CASE REPORT

The effect of spinach-derived thylakoids on anthropometric parameters and metabolic profile in antipsychotic treatment: A case report

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Abstract
Background: Antipsychotics is the first line, evidence-based treatment of schizophrenia and other primary psychotic disorders. Metabolic adverse effects are common, including body weight gain, hypertension and metabolic syndrome. There is still no safe treatment for these adverse effects, except from lifestyle changes. Studies of thylakoids have shown body weight loss and improved metabolic parameters in overweight women.
Case report: A 53-year old female with a history of unspecified nonorganic psychosis, treated with Quetiapin and Topimax (Topiramat), was given a supplement of 5g thylakoids daily for 12 weeks. She reported a rapid decrease of sweet craving and loss of body weight was observed.
Conclusion: We report a successful treatment with thylakoid supplements of the metabolic side effects of antipsychotics in a female adult with a history of body weight problems and sweet craving. Further investigation and larger studies are needed. A safe treatment of metabolic side effects could increase quality of life for patients in need of antipsychotic treatment.

Key words: psychosis, obesity, metabolic side effects, sweet craving, inflammation, hunger, satiety, weight loss

1. Introduction

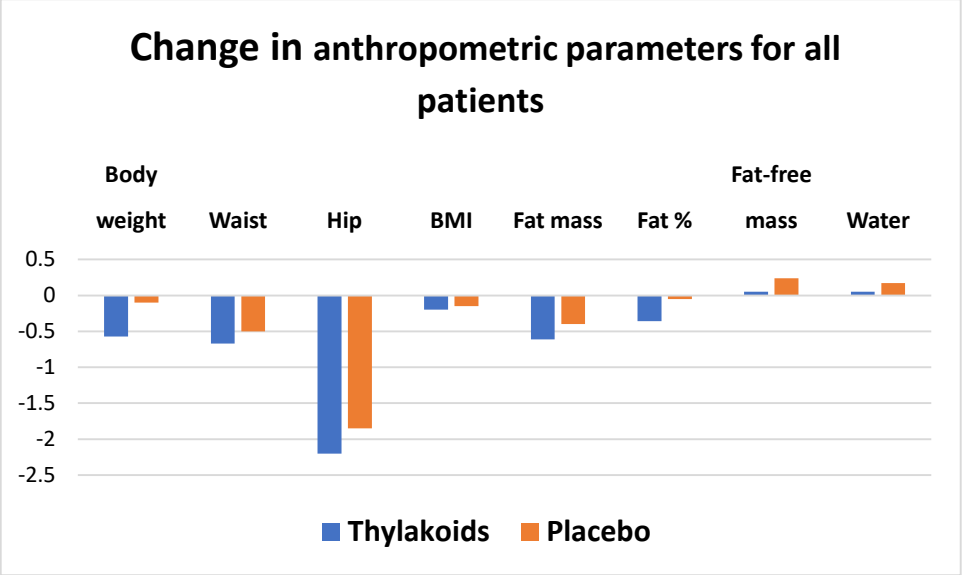
Schizophrenia is associated with suffering and often premature death. It is one of the most common and costly psychiatric disorders in the world. The evidence-based treatment of schizophrenia and other primary psychotic syndromes is antipsychotic medication (1). It is well-known that second-generation antipsychotic medications (SGA) are associated with metabolic disturbances such as body weight gain and type 2 diabetes mellitus (T2DM) (2). Comparative studies have shown that clozapine and olanzapine are the most strongly associated with this type of dysmetabolic events (3, 4). The SGAs interact with several receptors in the brain, including 5-Hydroxytryptamine Receptor 2C (5-HTR2C), regulating food intake, body weight, and glucose metabolism, resulting in overeating and obesity (5).

Body weight control is achieved through regulation of food intake and energy expenditure of the body, appetite regulation being the most important part of body weight control (6). Appetite control occurs centrally in the hypothalamus, with peripheral hormones such as cholecystokinin (CCK) and glucagon-like peptide 1 (GLP-1), acting to suppress food craving and promote satiety (7). This occurs through a reduction in dopamine reward signaling (8) and an activation of serotonin signaling(9).

