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Hypoglycemic and antioxidant activities of sulphureous mineral water

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Abstract

Literature demonstrated the correlation between oxidative stress and pancreatic β cells damage in diabetics. A few reports provided evidence that in animals and humans in vivo, sulphureous mineral water may exert an antioxidant role. The aim of our research was to evaluate the effects of sulphureous SPA therapy on the glycaemic status and the oxidative stress conditions in patients with type 2 diabetes mellitus. The study has been performed on 35 diabetics under drug therapy, randomized in 2 groups: A, who continued drug therapy, and group B, who continued drug therapy in association with a drinking treatment with sulphureous mineral water from Termae of Telese SpA (Benevento-Italy) for 14 days. After 2 weeks of treatments described above were evaluated fasting blood glycaemia; plasma ROM (reactive oxygen metabolites) and BAP (plasma Biological Antioxidant Potential) levels (used d-ROMs test and BAP test - Diacron International srl - Grosseto - Italy). This investigation suggests that combining drug therapy with the drinking of sulphureous water SPA treatment may be useful in type 2 diabetes mellitus for the improvement redox state in the organism.

Key Words: drinking SPA therapy, BAP, glycaemia, type 2 diabetes mellitus, sulphureous mineral water, ROM

Introduction

In the last decades, the scientific community has focused its attention on the chronic endocrine disorder Diabetes Mellitus [1]. It has been calculated that in the whole world, 300 million people will be affected by this disease within 2025 [2], with a reduced life expectance of 30% [3].

The highest incidence (90%) of diabetes mellitus belongs to type 2 diabetes. This pathology is often asymptomatic; and thus, the disease has a late diagnosis, when complications have already developed. In fact, cells exposed to an hyperglycaemic environment for weeks are thought to maintain a metabolic memory of damages, and thus, to continue the production of free radicals, even though normal conditions have been restored [4].

Recent reports in the literature demonstrated that the superoxide hyper-production by the mitochondrial respiratory chain and the increase of reactive oxygen species (ROS) represent the main mechanisms underlying the metabolic pathways, responsible for vascular alteration and pancreatic β cells damage in diabetics [5-8].

Some antioxidant agents are thought to be able to abolish the cell metabolic memory of the hyperglycaemic damage.

These antioxidant agents reconstitute the chemical equilibrium in free radicals through the restitution of the missing electrons. They may act alone, or together, with a reciprocal protection, when oxidized.

According to their internal production or introduction from outside, antioxidant are distinguished in endogenous and exogenous.

Several enzymes and endogenous antioxidant systems synergistically reduce free radicals or oxidation catabolites in the cells. For this function, enzymes need the presence of minerals, such as zinc, cuprum, manganese, magnesium, selenium, iron, which act as cofactors. This category of antioxidants is represented by superoxide dismutase (SOD), which eliminates superoxide, catalase and glutathione peroxidase, which eliminate hydrogen peroxide (H_2O_2), the systems eliminating lipid peroxides (selenium-peroxidase) and the systems reducing iron reactivity [9].

Above a threshold, a supplementation of antioxidants is needed. These are called exogenous or non-enzymatic antioxidants and can be soluble in water, as like glutathione (the most abundant intracellular thiol, which changes disulfide bridges (S-S) of oxidized proteins in thiols (2S-H) and acts as substratum of glutathione-peroxidase and of glutathione S-transferase), Vitamin C, uric acid, albumin or soluble in lipids such as Vitamin E, ubiquinone and carotenoids.

Some, but not numerous reports in the literature provided evidence that in animals and humans in vivo sulphureous mineral water may exert an antioxidant role [10-12].

In the light of the abovementioned reports and hypotheses, we carried out the present clinical and experimental study, in order to evaluate the effects of a drinking treatment with sulphureous mineral water on the glycaemic status and the oxidative stress conditions in patients with type 2 diabetes mellitus.

Patients and Methods

Thirty-five subjects (74% men and 26% women) (Age range: 46-74 years; Mean +/- SE: 64+/-1.1 years) affected by type 2 diabetes mellitus under drug therapy participated in the study. Patients were informed of the purpose of the study and gave their informed consent.

