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The effects of antioxidative treatment upon electrolyte and metabolic reactions of a chronically stressed group

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Key words
hypomagnesemia – Mg dynamics – hyperglycemia – mental agitation – prognosis – overcompensation

Abstract. The staff of a rehabilitation clinic was treated with an antioxidative nutraceutical during a demanding time of 8 weeks in a double blind, placebo controlled manner. Metabolic changes in metabolism and electrolyte state due to chronic workload, acute, standardized ergometry and, eventually to antioxidant treatment were recorded by capillary blood determination of pH, pCO_2, BE, blood glucose, lactate, K, Ca, Mg by Clinical Stress Assessment software. It turned out that those parameters changed significantly after 8 weeks of increased workload and also after standard ergometry. However, the antioxidant treated group showed significantly less chronic signs of metabolic distress due to the demanding working situation as well as a significantly calmer reaction to acute ergometric load, concerning lactate, base excess and pCO_2 changes. Electrolyte changes figure prominently among the workload effects both in group averages and in treatment dependent correlations with metabolic data. Mg changes are particularly sensible to a rise in metabolic dynamics, and therefore Mg is liable to be substituted to grant undisturbed energy turnover in a difficult situation.

Introduction

The staff of a rehabilitation clinic which successfully applies i.a. antioxidative substances to their stressed clientel, decided to try the same treatment on themselves during a demanding time of 8 weeks. The outcome of the placebo controlled, double blind investigation has been checked by Clinical Stress Assessment determinations (CSA, see material and methods), as it is done routinely with the patients to objectify the therapeutic success. We chose this kind of verification, as in a former paper [1] we could show, that the oxidative state of a person correlates linearly with concentrations of electrolytes and metabolic markers like pCO_2, base excess, lactate and blood glucose.

Material and methods

A group of 34 probands has been treated with a nutraceutical containing elderberry extract, acerola extract, grapestone extract, tocopherols and carotene of the Biogena corporation, Vienna, Austria, during 8 weeks in a double blind, placebo controlled investigation.

As placebo we used methyl-cellulose. Before and after a standard ergometrical load of 80 watts during 8 minutes, 100 µl **(■■■ Autor: oder ml?)** of capillary blood was taken from all participants before and after the 8 weeks of verum or placebo. The following parameters were determined from the blood samples using a NOVA Biomedical CCX Analyzer and CSA (Clinical Stress Assessment) software of PLK, Judendorf-Strassengel, Austria [2, 3]: pH, pCO_2, BE, blood glucose, lactate, K, Ca, Mg.

The volunteers were properly informed about possible risks of the study according to the Helsinki Charter [4].

Results

Average changes in pH, pCO_2, BE, ionized Ca, ionized Mg, ionized K, lactate, blood glucose and Ca/Mg quotient

All tables show the mean, its standard deviation and the standard error of means:

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Table 1. Placebo averages before workload before treatment.

	pH	pCO_2	BE	Ca	Mg	K	Lactate	BS	Ca/Mg
Mean	7.438	34.507	–0.673	1.077	0.487	4.419	1.787	111.800	2.220
SD	0.024	2.314	1.146	0.052	0.036	0.499	0.568	21.821	0.133
SEM	0.006	0.597	0.296	0.013	0.009	0.129	0.147	5.634	0.034

Table 2. Placebo averages after workload before treatmen.

	pH	pCO_2	BE	Ca	Mg	K	Lactate	BS	Ca/Mg
Mean	7.432	33.627	–1.440	1.086	0.490	4.737	3.653	94.133	2.220
SD	0.031	3.428	2.391	0.057	0.030	0.472	1.580	13.005	0.118
SEM	0.008	0.885	0.617	0.015	0.008	0.122	0.408	3.358	0.031
			$p < 0.05$				$p < 0.01$	$p < 0.05$	

Table 3. Placebo averages before workload after treatment.

	pH	pCO_2	BE	Ca	Mg	K	Lactate	BS	Ca/Mg
Mean	7.447	31.887	–2.093	1.077	0.524	4.557	1.500	103.200	2.058
SD	0.024	2.298	1.779	0.059	0.032	0.414	0.704	12.985	0.072
SEM	0.006	0.593	0.459	0.015	0.008	0.107	0.182	3.353	0.019

Table 4. Placebo averages after workload after treatment.

