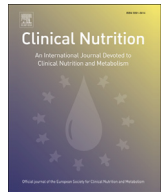




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Letter to the Editor

Green tea EGCG plus fish oil omega-3 dietary supplements rescue mitochondrial dysfunctions and are safe in a Down's syndrome child

Keywords:

Down syndrome
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Fish oil omega-3
Nutraceuticals

Dear Editor,

We would like to draw your and the readers' attention on the benefits of epigallocatechin-3-gallate (EGCG) plus fish oil dietary supplements, for the first time assumed by a child (10-year and 3-month-old) with Down syndrome (DS), in reversing alterations critical in DS pathogenesis without side effects.

The health benefits of fish oil omega-3 [1] and green tea extract EGCG [2], both available as nutritional supplements and safe for human use, are well known. We previously reported in DS cells the multimodal action of EGCG in counteracting oxidative stress and energy deficit, strongly associated with DS [3]. A pilot clinical trial on young adults with DS demonstrated mild positive effects of EGCG on cognitive performances [4] that reasonably, could be further improved by anticipating EGCG treatment in childhood.

The idea was to mix EGCG (Mega Green Tea Extract decaffeinated, from Life Extension, Europe) 10 mg/kg/die, dose safe in previous studies [4], with fish oil (Omega Kids Swirl Fish Oil from Barlean's, USA) 8 mg/kg/die of omega-3 fatty acids EPA and DHA, reported to enhance EGCG bioavailability and synergize its effectiveness [5]. The emulsion was added with orange juice containing ascorbic acid to prevent EGCG oxidation and to give a taste agreeable for children.

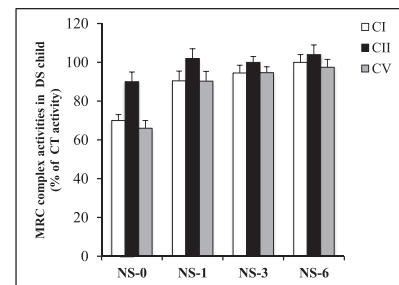
This nutraceuticals supplementation (NS) was assumed one dose daily for six months.

The DS child has been monitored before and during NS for biochemical and psychometric evaluation according to the guideline for DS follow up.

Measurement of mitochondrial respiratory chain (MRC) complex activities in lymphocytes from peripheral blood (5 mL) of DS child and his brother (13-year-old, as a control) performed as in [3], demonstrated a selective significant deficit of MRC complex I and ATP synthase activities before NS (NS-0) (Fig. 1). Remarkably, a complete restoring of MRC complex activities is observed already after one month (NS-1) and maintained for all NS-period, showing the efficacy of EGCG/fish oil to counteract mitochondrial dysfunction *in vivo*.

Laboratory analysis (see table in Fig. 1) reveals no alteration of hepatic function markers and lipid profile, demonstrating the safety of this NS in paediatric age. Interestingly, an ameliorative action on thyroid profile in the DS child suffering of a subclinical hypothyroidism is observed. Supplementation with folic acid (0.4 mg/2 dies) backs to the reference value the folic acid reduction observed after 1-month NS, possibly due to reduction folate availability by EGCG inhibition of dihydrofolate reductase.

In addition, the neuropsychological evaluation of the DS child through auditory attention and verbal strategic tests (according to Italian battery for ADHD), revealed an increased score (33%–



Laboratory analysis	EGCG/fish oil diet supplementation			
	Basal	1 month	3 months	6 months
Creatinine (ref 0.6–1.3 mg/dL)	0.69	0.66	0.69	0.65
GOT/AST (ref. 0–35 U/L)	23	27	26	30
GPT/ALT (ref. 0–45 U/L)	21	21	26	35
Total Cholesterol (ref. < 200 mg/dL)	166	162	172	165
HDL Cholesterol (ref. 30–75 mg/dL)	64	65	62	70
LDL Cholesterol (ref. < 150 mg/dL)	87	83	92	79
Triglycerides (ref. 40–160 mg/dL)	74	72	91	80
Folic acid (ref. 5–20 ng/mL)	3.01	1.90	18.40*	6.20**
FT3 (eu. 2.75–7.80 nmol/L)	5.36	5.46	6.25	7.90
FT4 (eu. 10.2–22.7 pmol/L)	13.9	14.3	13.8	16.1
TSH (eu. 0.40–4.00 uI/mL)	6.26	6.63	5.82	3.57
Thyroglobulin (ref 0–78 ng/mL)	112.70	44.8	37	57
Ab anti-Thyroglobulin (Neg. < 18.00 U/mL)	19.00	17.1	9.4	5.9
Ab anti-TPO (Neg. < 28.0 U/mL)	18.6	25	20.7	16

* supplementation of 1 cp (0.4 mg folic acid)/die
** supplementation of 1 cp (0.4 mg folic acid)/2 die

Fig. 1. Mitochondrial respiratory chain (MRC) complex I (CI), complex II (CII) and ATP synthase (complex V; CV) activities in lymphocytes of Down syndrome child (DS) vs MRC activities of not-treated brother (CT) before (NS-0), after 1 (NS-1), 3 (NS-3) and 6 (NS-6) months of nutraceutical supplementation. Bar represents mean \pm SD of three measurements.

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43%) after 3 months of NS respect to baseline, suggesting, as preliminary information, an improved ability to perform tasks requiring concentration after NS.

This report may support clinical trials with these nutraceuticals as potential therapeutic tool to prevent energy deficit-associated DS clinical signs.

Conflict of interest

RAV personal involvement (mother of the child with DS) has not influenced the results of the experiments, which were performed by DV. Both authors declare to have no competing interests that might be perceived to influence the results.

Informed consent was obtained from the child's guardian.

Contributors

DV designed, performed and analysed the biochemical experiments; RAV conceived the idea and coordinate the study. RAV and DV wrote the manuscript.

Acknowledgements

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