In recent years there has been an increased interest in natural products, called nutraceuticals. One such is thylakoids derived from green leafy vegetables (10). Thylakoids are the green chlorophyll-rich membranes responsible for photosynthesis and contain essentially proteins, lipids, pigments, antioxidants, minerals and vitamins. They could be isolated through a mechanical procedure involving centrifugation and filtration of green leaves, followed by drying into a green powder (11). This powder, as a food additive, has been found to promote body weight loss in overweight women when given at a dose of 5 gram per day for three months. In these patients, craving for sweets was reduced in a drastic way already the first day of treatment(12).

This paper describes a patient who during 3 months in 2019 participated in a study that was conducted to investigate if the intake of thylakoids would prove more effective compared to placebo in reducing metabolic side effects of antipsychotic medication. Due to dropouts during the study, there were too few participants at the end of the study for statistic analysis. The results are yet included in our report (Table 3 and Fig 1). Our patient differed clearly from the other participants by an immediate response on food cravings and body weight, making her case important to report. Consent was given by the patient to report the outcome of her experience.

Figure 1. Change in body weight, waist- and hip circumference, BMI, fat mass, fat percent, fat-free mass and total body water after intervention with thylakoids and placebo for three months in patients with psychiatric disease detailed in Table 3. Thylakoids (Blue)(n=7), Placebo (Orange) (n=7).



2. Case report

2.1 Background

The patient is a 53-year-old Caucasian female who first was admitted to a psychiatric ward in 1994, due to an acute stress reaction. At the time she had a history of childhood trauma, chronic pain, addiction to painkillers and was overweight. The woman had tried to commit suicide fourteen times and the last suicide attempt was in 2002. She suffered her first psychotic episode in 1997 with mostly auditory- and some visual hallucinations, hearing unknown male voices. Antipsychotic treatment was initiated and the patient reports that she went from overweight to obese. When the patient met her husband in 2001, her body weight was 137 kg with a height of 160 cm, equaling a BMI of 53,5. Her current diagnosis is Unspecified nonorganic psychosis and her antipsychotic treatment is Quetiapin and Topimax (Topiramat).

2.2 Intervention study

The patient participated in a 12-week randomized, double-blind, placebo-controlled clinical trial conducted from August 2019 through December 2019 in the psychiatric clinic of Västerås Hospital, Sweden. Prior to intervention, body length, body weight, body-composition (Tanita®), waist and hip circumference, pulse and blood-pressure were measured. Blood samples were collected for analysis of white blood cells count (WBCs), C-reactive protein (CRP), fasting blood sugar, glycated hemoglobin (HbA1c), cholesterol, triglycerides, low-density lipoproteins (LDL) and high-density lipoproteins (HDL). The patient was asked to estimate her cravings for sweets and salty foods, using a VAS scale from 1-10 (13). The estimation of cravings for sweets and salty foods was performed every 4 weeks during the study. At the end of the study, body-measuring and blood sample analysis were performed in a similar way as prior to the intervention.

The patient added a supplement of 5gram of thylakoid powder, divided into 4 capsules for breakfast and 5 capsules for lunch, daily during 12-weeks. There were no further

instructions given about diet or physical activity.

The thylakoid powder, Appethyl®, was derived from spinach and produced by GLM AB, Lund, Sweden, followed by encapsulation by Impac AB, Lund, Sweden. Laboratory samples were analyzed by the clinical chemistry department, Västerås Hospital, Sweden.

2.3 Results

After 3 months of intervention with thylakoids, total body weight was reduced with 9,3 kg, of which 6,8 kg consisted of fat (Table 1). This is a weight reduction of 8,6% from the baseline level, making it clinically significant (14). The waist circumference decreased with 7 cm, while no change was observed in hip circumference (Table 1).