	pH	pCO_2	BE	Ca	Mg	K	Lactate	BS	Ca/Mg
Mean	7.435	30.667	–3.667	1.083	0.517	4.541	3.340	92.067	2.097
SD	0.031	2.743	2.377	0.044	0.028	0.318	1.645	8.328	0.115
SEM	0.008	0.708	0.614	0.011	0.007	0.082	0.425	2.150	0.030
			$p < 0.05$				$p < 0.01$	$p < 0.05$	

Table 5. Verum averages before workload before treatment.

	pH	pCO_2	BE	Ca	Mg	K	Lactate	BS	Ca/Mg
Mean	7.438	35.256	–0.506	1.077	0.497	4.476	2.439	113.556	2.168
SD	0.019	3.133	2.098	0.056	0.026	0.365	1.517	27.942	0.099
SEM	0.004	0.739	0.494	0.013	0.006	0.086	0.358	6.586	0.023

Table 6. Verum averages after workload before treatment.

	pH	pCO_2	BE	Ca	Mg	K	Lactate	BS	Ca/Mg
Mean	7.439	32.506	–2.072	1.086	0.492	4.806	4.417	99.333	2.211
SD	0.040	3.396	3.807	0.055	0.031	0.474	2.345	27.442	0.122
SEM	0.010	0.801	0.897	0.013	0.007	0.112	0.553	6.468	0.029
			$p < 0.05$				$p < 0.01$		

Table 7. Verum averages before workload after treatment.

	pH	pCO_2	BE	Ca	Mg	K	Lactate	BS	Ca/Mg
Mean	7.443	31.789	–2.378	1.056	0.526	4.310	1.478	110.222	2.015
SD	0.016	2.353	2.067	0.040	0.034	0.306	0.487	22.180	0.119
SEM	0.004	0.555	0.487	0.009	0.008	0.072	0.115	5.228	0.028

Table 8. Verum averages after workload after treatment.

	pH	pCO_2	BE	Ca	Mg	K	Lactate	BS	Ca/Mg
Mean	7.437	30.344	–3.739	1.064	0.521	4.635	4.106	95.056	2.047
SD	0.026	2.427	2.799	0.053	0.027	0.385	2.281	18.444	0.120
SEM	0.006	0.572	0.660	0.012	0.006	0.091	0.538	4.347	0.028
						$p < 0.05$	$p < 0.01$	$p < 0.05$	

Table 9. Placebo and verum effects before and after workload.

	pH	pCO_2	BE	Ca	Mg	K	lactate	glucose	Ca/Mg
Placebo before load			▼		▲				▼
Verum before load			▼		▲	▲	▼		▼
Placebo after load			▼		▲	▲			▼
Verum after load					▲				▼

No significant differences between placebos and verum, either without or with workload before treatment.

No significant differences between verum either without or with workload before treatment

Schematic differences of pH, pCO_2, BE, Ca, Mg, K, lactate, blood glucose and the Ca/Mg quotient in the placebo and the verum group before and after eight weeks of antioxidant treatment (Table 9)

Placebo

Differences in the basal values of the placebo group before and after 8 weeks were due to an increase in Mg and a decrease in BE and Ca/Mg. Differences in the workload values of the placebo group before and after 8 weeks were documented by a further increase in Mg and K and a decrease in BE and Ca/Mg respectively.

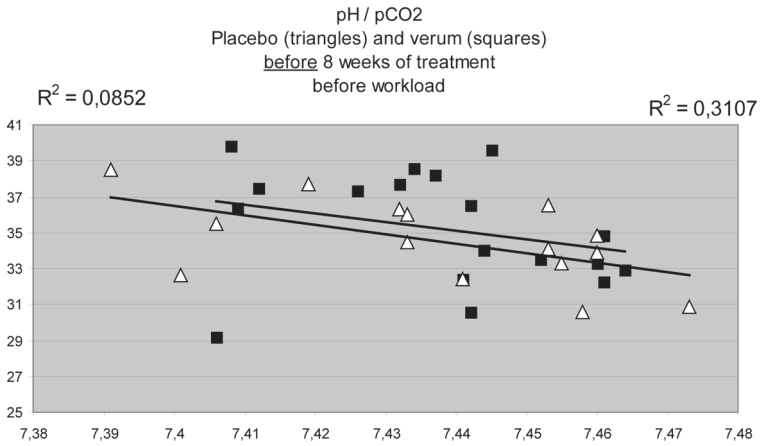

Figure 1. Abscissa: pH; Ordinate: pCO_2 in mmHg. Only the placebo group (triangles) showed a significant negative, linear correlation.

