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Table (2) Comparison of the difference between initial and follow up Anthropometric measurements between the two study groups. *Mann- Whitney U- test.

Index	Change From Study Beginning	Lactoferrin (n= 25)		Non LF (n= 25)		P- Value
		Mean	SD	Mean	SD	
Anthropometric	Body Weight (Kg)	−10.68	±3.04	−9.83	±3.55	0.410
	BMI (kg/m^2)	−10.66	±3.00	−9.87	±3.52	0.449
	Waist Circumference	−5.58	±1.31	−5.24	±2.56	0.676
	Hib Circumference	−4.61	±0.89	−4.71	±2.04	0.741

Table (3) Comparison of the change of serum leptin and lipid profile between the two study groups

Index	Change From Study Beginning	Lactoferrin (n= 25)		Non LF (n= 25)		P- Value
		Mean	SD	Mean	SD	
Biochemical	Serum Leptin (%)	−17.97	±22.14	−11.01	±13.03	0.002
	Serum LDL (%)	−10.2	22.7	−7.2	27.2	0.271
	Serum HDL (%)	9.6	28.4	7.7	22.6	0.165
	Total Serum Cholesterol (%)	−6.7	20.3	−2.9	29.9	0.020
	Serum Triglycerides (%)	−6.6	23.5	−4.8	27.5	0.332

This table shows significant difference regarding the change of serum leptin and cholesterol levels which decrease in the LF group more than the non LF group.

Discussion:

Our study included 50 obese school age children at age group of (6 to 12) years who attended the Pediatric follow up clinic. Those children have divided into two equal groups.

Regarding anthropometric measurements in our current study we found a decrease in weight, BMI, waist circumference, hip circumference and waist/ hip ratio in both LF and Non- LF groups after 12 weeks. We found a statistical significant difference between the two groups more in LF group after 12 weeks of intervention regarding waist circumference (p value< 0.001), hip circumference (p value <0.001) and waist/hip ratio (p value= 0.019) only.

Our study results are in contrast to Ono et.al. (2010), a double- blind, placebo- controlled design which was conducted on 26 Japanese human adult men and women aged (22- 60) years with abdominal obesity (BMI> 25 kg/ m^2, and visceral fat area (VFA)>100 cm^2)) measured from computed tomography images. They consumed bovine lactoferrin (300 mg/ day) or placebo tablets for 8 weeks. The study revealed a significant reduction body weight, BMI and hip circumference in the LF group and were significantly greater than with the placebo (P= 0.032, 0.013, 0.041, respectively). These differences of results may be attributed to difference in age group, dose of lactoferrin given and duration of the study.[15]

Also Zapata et.al. who performed their study on rats for 8 weeks concluded that lactoferrin, when compared to control groups, lactoferrin group had a decrease body weight by 14- 34% from day 7 onwards.[16] However, Ono et.al. revealed a significant reduction in Visceral Fat and subcutaneous fat in the LF group, as compared with the placebo controls (P= 0.009).[15]

Regarding serum leptin level, we found in our current study a decrease of serum leptin in both LF and Non- LF groups after 12 weeks of intervention. However, there was no significant difference of leptin serum levels between the two study groups after intervention. However there was a highly significant difference between the two study groups regarding the change (the decrease) of leptin level (p value= 0.002) which was more in LF group.

This is similar to McManus et.al. who demonstrated that lactoferrin significantly decreased leptin mainly due to decrease in their secretion and also because of accompanied decrease in expression of a hypothalamus associated genes linked to feeding behavior.[16][17]

Similarly, Zapata et.al. demonstrated that lactoferrin group of rats had more decreased plasma leptin concentrations when compared to control groups.

Regarding lipid profile, our current study has showed decrease of each of LDL, total cholesterol and triglycerides and increase of HDL in both LF and Non- LF groups after 12 weeks of intervention. No significant differences were found between the two study groups after intervention regarding LDL, HDL, total cholesterol or triglycerides. However, there was a significant difference between the two groups regarding the change (the decrease) of total cholesterol only (p value= 0.02) which was more in LF group. No significant differences between the two study groups regarding changes of levels of LDL, HDL or triglycerides levels were found.

