

Metabolic and Anthropometric Effects of NADH RAPID ENERGY® in Diabetic Type 2

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Abstract: Twenty patients with diabetes type-2, aged between 38 and 61 years, with at least one cardiovascular risk factor were divided in two groups (Group-1 included newly diagnosed type 2 diabetic patients without treatment with oral antidiabetic OAD, Group-2: patients with diabetes type 2 under OAD +/- insulin (N = 11)). Patients from both groups were taking Nicotinamide Adenine Dinucleotide (NADH) Rapid Energy® 80 mg/day in two takes for a period of 56 days. A greater reduction in average fasting glucose and HbA1c after 56 days was observed in the patients of group 1 not taking metformin compared to patients of group-2 which were taking metformin. Why metformin reduces the anti-diabetic effect of NADH will be discussed.

Key words: NADH, Coenzyme-1, diabetes, type 2, metabolic profile, anthropometry, mitochondrial diseases.

1. Introduction

Diabetes mellitus is a major public health issue. Its prevalence has increased exponentially over the last 20 years, 90% of which are Diabetes Type-2. The causes for this dangerous development are multiples from unhealthy diet (too many carbohydrates) to lack of physical activity. These reasons result in a pathophysiological process, the first step of which is insulin resistance. Initially this phenomenon is offset by a compensatory hypersecretion of insulin leading to pancreatic exhaustion and finally in an insulinopenia [1].

For the time being the percentage of the costs for diabetes care amounts to 15% of the total budget for health care. Based on the dramatic increase in diabetics worldwide in the next 10 to 15 years the health care system not only in Western countries but also in the Middle and Far East will end up with a deficit of more than 300 billion US dollar which no country will be able to cover. Furthermore all the anti-diabetic drugs on the market do not cure diabetes

but only slow the progression from insulin independent (Type-2 diabetes) to insulin dependent Type-1 diabetes. Hence it may be worthwhile to look for alternative substances which may cure diabetes type-2 before type-1 diabetes develops.

NADH, the abbreviation of Nicotinamide Adenine Dinucleotide (reduced form of NAD), also known as reduced form of coenzyme-1 is present in every living cell as it is essential for energy production in every cell [2]. The highest levels of NADH in our body are found in the heart, the brain and the muscles, as these are the organs which need the most energy [3]. In studies with isolated heart cells incubated with NADH an increase in intracellular ATP was detected. In addition, the vitality and the life-span of these heart cells did increase significantly [4].

One of the co-author (JGB) succeeded in developing a stabilized form of NADH which is available as food supplement [5]. The beneficial effect of this NADH formulation for Alzheimer's [6] and Parkinson's disease [7] as well as for Chronic Fatigue Syndrome (CFS) [8] and depression [9] has been substantiated by controlled clinical studies. Based on these findings and the Adenosine Triphosphate (ATP)

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increasing effect of NADH we wanted to find out whether this coenzyme has an antidiabetic effect, can improve metabolic and anthropometric profiles of type 2 diabetes and simultaneously reduce the cardiovascular risk factors, evoked by too high blood sugar levels.

2. Material and Methods

The study included 20 diabetic patients aged between 38 and 61 years, with at least one cardiovascular risk factor: overweight or obesity (BMI 26-44), low HDL rate, high rate of LDLc, waist circumference > 100 cm for both sexes. The patients were divided in two groups (Group-1: newly diagnosed type 2 diabetic patients without any oral antidiabetic treatment OAD (metformin and other antidiabetic) (N = 09); Group-2: diabetes type 2 patients under OAD +/- insulin (N = 11). Patients from both groups received NADH Rapid Energy® 80 mg per day in two takes (2 Tablets of 20 mg after breakfast and 2 Tablets of 20 mg after lunch) for a period of 56 days. The effects of this sublingually absorbed NADH on anthropometric and metabolic profile were determined by different methods of

biological assays (glucose, HbA1c and lipid) were performed by routine methods. Anthropometric parameters (BMI, fat mass, lean mass, body water), were measured by bioelectrical impedance kind Bodystat® 1500 MDD [10]. The software Statistical Package of Social Sciences (SPSS 17.0) was used for statistical analysis of the results [11]; ANOVA test was used for analysis of the comparison of the groups.