Verum

Similar to controls, the differences in the basal values of the verum group before and after 8 weeks of antioxidant treatment showed an increase in Mg, K and a decrease in BE and Ca/Mg a decrease in lactate. In contrast to placebos, differences in the workload values of the verum group before and after 8 weeks were solely marked by an increase in Mg and a related decrease in Ca/Mg.

Correlations

See Figures 1 – 6.

Discussion

A considerable part of the patients of a rehabilitation clinic in Maria Wörth/Wörthersee in Austria seeks recreation there after a demanding time in their life. A fully occupied house in the first half of the year provides an equally demanding time to the personnel of the clinic. Therefore it has been proposed by personnel and management, that physicians, technicians and nursing staff should be treated with the same antioxidative nutraceutic that empirically seemed to speed up recreation in their patients.

The theoretical basis was a paper of ours [1] where we could show, that the oxidative state of patients correlates linearly and significantly with stress markers like H-ions, buffer bases or electrolyte changes. By applying that correlative evaluation mode to people under antioxidant treatment, it could perhaps reveal some cause-effect relationship in those otherwise strictly statistically interpretable graphs.

Thus the clinic staff has been provided with the nutraceutic described in “materials and methods” during a challenging working

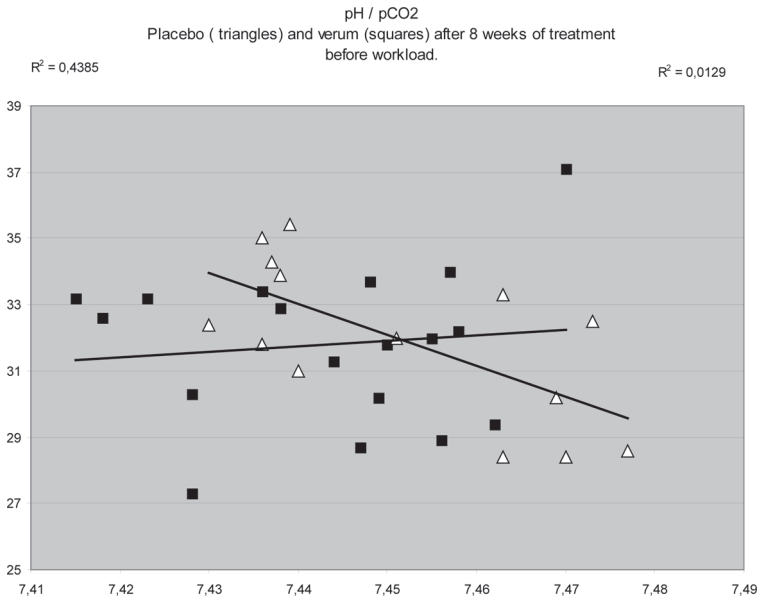

Figure 2. Abscissa: pH; Ordinate: pCO_2 in mmHg. Placebos (triangles) show a significant negative linear correlation with pH before workload. The more CO_2 has been exhaled, the higher the pH. There is no such correlation to be found in the verum group.

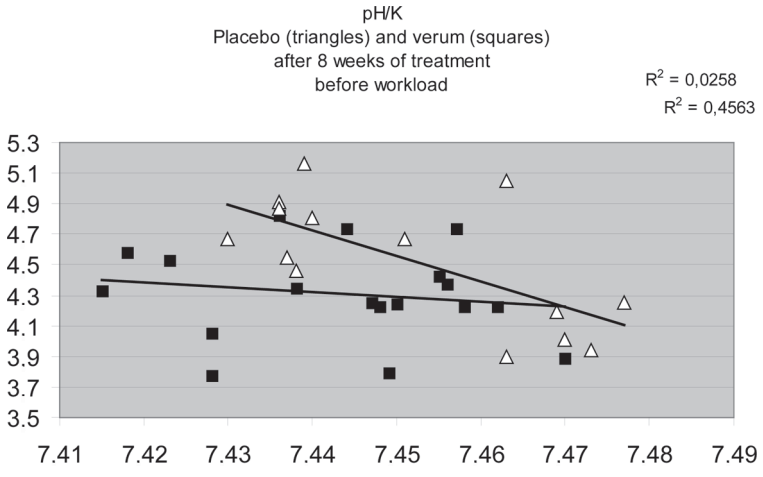

Figure 3. Abscissa: pH; Ordinate: ion K in mM/l. Those probands of the placebo group (triangles) with the lowest pH show the highest K concentrations. No such reaction could be found in the verum group.

period of 8 weeks. Capillary blood samples of about 100 µl **(■■■ Autor: oder ml?)** were collected before and after a short standardized ergometric workload, both before and after the treatment period. This was done to be able to get an idea not only about basal values of the determined parameters, but also about a possible influence of workload stress and treatment on the reserves of the participants.

