

Targeted Nutritional Intervention (TNI) for Children with Down Syndrome

M. J. Gelb
Down Syndrome Central Practice
Bretten, Germany

Key words: different metabolism-consequences for growth, purine metabolism and immunological problems – organization, results, side effects – contraindications, stopping questionnaires – outlook

Introduction

The metabolism of persons with Down syndrome differs, sometimes considerably, from persons with a normal complement of chromosomes. Pathological workups for purine, carbohydrate and homocysteine – cysteine metabolism are typical in persons with Down syndrome. These distinctive features correlate, at least partially, with gene – over – expression caused by the additional 3rd chromosome 21 characteristic of persons with Down syndrome. This gene – over – expression can result in an increase of chromosome 21 - encoded gene products. Gene dosage studies have shown an increase of gene products of up to 40-50% from genes located on chromosome 21. Two of these proteins in special interest are Zn/Cu peroxide – dismutase (POD) and cystathionine - β - synthetase (CBS).

Zn/Cu peroxide – dismutase catalyzes the dissimilation of peroxide that occurs with the metabolism to hydrogen peroxide, which is then processed in to water by the enzymes catalase or glutathionine peroxidase. A surplus of Zn/Cu peroxide-dismutase results in a surplus of hydrogen peroxide, which adversely reacts with cell membranes, DNA and enhances lipid peroxidation, especially in the presence of iron. Further investigations are needed to elucidate whether over - expression of this enzyme is also clinically correlated with disorders of maturation, aging and various degenerative diseases, like Alzheimer's.

The over - expression of cystathionine - β - synthetase interferes with methionine – homocysteine metabolism. This may be biochemically expressed as increased concentrations of cysteine or disorders in the metabolism of folate. Decreases in homocysteine can result in a reduction of the resynthesis of methionine.

Clinical Issues Associated with Aberrant Metabolism in Down Syndrome

Immunological Problems

Persons with Down syndrome have lower levels of IgA, fewer white blood cells and reduced numbers of T – cells. These decreases are, at least in part, responsible for the increased infections of the upper respiratory system, the ear and the digestive tract.

Growth

Persons with Down syndrome grow more slowly and are smaller than the diploid population.

Lipoprotein Metabolism

The author has often found higher circulating levels of cholesterol and lower circulating concentrations of ω - 3 and ω - 6 fatty acids in persons with Down syndrome. This has a negative effect on the HDL/LDL ratio and results in an increased risk of cardiovascular illnesses in these persons.

Alzheimer's disease

Persons with Down syndrome are at increased risk for developing Alzheimer's disease or Alzheimer's – like lesions in the brain. Some reports suggest that the incidence of Alzheimer's disease is as high as 40% for persons with Down syndrome over the age of 40.

Targeted Nutritional Intervention (TNI) – Real or Wishful Thinking?

Targeted nutritional intervention is the attempt to correct defects in intermediary metabolism in Down syndrome through the use of nutritional supplements such as vitamins, minerals and other metabolites found in the body. One should be aware that TNI does not cure Down syndrome and does not substitute for other medical interventions used to treat persons with Down syndrome. Recently, at the conference for Down syndrome specialists in Iserloh, a statement to the public was released that is in harmony with these observations.

A carefully designed double blind study is urgently needed to clarify the efficacy of TNI. A survey of patients with Down syndrome found that 15% of the parent caregivers “secretly” (without knowledge of the treating physician) supplemented the diet of their children with bach flowers, homeotherapeutics, *HapCaps*, TNI and other forms of nutritional additives. In contrast to the American market, there is, to my knowledge, no established retailer of TNI products in Europe.

In my practice, the choice of a TNI nutritional supplement for children with Down syndrome was based on the following criteria: 1) a complete disclosure of ingredients contained in the supplement, 2) its recommendation by Trisomy 21 Research, Inc., a non-profit parent and health care professional advocacy group for persons with Down syndrome located in the United States, 3) the length of time the supplement had been available, and 4) the availability of the TNI supplement in Germany. After deliberation, I chose the TNI supplement, *Nutrivene D*, which is marketed by International Nutrition, of Inc. of Owings Mills, MD., USA. The observations reported in this communication are based on the results observed when that dietary supplement was offered to patients with Down syndrome.