Some of these results were similar to results of Xiong et.al.[18] who demonstrated that Lactoferrin administration induced significant decreases in the serum FFA, total cholesterol (TC), and LDL concentrations (more in LF+ HFD group) when compared with the HFD group, but did not affect the serum triglycerides (TG) concentration. No significant difference was observed in the HDL level between the LF+ HFD group and HFD group. However, the HDL/TC ratio in the LF+ HFD group was significantly higher than that in the HFD group.

Lastly, we can come to a conclusion that administration of oral lactoferrin to obese children may have no significant effect on weight and BMI when compared with those who did not take lactoferrin when taken for 12 weeks. However, lactoferrin has showed a remarkable effect on leptin serum level, adipose tissue and lipid profile and increasing HDL after 12 weeks of administration. More studies has to be done on obese children with longer period of study time and measuring other satiety hormones and other serum parameters related to obesity in response to administration of lactoferrin and other whey proteins (e.g. lactalbumin).

Conclusion& Recommendations:

Daily 200 mg of oral lactoferrin supplementation for 12 weeks in school aged obese Egyptian children of age range of six to 12 years had no statistical significant effect on decrease of weight, BMI. However, daily 200 mg of oral lactoferrin supplementation for 12 weeks showed statistical significant effect on serum leptin level and serum cholesterol level.

Reference:

1. Ogden CL, Carroll MD, Fryar CD and Flegal KM. (2015). **Prevalence of obesity among adults and youth: United States 2011- 2014. NCHS Data Brief**; (219): 1- 8.

Introduction:

Obesity in children is considered the most prevalent nutritional disorder among children and adolescents in many countries. It is one of the most serious public health challenges of the 21st century. It is a complex disorder which is global and is steadily affecting many low- and middle- income countries, particularly in urban settings. Prevalence of obesity is increasing in all pediatric age groups, in both sexes, and in various ethnic and racial groups.(1) The rising prevalence of obesity is likely to result from contemporary environmental and lifestyle factors such as increased access to palatable foods and reduced requirements for physical exercise, when compared with ancient hunter- gatherer lifestyles characterized by unpredictable periods of feast and famine.(2)

The BMI is a continuous measure of body fatness. The BMI correlates closely with total body fat (TBF), which is estimated using dual- energy x-ray absorptiometry (DEXA) scanning in children who are overweight and obese.(3) Consensus committees have recommended that children and adolescents be considered overweight or obese if the BMI exceeds the 85th or 95th percentiles, on curves generated from the 1963- 1965 and 1966-1970 NHANES, or exceeds 30 kg/m^2 at any age.(4)

Obese children show less effective down- regulation of appetite after food consumption, have lower sensitivity to gastric motility. Thus, they have shown increase in their food intake more than normal- weight controls after exposure to food cues, have higher levels of snack consumption in the absence of hunger, and score higher on psychometrically assessed "external eating". They also fail to show the "normal" pattern of deceleration of eating during a meal.(5) Lactoferrin is a major iron- binding protein that has reported to have many beneficial biological effects including immunological, immunomodulatory, iron saturation enhancement and other clinical applies.(6) Lactoferrin receptors have been identified in the gastrointestinal tract, on leukocytes and macrophages, platelets, and on bacteria.(7)

Leptin is an adipocyte- secreted hormone which plays a key role in energy homeostasis and has an effect on obesity by regulation of expression of hypothalamic neuropeptides.(8) Lactoferrin produces a great and sustained reduction of food intake. This hypophagia is partly due to reduced meal size and/ or frequency, increased satiety, and decreased diet preference.(9)