The standardized workload mostly revealed the expected increase in lactate, a corresponding fall in base excess and blood glucose, likewise expected (Table 1 – 8).

But a significant change due to the general trying situation, common to both the placebo- and the verum group during the difficult 8-week period was already tangible in average basal values (Table 1 – 9). Mainly a decrease in base excess and increase in Mg, with a fall in the Ca/Mg quotient was common to placebos and the verum group and hence due to the temporary demanding working situation of the personnel [5, 6, 7]. But even in those basal values, the antioxidant treated group showed a significant peculiarity: in addition to the mentioned parameter changes, its members displayed an increase in ionized K and even diminishing lactate, the latter uncharacteristic for stressed people.

Such behavior could be the first hint towards a possible preference of a more protracted verum reaction to physical and mental load in contrast to the more acute stress reactions of the placebo group.

On top of the changes in basal values, the mentioned standard ergometry revealed another difference, already hinted in the group averages between verum and placebos due to treatment: While after exercise placebos show a further decrease in BE and the Ca/Mg quotient and an increase in Mg and K, the only reaction to workload in the antioxidant treated verum group is a further increase in Mg and a consequent diminishment of the Ca/Mg quotient. No acute workload induced changes e.g., in base excess or lactate were in evidence. We took that as a further indication of a "soothing" effect of antioxidative treatment on stress induced changes of electrolyte and metabolic parameters, with the notable exception of magnesium changes. We are quite aware that correlations between the oxidative state and stress parameters must not be interpreted as cause – effect relationships by the mere reason of their significance [1]. But our present experiments seem to invest such a deliberation with some credibility by unearthing additional facts:

Frequently we could demonstrate that behind the comparatively rough instrument of the calculation of mean values and their deviations a different dynamic of electrolyte/metabolic ratio can be hidden [6, 8, 9].

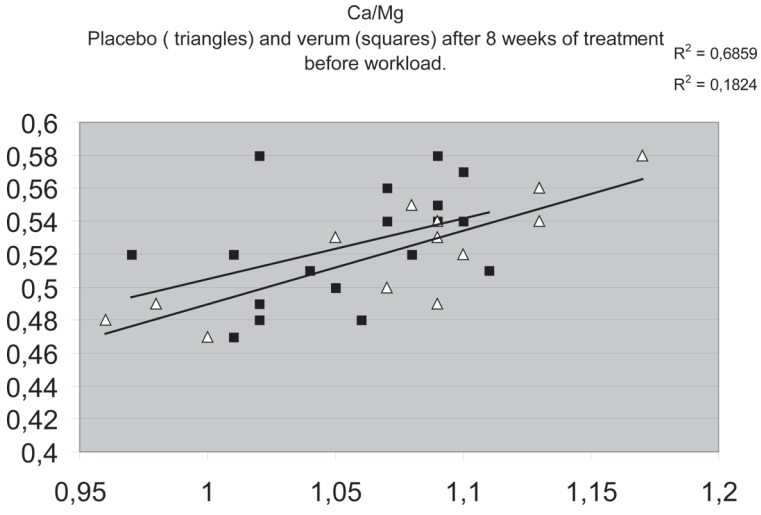

Figure 4. Abscissa: pH; Ordinate: ion K in mM/l. Only in the placebo group (triangles) a positive, significant correlation between ionized Ca and ionized Mg was visible.

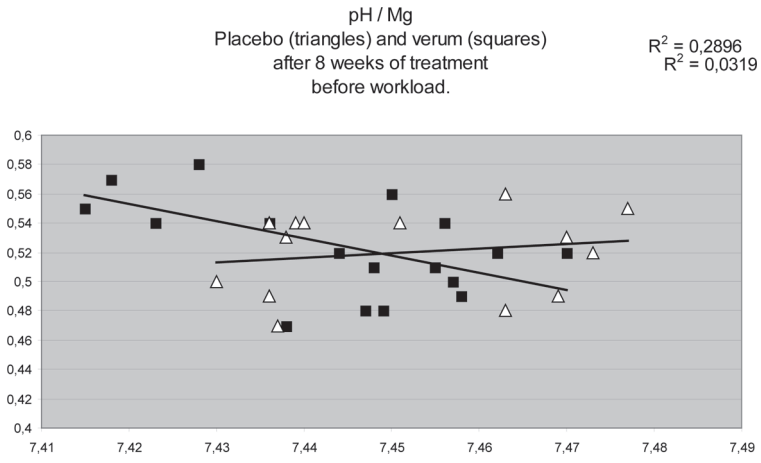

Figure 5. Abscissa: pH; Ordinate: ion K in mM/l. Higher Mg concentrations in the verum group (black rectangles) correlate with lower pH values linearly.