After medical examination, subjects were randomly divided into 2 groups: group A (21 subjects with Body Mass Index (BMI) 27.9+/-1.0), who continued drug therapy and group B (14 subjects with BMI 27.5+/-1.0), who continued drug therapy in association with a drinking treatment with sulphureous mineral water for 14 days.

Drugs used in group A were sulfanilureas (9%), biguanides (17%), meglitinides (9%), insulin (6%),

association between sulfanilureas and biguanides (14%), association between biguanides and meglitinides (6%). Drugs used in group B were sulfanilureas (9%), biguanides (11%), meglitinides (11%), association between sulfanilureas and biguanides (8%).

Drinking treatment (375 ml/day for 14 days) was performed with sulphureous-bicarbonate-calcic-magnesian mineral water (sulfhydryl degree=12.6 mg/L; bicarbonate=1811mg/L; calcium=462mg/L; magnesium=78mg/mg/L; sulfate=36.5mg/L) of Telese Thermae SpA (Benevento - Italy).

Assays: After 2 weeks of drinking treatment, the following parameters were measured:

a) fasting blood glycaemia (mg/dL); capillary blood was taken and immediately tested with Glucocard G+meter.

b) oxidative stress indices:

1. d-ROMs test (Diacron International srl-Grosseto, Italy). These test evaluate plasma ROM (reactive oxygen metabolites) levels. Normal healthy subjects show ROM values in a range between 250 to 300 U.Carr. (1 U Carr. = 0.08mg of H_2O_2).

2. Plasma Biological Antioxidant Potential (BAP) was measured with the BAP-test (Diacron International srl-Grosseto, Italy). Normal healthy subjects show BAP values higher than 2200 micromol/L of vitamin C.

c) Untoward side effects. All treatments were well tolerated by all subjects.

Statistical analysis was performed with the Student's t-tests for unpaired data. Data are presented as mean +/-SE.

Results

Fasting blood glycaemia

The comparison of mean values ‘3f‘3fof fasting blood glycaemia levels in the two groups of diabetics studied showed a significant ($p<0.05$) reduction of blood glycaemia in group B (110mg/dL±9), who continued drug therapy in association with drinking sulphureous mineral water, versus group A (139mg/dL±10), who continued only drug therapy (Fig. 1).

Plasma ROM (reactive oxigen metabolites) levels and BAP (plasma Biological Antioxidant Potential)

Even in this case the association of the sulphureous drinking treatment with hypoglycaemic drugs (group B) induced a statistically significant ($p<0.05$) reduction of plasma [ROM] levels (group A: 331U.Carr.±11; group B: 297U.Carr.±11) (Fig.2) and a significant ($p<0.05$) increase of BAP (plasma Biological antioxidant potential) levels (group B: 1487 µmol/L±61; group A:944µmol/L±71) (Fig.3).

Discussion

A variety of studies in the literature underline the role of oxidative stress in the pathogenesis and maintenance of several diseases, such as diabetes mellitus [13-17].

In this latter pathology, the oxidative stress caused by the production of reactive oxygen species (ROS) and by the reduction of antioxidants, due to hyperglycaemia and insulin resistance has been thought to be responsible for the development and progression of diabetic complications.

Therefore, to counteract the complications of diabetes is equivalent to reduce oxidative stress, the key factor of diabetes and other pathologies [18-20].

This gives the opportunity to preserve the patient's quality of life.

In addition to motor rehabilitation, an important role can be played by the metabolic-nutritional rehabilitation which includes the use of antioxidants, molecules capable of neutralizing free radicals.

Antioxidants can inhibit or block the oxidative damage that depends on intermediate radical substances. Antioxidants can act alone or together with others.

Their action inhibits or blocks oxidation, by preventing the development of free radicals or by giving an electron to radicals or to reactive oxygen

species. This mechanism stabilizes radicals and makes them unable to produce damages.

