TARGETED NUTRITIONAL INTERVENTION FOR DOWN SYNDROME

Author: Gabi Giacomin MHSc (Comp Med), BHSc (Comp Med),
Scientific Advisory Committee for Trisomy 21 Research Foundation (US)

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Introduction

The term Targeted Nutritional Intervention (TNI) was first used by W. James Croom Jnr, PhD, to describe the manipulation of gene expression through nutrition. In 1993, a team of prominent scientists from the USA, inspired by biochemist Dixie Lawrence, tested the theory of TNI. They formulated the first nutrigenomic supplement for people with Down Syndrome (DS).[1] The full protocol has been tested in three third-party clinical trials: the first published in the German Journal of Pediatrics in 2001 by Matthias Gelb,[2] and the second and third by N. Miguid from the University of Cairo, Egypt, published in 2002[3] and 2015.[4] TNI uses two specific formulas: *Nutrigenomic Support for Down Syndrome* and *Polyphenols for Down Syndrome*, which have been specifically designed to target gene overexpression, alongside *Tryptophan for Sleep and Growth* and *Digestive Support for Down Syndrome* to support healthy sleep and digestion, respectively. The full TNI protocol also includes fish oil, curcumin, glutathione and organic green papaya powder, used at very low and specific doses, as high dosing is counterproductive to treatment. EGCg is also recommended four hours away from folate supplementation.

Background

Genes located on chromosome 21 are triplicated, causing genetic overdose and the features of DS, including impairment in learning and memory, and craniofacial dysmorphology.[5] These genes actively produce enzymes and proteins which cause disruption to a large portion of the genome.[6] Nutrients and natural substances used in TNI have been researched for their ability to down-regulate or inhibit these genes.[6] By reducing this gene over-expression, we can also regulate the biochemical pathways they affect.

Gene Overexpression

The gene superoxide dismutase 1 (SOD1) is located on the long arm of chromosome 21 and is over-expressed. Elevated hydrogen peroxide results from high SOD1 and increases the level of free radicals in organs, particularly the brain,[7,8] and ROS (reactive oxygen species) are associated with premature ageing in DS. Therefore, supplementing with specific antioxidants, such as vitamins A, C and E, becomes imperative for cells to function properly. In addition, supplementation with selenium and vitamin D3 up-regulates glutathione peroxidase, which detoxifies hydrogen peroxide to balance the antioxidant system.

DYRK1A is also located on the critical region of chromosome 21. Over-expression of DYRK1A contributes to cognitive deficits and Alzheimer's pathology in DS. Epigallocatechin gallate (EGCG), the main catechin found in green tea, inhibits the expression of DYRK1A. In a landmark study by de la Torre (2014), EGCG reversed cognitive deficits in DS improving memory recognition, working memory and quality of life by reducing the activity of DYRK1a.[10] Craniofacial structure is also altered in DS due to triplication of DYRK1a, significantly affecting breathing, eating and speaking.[11] EGCG normalised some craniofacial characteristics when given prenatally.[12] Supplementing EGCG prenatally is carried out with caution due to its reducing effects on iron.

Research

In a published study by Gelb (2001), 38 patients with DS were treated with TNI for an average of 21 months, compared with 38 patients who didn't receive TNI. Laboratory measurements comparing the two groups are shown in Table 1.[13]

Table 1: Laboratory Measurements: Comparison of Children With DS Without and With TNI.[14]

Prameters/Child Group	Control Group Without TNI*	Children with TNI**	Normal Values
IgA	52 (32 - 211)	180 (80 - 325)	70 - 400
Cholesterol (fasting)	162 (98 - 265)	155 (102 - 232)	<200
HDL (fasting)	38 (23 - 76)	48 (33 - 95)	>35
LDL (fasting)	98 (76 - 164)	85 (54 - 143)	<155
Slenenium	32 (28 - 72)	81 (61 - 91)	53 - 105
Vitamin A	0.3 (0.1 - 2.0)	0.9 (1.5)	0.2 - 1.2
Vitamin E	4.2 (0.2 - 22)	8 (2.5 - 16)	3.0 - 14

* n = 80; ** n = 38

Miguid's (2015) research showed that at baseline (before taking TNI), DS patients had significant increases of SOD activity ($p<0.01$) and significant decreases in GST and GSH activities ($p<0.01$), compared to controls. Following TNI supplementation, increased catalase and glutathione activity balance the side effect of increased SOD1, hydrogen peroxide.[15]

Table 2: Mean Levels of Investigated Parameters in Controls and DS Children.[16]

Group	SOD (U/g Hb)	CAT (KU/gHb)	GPx (U/g Hb)	GR (U/g Hb)	GST (U/g Hb)	GSH (umol/g Hb)
Controls	705 +/- 65	391 +/- 56.4	19 +/- 0.6	2.92 +/- 0.235	6.60 +/- 0.69	10.3 +/- 4.2
Down Syndrome (pre)	1472 +/- 171	427 +/- 51.4	23.2 +/- 2.32	2.99 +/- 0.337	2.28 +/- 0.334	7.05 +/- 0.652
P1	<0.01*	>0.05	>0.05	>0.05	<0.01*	<0.01*
Down Syndrome (post)	1510 +/- 196	650 +/- 87	45.4 +/- 5.44	2.79 +/ 0.342	1.96 +/- 0.25	7.59 +/ 0.532
P2	>0.05	<0.05*	<0.01*	>0.05	>0.05	0.05

Each value represents the mean +/-SE:
Controls (n=20); Down Syndrome (n=21)
P1:DS versus control;P2; DS (Pre) versus DS (Post) p>0.05+ significant*

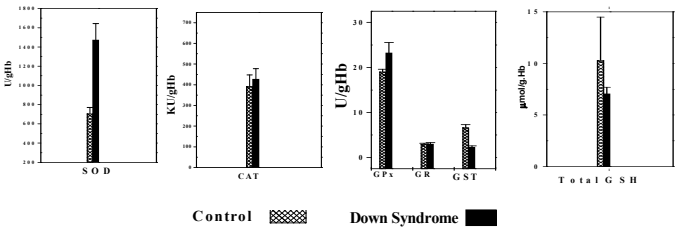

Figure 1: Antioxidant Enzymes Activities and in DS Children and Controls.[17]

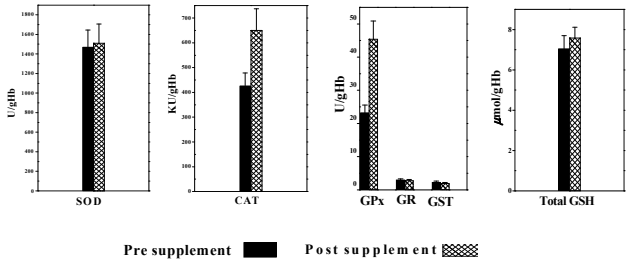

Figure 2: Antioxidant Enzymes Activities and in DS Children Pre- and Post-Nutritional Supplementation.[18]

Conclusion

Particular attention needs to be given to specific genetic subgroups, such as DS, when formulating nutritional plans. Substantial scientific evidence exists to support the use of nutritional supplements in this group and needs to be referred to in clinical practice. As TNI becomes better understood, nutritional treatment of people with DS will improve, allowing gene expression and cell functioning to occur normally and sustain homeostasis.

Reference

References available on request.

Contact Details

Gabriella Giacomin: c-pod@outlook.com
www.theconsciouspod.com

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