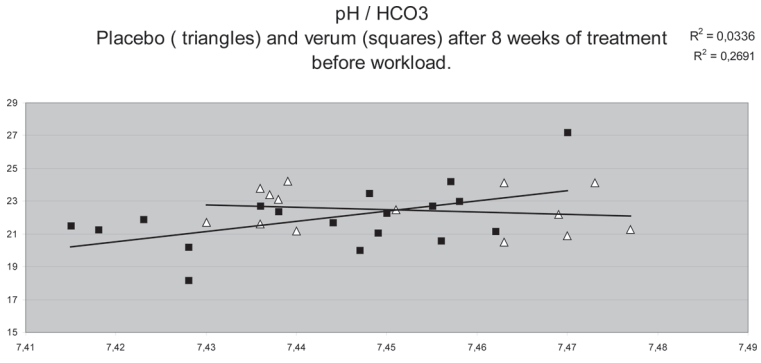

Figure 6. Abscissa: pH; Ordinate: HCO_3 in mM/l. The verum groups' pH values (black rectangles) in their turn do not correlate significantly with pCO_2 or lactate (not shown), but with HCO_3 changes.

Therefore we employed similar correlative tools for investigations about management of electrolyte- and metabolism as we have done to reveal oxidative state-metabolic interactions. This was mainly done to test our hypothesis about possible influences of antioxidants on stress markers after 8 weeks of treatment which may be hidden behind too equalizing average values.

First we observed a similar behaviour of the verum and placebo group (with the exception of an outlier) in their pH/pCO_2 management: The different sympatho-adrenal situations of the participants before ergometry already led to very similar correlations with slight overcompensation in both groups. The more CO_2 has been exhaled, the higher did pH values become.

But after 8 demanding weeks it needed 3 times as much CO_2 exhalation in the placebo group (curve slope 3 times steeper) to influence pH than before that period. In spite of this metabolic deterioration, the verum group does not show any pH/CO_2 interactions at all, the third suggestion for a possible damping of acute stress.

Exchange of H ions against K from tissue has been used as a sensible indicator of the sympatho-adrenal state already elsewhere [7, 8]. Indeed, placebos show increasingly high K concentrations in blood along with lower pH, while there is no such interaction in the verum group. Again, contrary to placebo, there is no hint for an acute compensatory reaction in the verum group.

Contrary to the findings with pH/K interrelationships, Mg values do correlate negatively with pH in the basal situation within the verum group, but not in placebos. In this context it is interesting that in the verum group pH does not correlate with pCO_2 as would be expected as reaction to workload, but linearly and significantly correlates with HCO_3. Though it is true, that metabolic compensation of a metabolic acidity should be met with suspicion, in our survey with healthy probands it seems to be rather the outcome of a calmer reaction to workload, probably brought about by a more efficient energy turnover as a result of successful radical – scavenging [10, 11, 12].

The livelier role of Mg in energy turnover of the verum group compared to Ca is reflected by both the increased average val-

ues and the inverse pH/Mg relation only in the verum group.

Since no differences between the groups could be found in pH/Ca relations, a certain exclusivity of Mg reaction in the verum group becomes apparent.

We conjecture, that the different reactions of Mg and K, both being cations, may derive from different dynamics. Low blood pH demands increased K output from tissue for H ion compensation, while increased ionized Mg without concomitant change in Ca points to pH induced dissociation out of the bound plasma fraction. This would explain Mg++ increases in the verum group in spite of calmer tissue reactions.

Conclusion

We think that there are good indications that antioxidative treatment in the described manner could counteract metabolic deterioration brought about by a demanding workload of some weeks. The role of electrolytes like K, Ca and Mg could be seen either from the viewpoint of sensible indicators of metabolic change or of eagerly required participants in a stress induced metabolic boost, whereby Mg is most involved. Its increase in times of most severe workload is an indication of loss, rather than that of a satisfactory situation.

Acknowledgment

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