EXPERIMENTAL TREATMENT INVOLVING APITHERAPY IN HEREDITARY HEMOLYTIC ANEMIA

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EXPERIMENTAL TREATMENT INVOLVING APITHERAPY IN HEREDITARY HEMOLYTIC ANEMIA (**Abstract**): Hemolytic anemia is a form of anemia in which red blood cells are destroyed and removed from the bloodstream before their usual lifespan is up. Anemia appears because the red blood cells are destroyed faster than the bone marrow can produce them. The etiology of premature erythrocyte destruction is diverse and can be due to conditions such as intrinsic membrane defects (hereditary spherocytosis, hereditary elliptocytosis), abnormal hemoglobins (sickle cell disease, thalassemia), erythrocyte enzymatic defects (G-6-PD deficiency, pyruvate kinase deficiency), immune destruction of erythrocytes, mechanical injury, and hypersplenism. Intrinsic hemolytic anemias are often inherited; these conditions produce red blood cells that do not live as long as normal red blood cells. Classical treatment of hereditary hemolytic anemia consists of corticosteroids, splenectomy, immunosuppressive drugs or plasmapheresis. The purpose of our study was to assess the effects of an experimental apitherapy treatment on a batch of mutant mice with hereditary hemolytic anemia.

Keywords: apitherapy, hereditary hemolytic anemia, honey, pollen

INTRODUCTION

Hemolytic anemia is a form of anemia in which red blood cells are destroyed and removed from the bloodstream before their usual lifespan is up. Anemia appears because the red blood cells are destroyed faster than the bone marrow can produce them. There are two types of hemolytic anemia: intrinsic - the destruction of the red blood cells due to a defect within the red blood cells themselves and extrinsic - red blood cells are produced healthy but are later destroyed by becoming trapped in the spleen, destroyed by infection, or destroyed from drugs that can affect red blood cells [1].

The etiology of premature erythrocyte destruction is diverse and can be due to conditions such as intrinsic membrane defects (hereditary spherocytosis, hereditary elliptocytosis), abnormal hemoglobins (sickle cell disease, thalassemia), erythrocyte enzymatic defects (G-6-PD deficiency, pyruvate kinase deficiency), immune destruction of erythrocytes, mechanical injury, and hypersplenism. Hemolysis is associated with a release of hemoglobin and lactic acid dehydrogenase (LDH). An increase in indirect bilirubin and urobilinogen is derived from released hemoglobin [2].

Some of the causes of extrinsic hemolytic anemia, also called autoimmune hemolytic anemia are: infections (hepatitis, cytomegalovirus (CMV), Epstein-Barr virus (EBV), typhoid fever, E. coli (escherichia coli), or streptococcus), medications (penicillin, antimalaria medications, sulfa medications, or acetaminophen), leukemia or lymphoma, autoimmune disorders (systemic lupus erythematous, rheumatoid arthritis, Wiskott-Aldrich syndrome, or ulcerative colitis), various tumors. Some types of extrinsic hemolytic anemia are temporary and resolve over several months. Other types can become chronic with periods of remissions

and recurrence. Intrinsic hemolytic anemias are often inherited, such as sickle cell anemia and thalassemia. These conditions produce red blood cells that do not live as long as normal red blood cells [3].

If symptoms are mild or if destruction of red blood cells seems to be slowing on its own, no treatment is needed. If red blood cell destruction is worsening, corticosteroids are usually the first choice for treatment. High doses are used at first, followed by a gradual tapering of the dose over many weeks or months. When there is no response to corticosteroids or when the corticosteroid causes intolerable side effects, splenectomy is often the next treatment. When destruction of red blood cells persists after removal of the spleen or when surgery cannot be performed, immunosuppressive drugs, such as cyclophosphamide or azathioprine, are used. Also, plasmapheresis is occasionally helpful when other treatments fail. When red blood cell destruction is severe, transfusions are sometimes needed, but they do not treat the cause of the anemia and provide only temporary relief [4].

Apitherapy is the use of products from the bee to promote health and healing. Also, standard type preparations have been developed and they are recognized as food supplements or medicines. The therapeutic effects of the bee products on anemia have been previously studied by Russian researchers in the ‘70s, with promising results [5]. Our study represents a bold experiment in which we tried to treat hereditary hemolytic anemia using an original apitherapic protocol.

Other conditions on which bee products have favorable effects are: chronic viral hepatitis (hepatitic virus B and C), even cirrhosis, female, male and couple sterility, autoimmune diseases, uterine fibromas and cists [6,7]. These results were attained in Apiregya Imunoastim private practice.

The main bee products used for apitherapy are honey, pollen, bee bread, apilarnil, royal jelly, propolis and beeswax.

Honey is a sweet, semi-fluid, viscous substance made from nectar/manna. It contains: sugars (sucrose, fructose, glucose, maltose etc.), minerals (Fe, Ca, Mg etc), organic acids (acetic, butyric, gluconic, citric, formic, lactic, maleic, malic, oxalic, pyroglutamic, succinic, glycolic, 2,3 phosphoglyceric, α ceto-glutaric, piruvic, tartric), vitamins (B1, B2, B3, B5, B6, B9, B12, C, provitamin A, D, E, K), pigments, aromatic substances, antibiotics (inhibine), antigerminative factors, enzymes (distase, invertase, sucrase, catalase, α and β amylase, peroxydase, superoxid dismutase, superoxid oxydoreductase, α and β glucosidase, tyrosinase), hormones, amino-acids (lysine, hystidine, treonine, arginine, valine, serine, methionine, glutamic acid, phenylalanine, tryptophane, prolyne, glycine, tyrosine, norleucine), fatty acids (palmitic, stearic, linoleic, oleic, lauric, miristoleic, linolenic).