Clinical Protocol

Our practice has been offering TNI since 1996. After 4 years experience with approximately 100 children, a protocol was developed that could be integrated into the normal clinical work of my practice. After extensive conversations with the parents of children with Down syndrome regarding the potential benefits and risks of TNI as well as a thorough medical assessment of the current health of the child (assessment made with consultations of various therapists as well as with various medical laboratory test results), the individual TNI dosage program was established and followed by a 3 month test phase.

After the testing phase, the health of the child was again assessed according to the procedures mentioned above. The data and medical evaluations from the testing period were used to determine if the TNI supplementation was continued for that child.

Results and Observations

Leichtman (1997) reported on the health of 113 patients with Down syndrome, ranging in age from one month to 12 years of age, who were supplemented with a TNI multivitamin supplement. His findings were:

1. An increase in growth ranking of the TNI patients from the 5th to the 19th percentile.
2. A significant reduction in the susceptibility to infections.
3. Seriological data demonstrating increased IgA levels and an increased number of leukocytes.
4. Significant developmental neurological improvements regarding language, motor skills and cognitive perception.

Current Observations

I treated 38 patients, aged 6 months to 15 years of age for an average of 21 months (range 12-48 months) with TNI and compared them with a group of 38 patients aged 5 months to 17.2 years of age who had not been supplemented with a TNI product. The growth scales of Swets and Zeitlinger were used for the determination of the percentile ranking of the children.

Table 1.
Increase in percentile ranking of children

<p><u>Children with TNI</u></p> <p>52.6% (n=20 children) averaged from the 25th (10th - 50th) to the 50th percentile (30th - 70th).</p> <p><u>Children without TNI</u></p> <p>13.1% (n=5 children) averaged from the 25th (5th - 25th) to the 30th percentile (10th - 60th)</p>

Table 2.
Reductions in Infections

Laboratory Measurements

Parameters	Intraindividual changes of the TNI children	Changes compared to the control group
Reductions of doctor's visits because of infections	42.1%	39.4%
Reductions of infections treated with antibiotics	31.5%	36.8%

We compared our TNI group with a control group of 80 children from 1 month to 17.2 years of age. The laboratory measurements (Table 3) have been chosen as examples. In contrast to Leichtman (1997) we did not find an increased number of leukocytes.

Table 3.
Laboratory Measurements: Comparison of children with Down syndrome without and with TNI

Parameters/Child Group	Control group without TNI*	Children with TNI**	Normal Values
IgA	52 (32-211)	180 (80-352)	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
Selenium	32 (28-72)	81 (61-91)	53-105
Vitamin A	0.3 (.01-2.0)	0.9 (.03-1.5)	0.2-1.2
Vitamin E	4.2 (0.2-22)	8 (2.5-16)	3.0-14

* n=80; ** n=38

Development

Leichtman (1997) describes significant neurological improvements of the TNI children. I believe that I can see the same tendency based on my observations and tests (**MFED, Denver, Wet**, among others).

Assessment by the parents

All parents of TNI children were asked to fill out questionnaires and to submit them to us at regular intervals. These questionnaires help us to document unwanted side effects and the observations of the parents. I am aware of the subjectivity of this method. I also recognize the danger of false observations because of the placebo effect. Nevertheless, the results of 321 questionnaires of the 38 long-term TNI supplemented children are listed in Table 4.

Side Effects

I did not find any information on the side effects of TNI supplementation in the literature. In my own patient group of approximately 100 TNI supplemented children,

among them 38 long-term supplemented children, I observed the following side effects:

1. 2 patients had reversible sleeping disorders (sleeping through the night)
2. 3 patients experienced short term eating disorders (they ate too little or too much)
3. 4 patients had reversible digestive problems such as diarrhea where no pathogen could be found.
4. 10 patients experienced increased restlessness with affective instability and increased motor activity at the beginning of the TNI supplementation (3 of these patients experienced this for more than 3 months).

All observed side effects during the TNI supplementation eventually subsided and were not considered dangerous. TNI supplementation did not have to be stopped for any patient.