3. Results and Discussion

As you can see from the blood readings of patient # 02 the glucose level decreased from 3.6 g/L to 1.55 g/L and the HbA1c from 12.06% to 8.9% after 56 days treatment with NADH.

In Table 2 the blood readings of patient # 04 show a drop in the glucose level from 4.10 g/L to 1.59 g/L and in the HbA1c from 13.3% to 9.6% after 80 mg NADH per day for 56 days.

Patients # 02 and # 04 have not been taking any metformin so far.

As you can see from the blood readings of patient # 07 the glucose level changed from 1.61 g/L to 1.28 g/L and the HbA1c from 7.9% to 7.7% after 56 days treatment with NADH.

Table 1 Blood readings of patient #02.

Blood readings	Day 1	Day 14	Day 28	Day 56
Fasting blood Glucose g/L	3.66	2.18	1.87	1.55
HbA1c %	12.6	/	/	8.9
Blood cell count:				
-White cells /L	5.9×10^3			4.6×10^3
-Red cells /L	4.2×10^6			4×10^6
-Hemoglobin g/dL	10.9			11.2
-Hematocrit %	34.3			36
-MCV fL	86			82
-MCHpg	31.8			30.4
-Platelets /L	238×10^3			277×10^3
-Neutrophil granulocytes /L	2.2×10^3	/	/	2×10^3
-Lymphocytes /L	3.5×10^3			2.2×10^3
-Monocytes /L	0.2×10^3			0.2×10^3
Cholesterol g/L	1.92	/	/	1.66 g/L
HDL g/L	0.55	/	/	0.50 g/L
LDL g/L	1.42	/	/	1.24 g/L
TG g/L	1.39	/	/	1.07 g/L
BUN g/L	0.19	/	/	0.32
Creatinine mg/L	8.3	/	/	10
GOT U/L	17	/	/	20
GPT U/L	23	/	/	26

Table 2 Blood readings of patient #04.

Blood readings	Day 1	Day 14	Day 28	Day 56
Fasting blood Glucose g/L	4.10	2.05	2.46	1.59
HbA1c %	13.3	/	/	9.6
Blood cell count:				
-White cells /L	6.6×10^3			4.2×10^3
-Red cells /L	3.8×10^6			4.5×10^6
-Hemoglobin g/dL	10.7			11
-Hematocrit %	33.8			39
-MCVfL	87.1			92
-MCHpg	31.3			32
-Platelets /L	254×10^3			277×10^3
-Neutrophil granulocytes /L	3.4×10^3	/	/	2.3×10^3
-Lymphocytes /L	2.5×10^3			1.5×10^3
-Monocytes /L	0.7×10^3			0.2×10^3
Cholesterol g/L	2.88	/	/	2.14 g/L
HDL g/L	0.35	/	/	0.42 g/L
LDL g/L	2.2	/	/	2 g/L
TG g/L	1.63	/	/	1.43 g/L
BUN g/L	0.32	/	/	0.24
Creatinine mg/L	11.1	/	/	10
GOT U/L	19	/	/	24
GPT U/L	26	/	/	36

Table 3 Blood readings of patient #07.