Royal jelly is produced in the glands of worker bees and is a complex mixture of glandular secretion and honey with a 1:1.7 ratio. It is the most valuable substance known by biochemistry, pharmacology and medicine. Its chemical composition includes: proteins, glucides, gammaglobulin, gelatine, 10-hydroxi-2-decenoic acid with antitumoral properties, 9-hydroxidecenoic acid, formic, tartaric, citric, acetic, butyric acid, hydrosoluble and liposoluble vitamins and a vitaminic substance which prevents aging. Also, it contains all the minerals found in pollen and honey, enzymes, hormones, antibiotic, bactericide and antiviral substances. It has energizing effects, stimulates cellular regeneration, the enzyme system and hematopoiesis; it also has antioxidant, immunomodulating, hepatoprotector, remineralizing, antianemic, antileucemic and antitumoral properties.

Apilarnil is a triturate of drone larvae which includes the specific food content of the larvae cells (honey, bee bread, glandular secretions of the nurse bees). Apliarnil contains proteins (9-12%), glucides, lipids, hydrosoluble and liposoluble vitamins, minerals, enzymes, hormones, antiviral substances. It has antianemic, antileucemic, biostimulant, immunomodulating, energizing properties and stimulates cell regeneration [7].

Pollen is the male element of the flowers. It contains nourishing and biostimulating substances: enzymes, hormones, growth factors, reducer sugars (polein, fructose), non-reducer sugars, azotate compounds (xantine, hypoxantine, geranine, trimethylamine), lipids, organic acids (citric, tartaric, malic, malonic, succinic, acetic, fumaric, α ceto-glutamic), proteins, essential amino-acids, liposoluble vitamins (A, D, E, K), B vitamins complex, C vitamin, minerals (calcium iron, magnesium, zync), ribose, dezoxyribose, pectine, pigments (rutine, which increases the resistance of the capilaries), inositol, enzymes (amylase, invertase, protease, lipase, phosphatase, catalase, lactase). It stimulates cellular regeneration, hematopoiesis and capillary blood flow and has antioxidant, antianemic and antileucemic effects.

Bee bread has a therapeutic value ten times higher than pollen. It is an outstanding biostimulant [8].

Propolis is a resinous substance collected by the bees from plants and trees and is used to coat the inside of the beehive and the honeycomb cells with an antiseptic layer. It is a combination between plant and bee glandular secretions. It contains resins and balms, volatile oils, aliphatic acids, aliphatic acid sterols, vitamins, minerals, amino-acids, enzymes, flavonoids. It has antioxidant, phosphorilating, antitumoral, antileucemic, antianemic and immunostimulating properties [7,8].

MATERIAL AND METHOD

We conducted our study on a batch of 4 mutant mice with hereditary hemolytic anemia. Based on the physiopathologic mechanisms we developed an experimental therapeutic protocol based on bee products. All products used were provided by "Stupina" and are approved by the Institute of Bioresources of Bucharest.

According to the protocol, mutant mice were given the following apitherapics: "Vestala", "Centaurus I", „Centaurus II", pollen ("Polen – Prisaca") and honey – 10 g in three doses per day. Also the batch food included olive oil (approximately 5 ml per day, depending on the mice tolerance), vegetal extracts as powder (*Ribes Nigrum, Apium graveolens, Petroselinum crispum, Beta vulgaris, Armoracia rusticana*) or infusion *(Calendula officinalis, Lamium Album, Equisetum arvense/E. maxima, Basilici herba, Juglans regia folium, Serpylli herba, Rosa canina, Trigonella foenum graecum*). All alimentary products containing potassium were excluded from the mice diet; also, we opted for a low sodium diet.

RESULTS

Our experimental apitherapeutic protocol resulted in an increase of the survival period from 2 weeks (the mice were assumed to be in terminal phase) to 7 month for 50% of the batch (2 mice), to 10 month for 25% (1 mouse) and 11 month for the remaining 25% (a mouse).

DISCUSSION AND CONCLUSIONS

Because hereditary hemolytic anemias are due to some innate defects of one of the three main components of the red blood cells, including the enzyme equipment, we administered the "Polen – Prisaca" product for its tremendous enzyme variety and its content rich in essential amino-acids.

It is known that hereditary spherocytosis is due to a erythrocyte membrane protein defect which results in alteration of the surface/volume ratio. Given the fact that erythrocyte hemolysis is prevented by glucose addition, we administered to he study batch 10 g of honey in three portions daily. It is known that the circulating mature erythrocyte has a relatively simple intermediary metabolism due to its modest metabolic needs (approximately 10% of the glucose consumed by erytrocytes is metabolized by hexozomonophosphate shunt).

Also, in hereditary hemolytic anemia pathogeny is implicated a molecular anomaly which affects the cytoskeleton proteins, mainly those responsible for stabilizing of the lipid double layer. In order to compensate this defect we administered olive oil mixed in the daily diet, adjusting the dose according to the subject tolerance.

The efficiency of the "Stupina" apitherapeutic products was acknowledged by this study conducted in "Gr.T. Popa" University of Medicine and Pharmacy of Iasi biobase, within the Physiopathology Department.

The results obtained with the experimental model for hereditary hemolytic anemia, represented by the important increase of the survival of the mutant mice, suggests a potentially efficient therapeutic protocol for hereditary hemolytic anemia. This first success imposes the continuation of this study with the support of laboratory analyses specific for diagnosis of hemolytic anemia and treatment follow-up.

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