Lactoferrin produces great reductions in body weight and fat mass, enhancement in energy expenditure, and improvement in glucose tolerance. However, it is demonstrated that the improvement in energy balance, lipid metabolism, and glucose tolerance by lactoferrin are beyond its hypophagic effects.(10) Bovine whey- derived lactoferrin and immunoglobulins are isolated milk proteins shown to have immunomodulating properties. Modulation of the intestinal microbiota and reduction of intestinal permeability thus have the potential to counteract obesity related inflammation, and that suggests that lactoferrin supplementation may have direct anti- obesogenic effects.(11) Some studies on animals and human being have reported that lactoferrin had a decreasing effect on appetite, serum leptin level and had a role in changing lipid metabolism and decreasing weight gain rate.(12)

Aim of The Study:

To correlate between lactoferrin intake, changes in serum lipid profile and changes in serum leptin level in obese school age children.

Methodology:

This study was a randomized double armed prospective clinical trial study which included 50 obese school- aged Egyptian children with an age range of (6 to 12) years old. Children with BMI >2 SD (standard deviation) according to WHO growth chart presenting to the Pediatric outpatient department are included.

Those children have divided into two equal groups. The first 25 children have received oral lactoferrin supplementation in the form of sachets, the dose was 100 mg twice daily dissolved in ¼ glass of water or juice before meals for 12 weeks in addition to diet regimen and exercise performance and named as "Lactoferrin group" (LF group). The second 25 children did not take lactoferrin and put only on a diet regimen and exercise program for the same 12 weeks and named as "Non- Lactoferrin group" (Non- LF group).

BMI was calculated by the formula, BMI= weight (kg)/height (m^2) (Weight in kilograms over height squared in squared meters).(13)

Two samples for lipid profile (LDL, HDL, Triglycerides and cholesterol) and serum leptin were taken from each patient of two groups; first baseline sample before supplementation and second one after 12 weeks. The normal range of serum leptin hormone is 2.2- 4.8 ng/ ml.(14)

Results Data were analyzed using IBM© SPSS© Statistics Version-23 (IBM© Corp., Armonk, NY).

Results:

The children were randomly divided into two groups:

- Group A "Lactoferrin (LF) group": It included 25 obese children who received lactoferrin. They also were on exercise and diet regimen.
- Group B "Non- Lactoferrin (Non- LF) group": It included 25 obese children who did not take lactoferrin and were only on exercise and diet regimen for 12 weeks.

Table (1) Comparison of Anthropometric measures after intervention between both study groups

Variable	Lactoferrin (n= 25)		Non LF (n= 25)		Difference	95% Ci	P- Value*
	Mean	SD	Mean	SD			
Weight (Kg)	48.9	13.0	50.8	16.3	1.9	-6.4 to 10.3	0.647
BMI (kg/m^2)	28.3	3.8	27.6	4.1	-0.7	-3.0 to 1.5	0.526
WC (Cm)	76.12	7.84	84.56	7.23	8.44	4.15 to 12.73	<0.001
HC (Cm)	80.40	7.83	88.76	7.33	8.36	4.05 to 12.67	<0.001

Data are mean and standard deviation (SD). 95% CI= 95% confidence interval.
*Unpaired t- test.

This table shows highly significant difference between the two groups after intervention regarding waist circumference.

Lactoferrin intake and changes in serum leptin level in obese school age children

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Summary

Background: Obesity in children is considered the most prevalent nutritional disorder among children and adolescents in many countries. Lactoferrin is a protein that derived from bovine and human milk and has biological effect on appetite and obesity.

Aim: We aim in this study to determine the effect of lactoferrin intake on weight loss and changes in serum leptin level in obese school age children.

Methodology: This study was a randomized double armed prospective clinical trial study which included 50 obese school- aged Egyptian children who were divided into two equal groups. Two samples for lipid profile (LDL, HDL, Triglycerides and cholesterol) and serum leptin were taken from each patient of two groups.