Table 1. Anthropometric measurements before and after intervention in single case

Analysis	**Start**	**End**	**Change**
Body length (cm)	160		
Body weight (kg)	108,4	99,1	-9,3
Waist circumference (cm)	116	109	-7
Hip circumference (cm)	124	124	0
BMI (kg/m^2)	42,3	38,7	-3,6
Fat mass (kg)	55,9	49,1	-6,8
Fat%	51,6	49,6	-2
Fat free mass (kg)	52,5	50	-2,5
Total body water (kg)	38,4	36,6	-1,8

When estimating her cravings for rewarding food the patient noticed that her cravings for sweets disappeared after 3 days of thylakoid supplement. When she was at the grocery store, she could walk by the candies without feeling the need to buy some, which she had not been able to do previously. The effect was persistent throughout the entire period of the study. Her cravings for salt also disappeared and she stopped putting extra salt on her meals. The patient also experienced that she ate less and felt satiated more rapidly than before. Her husband noticed a significant difference in her eating habits.

Post intervention the patient noticed that her cravings for sweets returned as soon as she stopped the treatment of thylakoids. She therefore decided to continue treatment on her own account. On a 1-year follow up interview the patient reports a total body weight loss of 20 kg. She reported no side effects of the treatment.

Blood analysis of metabolic parameters indicated a healthy patient (Table 2), apart from CRP which is slightly elevated. During the 12-week intervention, there was no drastic change in these parameters.

Table 2. Fasting values of patient before and after intervention

Analysis	**Unit**	**Ref.int**	**Start**	**End**
White blood cell count (WBCs)	10e9/L	3,5-8,8	8,0	7,3
C-reactive protein (CRP)	mg/L	<5	9,1	11,0
Glycated hemoglobin ($HbA1_C$)	mmol/mol	31-46	35	36
Blood sugar	mmol/L	4,0-6,0	5,7	5,6
Cholesterol (total)	mmol/L	3,9-7,8	7,5	6,8
Triglycerides	mmol/L	0,5-2,6	1,9	2,2
HDL- cholesterol	mmol/L	>0,99	1,43	1,40
LDL-cholesterol	mmol/L	2,0-5,3	5,10	4,90

Table 3. Anthropometric measurements in patients with psychiatric disease, receiving either 5 g thylakoids (n=7) or placebo (n=7) daily during 3 months. The values are presented as means±S.D.

	Thylakoids (n=7)			**Placebo (n=7)**		
	Start	End	Change	Start	End	Change
Body weight (kg)	90,7±13,1	90,0±13,7	-0,57±5,5	114,3±34,6	114,1±31,9	-0,10±4,1
Waist circumference (cm)	105,0±8,6 n=6	104,3±13,7 n=6	-0,67±8,8 n=6	120,6±14,2	120,1±14,2	-0,5±3,3
Hip circumference (cm)	113,3±9,2	111,2±12,8	-2,2±4,4	124,3±7,1	122,4±7,2	-1,85±1,8
BMI (kg/m^2)	31,0±5,9	30,8±13,5	-0,20±2,0	39,1±10,9	38,9±10,0	-0,15±1,4
Fat mass (kg)	32,4±13,9	31,8±13,5	-0,61±3,7	45,5±24	45,1±23,2	-0,40±1,8
Fat%	34,9±11,0	34,5±11,0	-0,36±1,8	38,2±9,5	38,2±10,5	-0,05±1,36
Fat free mass (kg)	58,3±8,5	58,4±8,8	0,05±2,5	68,8±13,7	69,0±13,8	0,24±3,26
Total body water (kg)	42,6±6,2	42,7±6,4	0,05±1,8	50,4±10,0	50,5±10,1	0,17±2,4