Inside the cell, the first defence barrier is represented by antioxidants which inhibit or block free radicals. This category includes enzymes, such as superoxide dismutase (SOD), catalase and glutathione peroxidase. In addition, there are chain-breaking antioxidants, which are rapidly oxidized; they capture radicals present within the system and extending the chain. This class includes Vitamin E (or á-tocopherol), ubiquinone etc.

A few studies showed that sulphureous waters can be useful, because they may exert an antioxidant role [11,12].

For example, in retrospective studies [22,23], sulphureous mineral water has been reported to have antioxidant actions and a positive effects on the oxidative defence mechanism on both rabbits and rats.

Antioxidant activity of drinking sulfureous mineral water has been found in normal rats; in contrast, no effect was observed in normal rats submited to drinking tap water (control group) [10].

Sulphur is a non-metallic essential element, wide spread in the human body [24]. It is involved in the biosynthesis of important co-factors, and is present in a variety of fundamental molecules, proteins, enzymes, hormones, such as insulin, and antioxidant molecules, such as glutathione [25-27].

In the light of these studies, we carried out an experimental research in humans, with the purpose to evaluate the antioxidant actions of drinking SPA therapy with sulphureous mineral water in type 2 diabetics treated with hypoglycaemic drugs.

In agreement with previous reports in the literature [11,13], basal data showed an elevated free radicals production in diabetes mellitus; in fact, in all diabetic subjects, ROM levels were higher, whereas BAP levels were lower than normal values. Both these parameters indicated a condition of oxidative stress in our diabetics.

The association of the hypoglycaemic drug therapy for regulation of blood glucose levels along with the drinking treatment with sulphureous mineral water produced significantly lower plasma ROM concentrations in group B, in comparison with group A (treated with drug therapy alone). Furthermore, in group B we observed a significant increment of the plasmatic barrier defence against free radical attack, documented by the higher BAP levels after treatments in group B than in group A.

Simultaneously, a significant reduction of blood glycaemia was observed.

The antioxidant effect might be attributed to the chemical characteristic of the mineral water; in particular, to the presence of elements, such as magnesium, which are indispensable for the endogenous antioxidant enzymes activity [27-31].

Furthermore, the sulfureous water provides the body with one of the its main constituents, sulphur, which may contribute to reconstitute glutathione activity for neutralization of free radicals [22-24,27,32-35].

Conclusion

In conclusion, our results suggest that sulphureous mineral water drinking treatment together with hypoglycaemic drug therapy for regulation of blood glucose levels can improve the oxidative-reductive status of the body, and thus reduce risks of complication. In turn, these effects improve quality of life and wellness in type 2 diabetic patients.

Therefore, Drinking treatment with sulphureous-bicarbonate mineral water could be inserted as an adjunct to other therapeutic and nutritional therapies usually adopted in the treatment of Type 2 Diabetes Mellitus.

Conflict of Interests

The authors have no conflict of interests to declare.

