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The Effect of a Colostrum Extract of Proline Rich Polypeptides (PRP) on Immune Status in Guinea Pigs and its Implications on the Potential of PRP in Aging Humans

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Study funded by BioPharma Scientific, which developed, manufactures and distributes the green phytonutrient powdered drink mix used in this study.

Assessment of anti-allergic properties of Proline Rich Polypeptide Extract (PRP) on systemic anaphylaxis in guinea pigs

INTRODUCTION

Proline rich polypeptides are active immune modulating peptides from colostrum. Specifically, they are thought to help modulate Th1/Th2, favoring a "shift to the left", meaning they tend to up-regulate Th1 and down-regulate Th2. In order to test PRP's ability to down regulate Th2, a study was designed to measure PRPs effect the allergic reactions of guinea pigs sensitized to egg protein. Simultaneously, another group of sensitized guinea pigs were used to see the direct antihistamine effect on PRP, if any, upon their exposure to histamine.

MATERIAL AND METHODS

This study was conducted on both male and female guinea pigs. Egg white protein (ovalbumin, GIII Sigma) and histamine (histamine dihydrochloride, Sigma) were used as antigens. Ovalbumin and histamine were injected into animals by using compressor nebulizer (Pari).

P. Anderson Method (1980) of active sensibilisation of guinea pigs

Guinea pigs (250-300 g) were sensibilized by one time injection of 10 gm ovalbumin (OA) and 100 mg aluminum hydroxide (Al(OH)3) in 1ml total volume: 0.2 ml intramuscularly in thigh on two sides and 0.6ml intra-abdominally. Experiment began 5 weeks after sensibilisation, when IgE antibodies are formed in high enough quantities. Bronchial spasms in animals are developed after injection of permissive dose of antigen.

EXPERIMENTAL DESIGN

1. Measurements of bronchial spastic duration time after histamine introduction - internal control.
2. Measurements of bronchial spasm with exposure to ovalbumin.
3. Measurement of bronchial spasm after exposure to histamine (first group) and ovalbumin (second group) preceded 30 minutes by oral introduction of exposure to PRP by spray.

Histamine Model: induced bronchial spasm in guinea pigs via histamine.

0.2% histamine solution containing 0.9% of NaCl was inhaled by guinea pigs, which had been kept in special chamber, until the first signs of bronchial spastic reaction. Duration time of this reaction was measured. Development of bronchial spastic reaction is characterized by 2 phases: 1) acute phase – guinea pigs lie on their side, deep breath, frequency of breathing 10-15 per minute; 2) subacute phase – sitting position, increase of chest muscular activity, more frequent breathing 40-50 per minute. Introduction of PRP was done by spray 5 or 10 times into animal mouth-throat 30 minutes before histamine introduction.

Antigen Model: induced bronchial spasm mode in immunized guinea pigs via ovalbumin.

Experiment was conducted on guinea pigs actively sensibilized by ovalbumin in accordance with P. Anderson-method. Ovalbumin was used as inductor of bronchial spastic reaction. Animals were dived into two groups. Ovalbumin in dose of 2.5 g/kg was given to the animals of first group. Ovalbumin, dissolved in 1 ml of 0.9 % NaCl solution, was inhaled during 3 min with nebulizer followed by assessment of acute and sub-acute bronchial spasm. Animals in the second group received PRP 30 min prior to similar ovalbumin injection. PRP was delivered by the spray into mouth-throat in the amount of 10-12 sprays. Antiallergenic effect was evaluated on the basis of difference in extent of acute and sub-acute bronchial spasms between experimental and control groups.

EXPERIMENTAL RESULTS

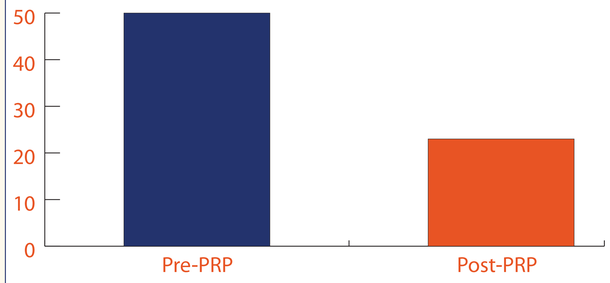
PRP in the dosages of 5 and 10 sprays didn't affect the development of bronchial spasms induced by histamine inhalation in guinea pigs. The several minutes of histamine induced acute and sub-acute phases of bronchial spastic reaction experienced by all the test subjects were practically the same in the control and experimental groups. There were no deaths in either group.

However, in the case of ovalbumin induced bronchial spasms the antiallergenic effect of PRP was significant. Delivery of a permissive dose of ovalbumin resulted in development of bronchial spastic reaction in 100% of animals (6 out of 6), 3 (50%) of whom died from suffocation. The duration of acute phase in the surviving animals (3) was 313 seconds in average; the sub-acute phase averaged 547 seconds. Introduction of PRP prior to ovalbumin inhalation resulted in death of 2 animals out 7 (28.6%).
(Table 1). In the surviving animals, development of acute bronchial spastic reaction on the permissive dose of antigen-ovalbumin was completely blocked by PRP. Sub-acute phase was experienced by only one survivor and that for only 16 seconds. (Table 2). Statistically significant difference was determined in accordance with Fisher criteria $p<0.05$.

CONCLUSIONS

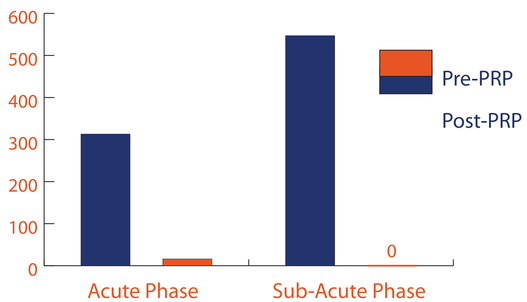
- PRP didn't affect the development of systemic anaphylaxis induced in sensibilized guinea pigs by exogenic histamine. Proline rich polypeptides do not appear to act as anti-histamines
- PRP has shown clear anti-allergic activity and inhibited the development of systemic anaphylaxis, induced in sensibilized guinea pigs by ovalbumin. These findings support their purported function of down-regulating Th2 mediated allergic cascades.

Death Rate in Sensitized Guinea Pigs from Allergy Induced "Asthmatic" Bronchial Spasm Pre PRP and Post PRP*



Death % Rate by Pre PRP and Post PRP
*Proline Rich Peptides

"Asthmatic" Allergic Reaction Duration Time in Surviving Guinea Pigs – Pre and Post PRP*, Acute and Sub-Acute Phases



Average Time in Seconds
*Proline Rich Peptides