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Effects of NO/cGMP inhibitors in a rat model of anaphylactic shock

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Introduction: Anaphylaxis has been defined as an acute syndrome, being the most severe clinical manifestation of allergic diseases. Many substances can mediate the anaphylactic shock. Among these substances, the histamine, the main secretory product of basophils and mast cells, induces nitric oxide (NO) release and the consequent cardiovascular manifestations observed in anaphylactic shock. The compound 48/80 (C48/80) can be used to induce anaphylactic shock since it promotes histamine release. **Objective:** To evaluate the effect of Nω-nitro-L-arginine methyl ester (L-NAME, a NO synthase inhibitor), methylene blue (MB, an unspecific guanylyl cyclase inhibitor) and/or terbutaline (Terb, a β2 adrenergic agonist) in C48/80-induced shock in rats. **Methods:** Animals were randomly assigned into twelve groups (n=6 in each group): Control, C48/80, L-NAME, MB, Terb, L-NAME+C48/80, C48/80+L-NAME, MB+C48/80, C48/80+MB, Terb+C48/80, C48/80+Terb and Terb+MB+C48/80. The animals were maintained in spontaneous ventilation and after complete anesthesia the femoral artery and vein were cannulated for mean blood pressure (MBP) measurement and drugs administration, respectively. The L-NAME (1mg/kg), MB (3mg/kg) and Terb (0.3mg/kg) were administered 5 minutes before or after the C48/80 (4.5mg/kg) administration. The MBP and the survival were analyzed over a period of 60 minutes. The MBP was analyzed every 10 minutes and the values in the results represent the final measurement that represent 60 minutes or less, depends of the survival. **Results:** Administration of C48/80 decreased the MBP (89±5 mmHg to 27±7 mmHg), led to cyanosis and killed 60% of the animals within 60 minutes. The use of MB and L-NAME prior to shock induction does not significantly prevented the MBP reduction (38±7 mmHg and 44±8 mmHg respectively), but increased the survival in approximately 50%. The administration of Terb before C48/80 administration partially inhibited the decrease in MBP (51±4 mmHg); this effect was not observed when Terb was associated with MB (36±7 mmHg), however in both groups (Terb+C48/80 and Terb+MB+C48/80) the survival was 100%. When L-NAME, MB and Terb were administered after shock induction, no improvements in MBP were observed (30±6 mmHg, 29±3 mmHg and 19±3 mmHg, respectively). Concerning the survival, the drug administration after C48/80 promoted an increase of the mortality (100%, 70% and 90% respectively). The administration of L-NAME, Terb and MB did not affect the MBP or survival. **Conclusion:** In this rat model of anaphylactic shock the blockade of NO/cGMP pathway with L-NAME or MB did not alter the decrease in MBP, but increased animals survival and Terb partially inhibited the decrease in MBP and prevented animals death when administered alone or associated with MB.

Keywords: anaphylaxis, compound 48/80, methylene blue, nitric oxide, histamine.

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