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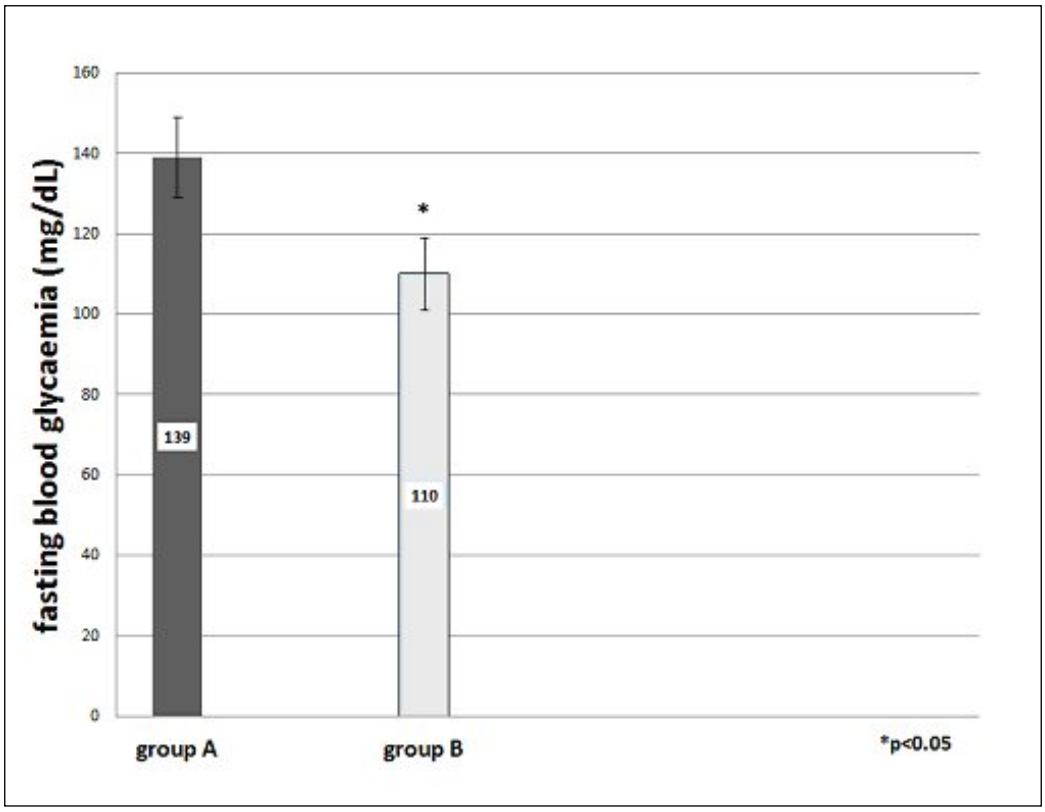

FIGURE 1: Comparison of mean values of fasting blood glycaemia (mg/dL±SE) in groups A and B of diabetic patients examined after 2 weeks of therapy.