Blood readings	Day 1	Day 14	Day 28	Day 56
Fasting blood glucose g/L	1.61	1.44	1.50	1.28
HbA1c %	7.9	/	/	7.7
Blood cell count:				
-White cells /L	7.1×10^3			6.3×10^3
-Red cells /L	4.8×10^6			5.1×10^6
-Hemoglobin g/dL	15.1			14.6
-Hematocrit %	44.2			42.7
-MCVfL	85			90
-MCHpg	34.2			34
-Platelets /L	192×10^3			224×10^3
-Neutrophil granulocytes /L	3.6×10^3	/	/	2.6×10^3
-Lymphocytes /L	2.6×10^3			3.3×10^3
-Monocytes /L	0.5×10^3			0.3×10^3
Cholesterol g/L	2.55	/	/	2
HDL g/L	0.30	/	/	0.42
LDL g/L	1.52	/	/	1.29
TG g/L	3.5	/	/	1.95
BUN g/L	0.33	/	/	0.41
Creatinine mg/L	9.3	/	/	10.8
GOT U/L	26	/	/	21
GPT U/L	28	/	/	31

The blood readings of patient # 10 showed a change in glucose level from 1.92 g/L to 1.73 g/L and almost no change in the HbA1c concentration from 8.7 % to 8.8 %.

Patients # 07 and # 10 have been taking metformin before the start of the study but stopped it at the

beginning when all patients were taking NADH.

After statistical analysis of the values of all 20 patients an overall a greater reduction in average fasting glucose and HbA1c after 56 days in Group-1 (newly diagnosed diabetic subjects without metformin) compared to those of Group-2 taking metformin (glucose

Table 4 Blood readings of patient #10.

Blood readings	Day 1	Day 14	Day 28	Day 56
Fasting blood glucose g/L	1.92	1.79	2.06	1.73
HbA1c %	8.7	/	/	8.8
Blood cell count:				
-White cells /L	8.7×10^3			6.3×10^3
-Red cells /L	4.3×10^6			4.9×10^6
-Hemoglobin g/dL	11.9			12.4
-Hematocrit %	41.7			48
-MCVfL	92			94
-MCHpg	32.8			32.3
-Platelets /L	320×10^3			311×10^3
-Neutrophil granulocytes /L	4.2×10^3	/	/	3.2×10^3
-Lymphocytes /L	2.8×10^3			2.5×10^3
-Monocytes /L	0.6×10^3			0.4×10^3
Cholesterol g/L	2.9	/	/	2.2 g/L
HDL g/L	0.45	/	/	0.52 g/L
LDL g/L	1.75	/	/	1.42 g/L
TG g/L	1.45	/	/	1.10 g/L
BUN g/L	0.4	/	/	0.33
Creatinine mg/L	13	/	/	11.7
GOT U/L	22	/	/	32
GPT U/L	26	/	/	38

fasting = D0: 2.62 +/- 0.24 g/L, D56: 1.31 +/- 0.11 g/L versus D0: 1.90 +/- 0.19 g/L, D56: 1.56 +/- 0.13 g/L); (HbA1c = D0: 10.8 +/- 1.4%, D56: 7.8 +/- 0.8% versus D0: 8.4 +/- 0.5% D56: 7.9 +/- 0.3%). The difference is significant at $p < 0.001$.

Regarding the lipid profile, it was found an improvement in various parameters of lipid profile in all subjects who took the NADH RAPID ENERGY®, reducing their cardiovascular risk with a decrease in total cholesterol levels (D0: 2.12 +/- 0.6 g/L, day 56: 1.70 +/- 0.22 g/L) ($p < 0.002$) and LDLc (D0: 1.21 +/- 0.4 g/L, day 56: 1.01 +/- 0.22 g/L) ($p < 0.02$) and increased HDL (D0: 0.45 +/- 0.04 g/L, D56: 0.49 +/- 0.09 g/L) ($p < 0.02$).

Regarding the anthropometric data, it was observed a weight loss in different subjects either -3 kg after 2 months of taking NADH RAPID ENERGY® (D0: 88 +/- 16 Kg D56: 84.9 +/- 11 kg) ($p < 0.001$) and in parallel lower BMI (D0: 31.6 +/- 5.6 kg/m², day 56: 30.4 +/- 2.7 kg/m²) ($p < 0.001$); this weight loss has affected mainly the fat mass (D0: 31.4 +/- 7.2 kg, J56: 28.1 +/- 3.1 kg) ($p < 0.001$), with a stabilization of lean mass during the whole period. The body water

was only slightly increased after 3 months with an increase in its average of 1.8% (D0: 47.8%, D56: 49.5%) ($p < 0.02$).