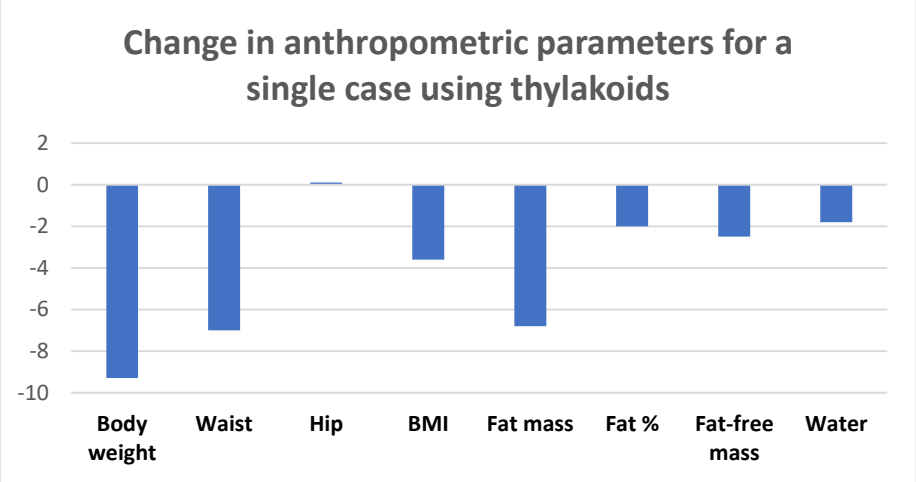
3. Discussion

Metabolic side effects are common in antipsychotic medication. Yet these medications are important in the treatment of psychosis, improving the quality of life of the patient. It would however be desirable to find a safe way to prevent and treat the metabolic side effects, since they may lead to somatic complications and premature death. Advice of lifestyle changes are often given, even though mostly not effective. In this case report a female with antipsychotic treatment, markedly changed her eating habits after having taken thylakoid supplements daily for 12 weeks. After 3 days of intervention, the patient reported a suppression of craving for sweets and salt, resulting in a clinically significant body weight loss of 8,6 % after 12 weeks.

During treatment the patient lost a total of 9.3 kg in body weight, which corresponds to an average weight loss of 3 kg per month. This is an optimal rate for preventing counterregulatory hunger signals (14). The loss of body weight occurred mainly through the loss of fat mass, equal to 6.8 kg of fat (Table 1). This may be related to an increased fatty acid oxidation, as has been described for thylakoids in earlier studies(15).

Furthermore, the waist circumference decreased with no change in hip circumference, suggesting a loss of abdominal fat. When comparing the results of this single case receiving thylakoids with the whole group of patients receiving thylakoids the pattern of metabolic change appeared similar and different from the placebo group, illustrated in figure 1. As indicated the thylakoid group had a loss of body fat, a seemingly specific loss of abdominal fat with a reduction of waist circumference and a decreased hip circumference as did the placebo group. For comparison the same parameters for the single case is illustrated in figure 2.

Figure 2. Change in body weight, waist- and hip circumference, BMI, fat mass, fat percent, fat-free mass and total body water after intervention with thylakoids in the single case reported.



Apart from CRP, all blood parameters were within the normal range both before and after the intervention (Table 2). The CRP was elevated from the start of intervention and remained elevated after three months, indicating a low-grade inflammation, as is common in obesity. One might expect that weight loss would induce a reduced inflammatory status. It has however been demonstrated that the inflammatory status is gradually lowered during the following 3-9 months after a short-term weight loss intervention(16).

Earlier studies have demonstrated an activation of gut hunger- and satiety hormones by thylakoids, mainly ghrelin, cholecystokinin and glucagonlike peptide (17). This suggests that it would have been more relevant to analyze these parameters, since the subject reported such a radical change in cravings and satiety.

The subject in this case report, participated in an intervention study that contained too few participants to draw any conclusions. Furthermore, the inclusion criteria were too wide. Future studies are suggested to narrow down the inclusion criteria, restricting the study for overweight patients with craving for sweet and salt associated with antipsychotic medication.

4. Compliance with ethical standards

Ethical permittance of the study was approved by the Regional Ethical Review Board (Dnr 2019-00447). The patient of this case report has given her consent for sharing this information.

5. Conflict of interest

CEA is the founder of the Research Company Thylabisco AB at Lund University, Sweden and a board-member in Green Leaf Medical AB.

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