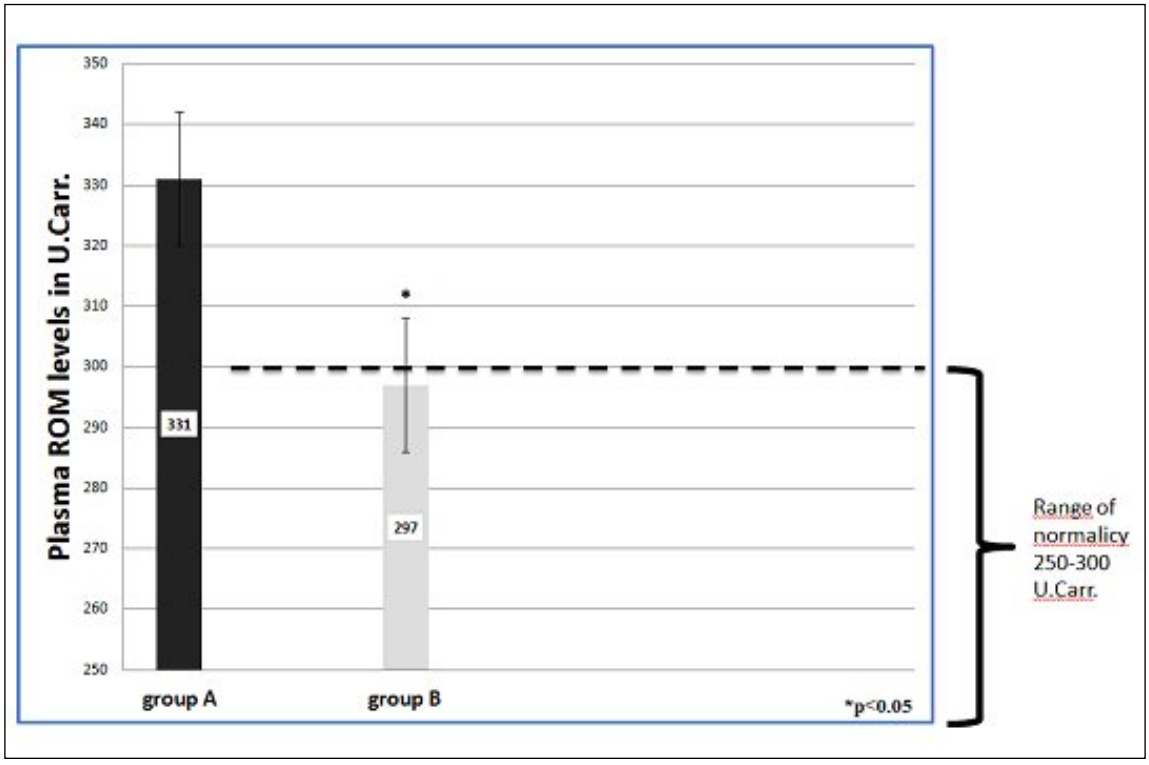

FIGURE 2: Comparison of mean values of plasma [ROM] levels (U.Carr.±SE) in groups A and B of diabetic patients examined after 2 weeks of therapy.

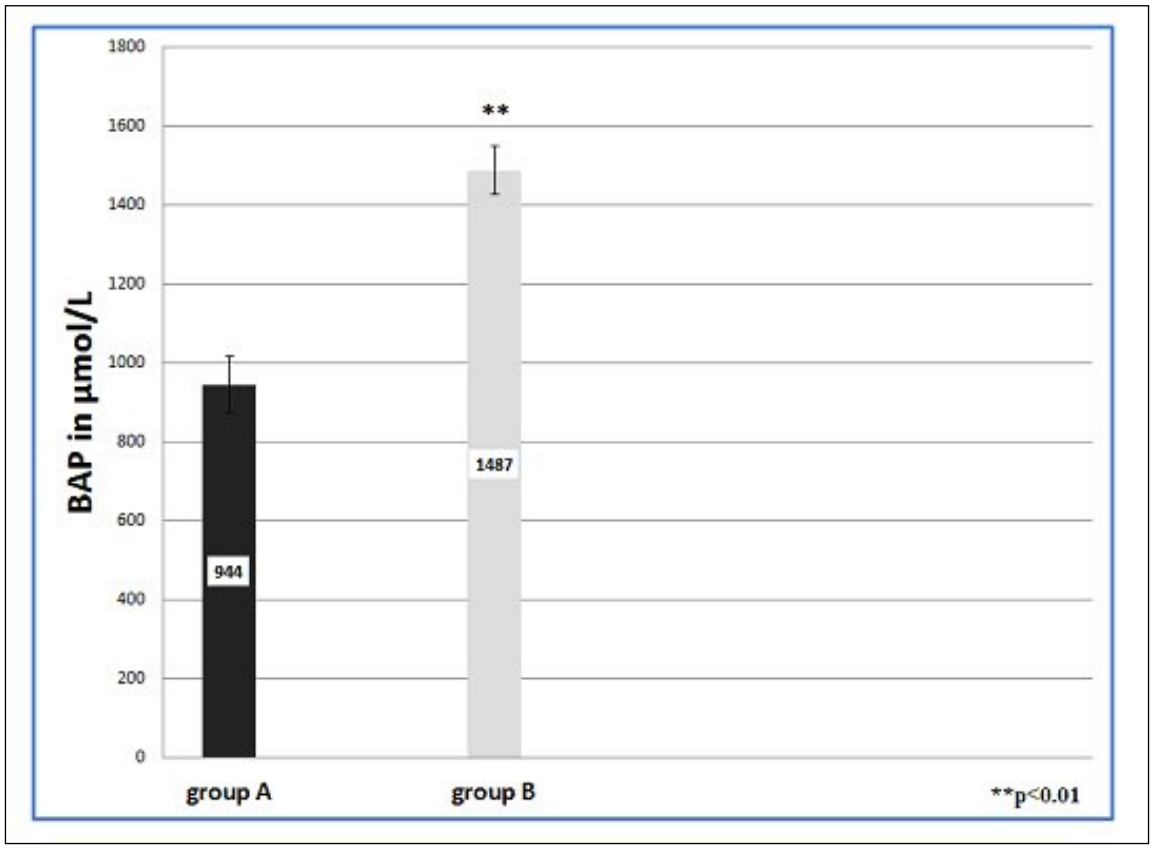

FIGURE 3: Comparison of mean values of BAP (µmol Vitamin C /L ±SE) in groups A and B of diabetic patients examined after 2 weeks of therapy.