The results of this study show NADH normalizes blood glucose and hemoglobin HbA1c values in newly diagnosed diabetes type-2 patients who have not taken metformin before. NADH is also improving their metabolic and anthropometric profile. In diabetic patients who have taken metformin for a longer period of time the effect of NADH was not as significant.

Metformin inhibits the uptake of glucose through the gut, reduces glucose production in the liver and lowers insulin resistance. The consequence of this effect of metformin is: Glucose cannot be used sufficiently for ATP energy production. Hence glucose is mainly fermented to lactate, which causes a lacticidose. Due to this phenomenon blood sugar rises again. The metabolic situation is not at all improved but worsens by metformin. This drug will never cure diabetes.

However, what is the reason for our observation that metformin inhibits the glucose lowering effect of NADH. For the time being we can only speculate about

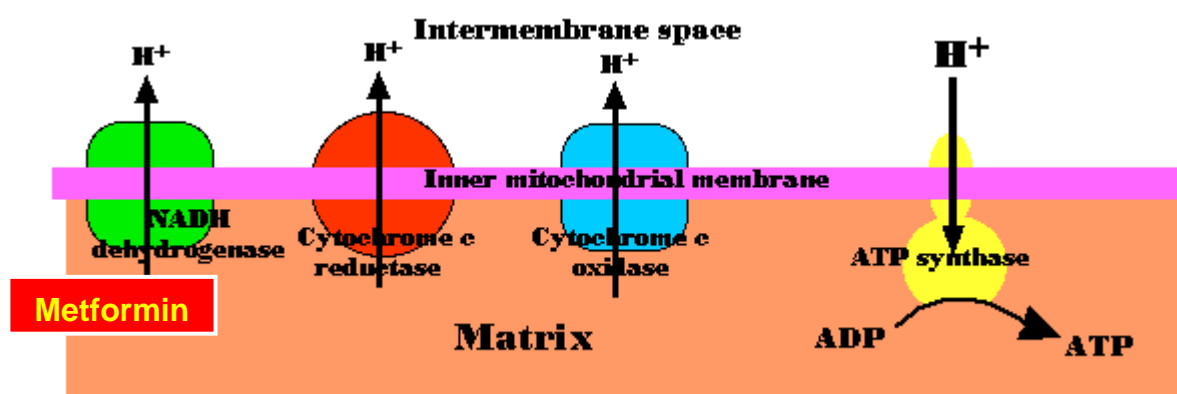


Fig. 1 Enzyme cascade of the respiratory chain essential for ATP production in the mitochondria.

the mechanism underlying this phenomenon. One possibility is the inhibitory effect of metformin on the NADH-dehydrogenase and cytochrome c reductase, the first and decisive enzyme in the ATP energy production via the mitochondrial respiratory chain [12] (Fig. 1).

The inhibition of NADH dehydrogenase by metformin leads to an energy deficiency in all cells of our body and of course also in the beta-cells of the pancreas. If the pancreas has not sufficient ATP available it cannot produce the amounts of insulin necessary for regulating blood sugar levels.

As shown on Fig. 1 NADH dehydrogenase is the first and most important enzyme in generating ATP via the oxidative phosphorylation. It has been demonstrated that NADH, supplied from outside the cell, increases the intracellular ATP level [4]. Cells fed with NADH produce more ATP. Hence they function better and live longer.

In further studies it should be investigated if NADH leads to a stimulation of insulin production in beta-cells of the pancreas. If this is actually the case, then NADH would be the ideal substance in healing diabetes type-2.

NADH may also have a preventive effect for diabetes. This could be found out by an epidemiological study with a population at a certain age in which the prevalence of diabetes is known. These people should be split into 2 groups, one taking NADH and the other group a placebo or nothing at all.