Results: The results of our study revealed low serum leptin after lactoferrin supplementation. There is significant difference (P0.002) regarding the change of serum leptin and cholesterol levels which decrease in the LF group more than the non LF group.

Conclusion& Recommendations: lactoferrin supplementation in school aged obese Egyptian children of age range of six to 12 years had no statistical significant effect on decrease of weight, BMI and adiposity. However, it showed statistical significant effect on decreasing serum leptin level and serum cholesterol level.

تناول اللاكتوفيرين والتغيرات في مستوى الليبتين في الدم لدى الأطفال الذين يعانون من السمنة المفرطة في سن المدرسة

الخلفية: تعتبر السمنة من أكثر أنواع الخلل الغذائي انتشارا بين الأطفال والمراهقين في دول عديدة عبر العالم. وقد تتسبب هذه السمنة في مشكلات بسيطة وأخرى خطيرة، معظمها لها تأثير يعتد به على جودة الحياة وأحيانا قد يقلل من توقعات المدة العمرية في حياة الإنسان. ومن المعروف أن هناك عوامل عديدة تلعب دورا في تشكيل السمنة وظهورها منها العوامل الجينية والبيئية والأيضية وبالتأكيد العادات الغذائية. لكن يبقي السبب الرئيسي لحدوث السمنة في الأطفال غير معروف تحديدا. يعتبر اللاكتوفيرين بروتين حيوي تم استخلاصه من لبن الأبقار وأيضا من اللبن البشري. هذا البروتين له أدوار حيوية ومناعية واستخدامات حيوية متعددة. واحد من هذه الأدوار الحيوية هو تأثيره علي السمنة والشهية في الأطفال ذوي السمنة. أما الليبتين فهو هرمون يفرز من الخلايا الدهنية بالجسم وله دور رئيسي وفعال في التحكم وتنظيم الشهية في جسم الإنسان متضمنا الأطفال ذوي السمنة.

الاهداف: تهدف هذه الدراسة إلي تحديد تأثير تناول اللاكتوفيرين علي إنقاص الوزن في الأطفال ذوي السمنة في سن المدرسة. كما تعمل هذه الدراسة علي تقرير تأثير تناول اللاكتوفيرين علي مستويات الدهون ومستوي هرمون الليبتين بالدم. توصف هذه الدراسة بأنها دراسة تجريبية سريرية مستقبلية ثنائية الذراع، تم إجراؤها علي ٥٠ طفل ذي سمنة في سن المدرسة الذين تتراوح أعمارهم من ستة إلي اثني عشرة عاما والذين تم متابعتهم طوال فترة الدراسة.

العينة: تم تقسيم هذا العدد من الأطفال إلي مجموعتين متساويتين العدد. المجموعة الأولي عبارة عن ٢٥ طفلا تم إعطائهم أكياس اللاكتوفيرين لتناولها عن طريق الفم يوميا ولمدة ثلاثة أشهر بالإضافة إلي التزامهم بنظام غذائي وأخر رياضي محدد ومتابعتهم طوال فترة الدراسة، وتم تسمية هذه المجموعة بـ"مجموعة اللاكتوفيرين". أما المجموعة الأخري فهي تتكون من ٢٥ طفلا لم يأخذوا اللاكتوفيرين وتم وضعهم فقط علي النظامين الغذائي والرياضي، وبالتالي تم تسمية هذه المجموعة بـ"مجموعة اللا-لاكتوفيرين".

الخلاصه: استنتاجا مما سبق، تم إثبات وتوضيح عن طريق هذه الدراسة أن تناول اللاكتوفيرين في الأطفال ذوي السمنة في سن المدرسة لمدة ثلاثة شهور كان له تأثير ملحوظ في تقليل الشهية وتقليل مستويات الكوليستيرول وهرمون الليبتين بالدم. بالرغم من ذلك لم يكن هناك تأثير يعتد به في تناول اللاكتوفيرين علي تقليل الوزن ومؤشر كتلة الجسم في هذه الدراسة.

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