Table 4.
Results of 321 questionnaires of 38 long-term TNI supplemented children

Parameter/Score	-5	-4	-3	-2	-1	0	1	2	3	4	5
Falling asleep						165	32	4	72	38	10
Sleeping through night			2	1		98	64	42	52	34	28
Appetite		1		6	5	62	65	76	4	54	9
Digestion			10	14		57	11	65	45	76	43
Frequency of illness						39		43	58	76	105
Length of illness						78	43	78	72	15	35
Seriousness of illness						22	65	23	89	54	68
Coordination						48	43	101	65	21	43
Cooperation					2	55	28	87	96	43	10
Emotional stability				5	10	145	98	45	22		1
Activity		2		10		73	21	108	76	32	11
Restlessness			11	5	2	89	28	57	89	32	8
Motor skills						46	67	72	65	50	21
Language						52	65	76	87	39	2

Contraindications, Renunciation and Stopping

Possible contraindications for TNI and reasons for renunciation of TNI are:

1. Cost of the treatment. It is not covered by the state health insurance plan and only a few private health insurances cover it. – of concern to parents
2. Not enough data, because there are no comprehensive studies. – of concern to parents
3. Excessive time and effort needed for blood tests, recording results and assessing the health of the child – of concern to parents
4. “No free skating without the compulsory program” that is, TNI is just another part in the optimization of the management of Down syndrome. TNI does not replace other therapies (for example medical gymnastics, speech, occupational therapy, etc). – of concern to physicians
5. “Wrong” expectations of the parents about possible effects. – of concern to physicians
6. Lack of cooperation of the parents. – of concern to physicians

Table 5.
TNI consultation, test substitution from January to November 2000

TNI consultation	97
TNI experiment considered	31
TNI experiment	45
No TNI experiment (parents)	12
No TNI experiment (physician)	9
Termination of experiment during the test phase	2
Termination of the experiment during long term supplementation	3
Resumption of long term supplementation	2

Discussion and Outlook

Targeted nutritional intervention, it seems to me, is an interesting way to improve the health and the development of children with Down syndrome. Under the conditions described, that is, close cooperation with parents and the treating physicians as well as the availability of a control population, this supplementation appears safe and does not constitute an endangerment to the children. A sizeable number of parents use TNI as a supplement to their children's diet without the consultation of the treating physician and this number is increasing.

Since I was able to reduce the number of cases of infection dramatically and the growth of some of the children increased (even though their final height remains unknown), I find this treatment justified. It is still an open question if the observed developmental and neurological improvements were caused by TNI, as speculated by Leichtman (1997), or if the general health of the children was improved and they responded in a more favorable manner to conventional therapies. It is time for medical schools to study TNI and develop research programs to answer these questions. Our results, even though they are not statistically conclusive, should serve to stimulate studies that verify the correctness of our observations.

Summary

The metabolism of persons with Down syndrome differs, sometimes considerably, from persons with a normal complement of chromosomes. This difference can cause immunological dysfunction, retardation of growth and disorders in lipid metabolism. TNI (Targeted Nutritional Intervention) is designed to correct these problems. I have been supplementing the diets of Down syndrome patients with TNI since 1996 and I am currently treating approximately 100 children.

In the current study, I report on the effects of TNI supplementation for more than 12 months (average = 21 months; range 12-48 months). I observed a reduction of infections, increases in percentile ranking of growth and improvement and normalization of various laboratory parameters. Parents and therapists have reported considerable improvements in the behavior, cooperation and development of children administered TNI supplementation. Since my observations have not been statistically analyzed and are not organized as a double blind study, my results have to be critically assessed, especially the subjective evaluations of parents and therapists. More extensive, controlled studies need to be conducted since my survey indicates 15% of Down syndrome children are being supplemented by their parents without the supervision or approval of their attending physician.

Literature available from the author:

Dr. M. J. Gelb
Anne-Frank-Str.27
75015 Bretten, Germany
Email: Gelb@kinderarzt-bretten.de

Translated by:

Dr. Lutz Kube, Visiting Lecturer in Germanic Studies, North Carolina State University

Translation edited by:

James Croom, Ph.D., FACN, Professor of Nutrition and Physiology, North Carolina State University