After a certain period of time the incidence of diabetes in both groups should be compared. If the incidence of diabetes in the group taking NADH is lower than in the placebo group this would be scientific proof for the preventive effect of NADH for diabetes.

For the time being NADH is available as a nutritional supplement which according to our findings may be a promising agent in fighting overweight and all the risk factors related to it such as cardiovascular and metabolic complications.

4. Conclusion

NADH normalizes blood glucose and hemoglobin HbA1c values in newly diagnosed diabetes patients and is improving their metabolic and anthropometric profile. In diabetic patients who have taken metformin for a longer period of time the effect of NADH was not significant. These findings indicate that metformin blocks the antidiabetic effect of NADH. Hence metformin is not a meaningful antidiabetic medication.

References

- [1] International Diabetes Federation. IDF Diabetes Atlas, 7th ed. Brussels, Belgium, International Diabetes Federation, 2015.
<http://www.diabetesatlas.org/resources/2015-atlas.html>.
- [2] Alberts, B., and Johnson, A., and Lewis, J. 2002. "Energy Conversion: Mitochondria and Chloroplasts." *Garland Science*.
- [3] Alberts, B., and Johnson, A. 1994. *Molecular Biology of the Cell*. 3rd ed. New York: Garland Publishing, 653-720.

- [4] George, D. B. 2009. *NADH—The Biological Hydrogen—The Secret of Our Life Energy*. Basic Health Publications, Inc.
- [5] Pelzmann, B., Hallström, S., Schaffer, P., Lang, P., Nadlinger, K., Birkmayer, G. D., Vrecko, C., Reibnegger, G., Koidl, B., and Pharm, B. J. 2003. "NADH Supplementation Decreases Pinacidil-primed I K ATP in Ventricular Cardiomyocytes by Increasing Intracellular ATP." *Br. J. Pharmacol.* 139 (4): 749-54.
- [6] Birkmayer, J. G. D. 1994. Stable, Ingestible and Absorbable NADH and NADPH Therapeutic Compositions, United States Patent, No. 5,332,727.
- [7] Demarin, V., Podobnik-Sarkanji, S., Storga-Tomic, D., and Kay, G. 2004. "Drugs Exptl. Treatment of Alzheimer's Disease with Stabilized Oral Nicotinamide Adenine Dinucleotide: A Randomized, Double-Blind Study." *Clin. Res.* 30: 327-37.
- [8] Birkmayer, J. G. D., Vrecko, C., Volc, D., and Birkmayer, W. 1993. "Nicotinamide Adenine Dinucleotide (NADH)—A New Therapeutic Approach to Parkinson's Disease: Comparison of Oral and Parenteral Application." *Acta Neurol Scand* 87: 32-5.
- [9] Forsyth, L., Preuss, H., Carneiro, M. L., Chiazze, R., Birkmayer, G. D., and Bellanti, J. 1999. "The Therapeutic Effect of NADH in Patients with Chronic Fatigue Syndrome." *Allergy Asthma and Immunol* 82: 185-91.
- [10] Birkmayer, J. G. D., and Birkmayer, W. 1999. "The Reduced Nicotinamide Adenine Dinucleotide (NADH) as Biological Antidepressive Agent. Experience with 205 Patients." *New Trends in Clinical Neuropharmacology* 5: 75-86.
- [11] Ross, B., Leger, L., and Boulier, A. 1990. "Comparison of Tetra- and Bipolar Impedance to Assess Body Composition." *Journal of Sports Sciences* 8: 159-94.
- [12] SPSS Ins. 2007. SPSS 17.0—Statistical Package for Social Sciences, Chicago, IL 60606-6412. Patent No. 7,023,453.
- [13] Bridges, H. R., Jones, A. J., Pollak, M. N., Hirst, J., and Biochem, J. 2014. "Effects of Metformin and Other Biguanides on Oxidative Phosphorylation in Mitochondria." *Biochem J.* 462 (3): 475-87.