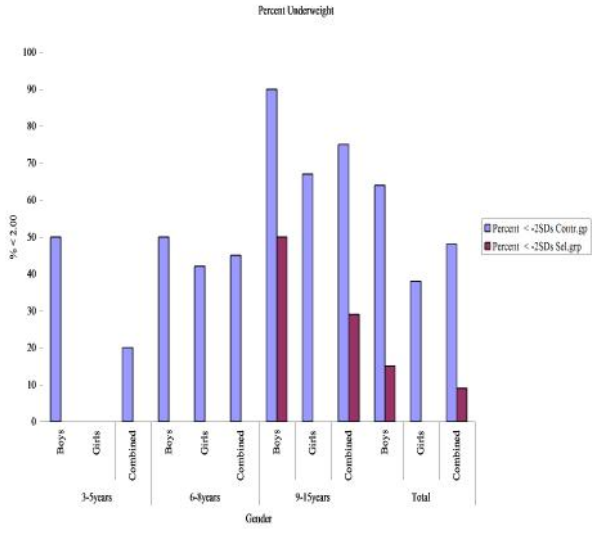

Figure 3

Table 7 Change on WAZ by Gender and Age Category among the children on Control

	Weight For Age Z Score For Boys in Control			Weight For Age Z Score For Girls in Control		
	Baseline	3 Months	6 Months	Baseline	3 Months	6 Months
3-5 years	-2.48	-2.21	-2.22	-3.24		
6-8 years	-2.30	-2.89	-1.81	-1.87	-0.90	-1.32
9-15 years	-1.37	-1.44	-2.08	-2.50	-1.64	0.001

DISCUSSION

The Weight for age Z score of the children in both groups were established at baseline. The cut-off of -2.00 Standard Deviations (WHO) was used to determine underweight among the children. Over all 49% of children were established to be underweight at baseline, 48% of those in control being underweight compared (1%) of those in selenium group at six months. Significant increase of body weight, and-Weight-for-Age Z Scores was observed in all age groups among the children on selenium as compared to the matched controls ($p< 0.05$), at six months, thus the WAZ score increased among the children who were given selenium.

Selenium forms active site (SeCy) of a group of isoform enzymes iodothyronine 5‘ deiododinases which catalyzes activation and deactivation of thyroid hormones, 3’3 5-T3 (Gibson *et al*., 2005) and anti-oxidant GSH-px which protects thyrocytes from damage by hydrogen peroxides produced during iodination of thyroglobulin.In this study, significant increase of body weight and weight for age Z score was observed in all age categories among children taking yeast selenium as compared to the controls. This observation therefore suggests that selenium intake likely increased the level and activity of iodothyronine 5’ deiodonases and GSH-px hence resulting in gene mediated protein deposition leading to the weight increase and thyroid tissue protection.

The data analyzed shows that mean WAZ for girls changed from-0.343 at baseline initially decreasing and then making sharp rise to 0.314 for those on selenium compared to the mean WAZ for boys which gradual increasing from to -0.491 to 0.201. This observation tends to suggests that when girls are given selenium there is a lapse in response of WAZ initially (tick phenomenon) and is probably influenced by some other factors. It is not clear whether the “tick phenomenon” could be due to differences in gender adherence, stigma, or non-availability of home support. How ever these findings are consistent with earlier observations by Rasmussen *et al*.,2011, and Deameaux *et al*., 2003; Massafra *et al*., 2002 which may suggest genetic link to the tick phenomenon in females.

This study therefore confirms earlier observations made by Baum *et al*.,2001 that selenium administration reduces the morbidity and hospitalization amongst the children. This observation also tends to confirm other observations by Niekerk *et al*., (2002) in South Africa that increase of micronutrient intake tends to maintain the body weight of People Infected with AIDS hence is cost effective way of promoting their health.Further studies by Sharpstone *et al.*,1997 showed that maintenance of and improved body weight in asymptomatic HIV –seropositive patients are associated with longer latency period to AIDS.

CONCLUSION

Supplementation of yeast selenium led to increased weight and improved Weight for Age Z Score over six months in asymptomatic HIV positive children. There were gender differences in response to selenium supplementation with female children having amore steeper response compared to boys.

Recommendation

Yeast selenium supplements are given to asymptomatic HIV positive children 3-16 years old to maintain their body weight and reduce their progression to AIDS. When supplementation regime is designed, the girls need to start supplement intake earlier than boys to address the tick effects.

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