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Title: Experimental airways hyperreactivity and modulation of glutamatergic and nitrergic signalling

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Body: In the literature is very little information on possible interactions of glutamatergic and nitrergic system in the airways hyperreactivity. Therefore, we focused on the monitoring of possible relationship of excitatory neurotransmission involving NMDA receptors and inhibitory nitrergic system with nitric oxide (NO) in the conditions of the ovalbumin-induced airways hyperreactivity. We used the agonist of NMDA receptors monosodium glutamate (MSG), non-specific inhibitor of NO synthases (NOS) Nω-nitro-L-arginine metylester (L-NAME) and aminoguanidine (AG) as inducible NOS (iNOS) selective inhibitor. Agents were administered to guinea pigs orally for 14 days. Thereafter, was evaluated the airways responsiveness to histamine or acetylcholine in in vitro conditions. We studied as well the changes in the levels of exhaled NO (eNO). Both NOS inhibitors showed more expressive effect on the airway reactivity to histamine, less to acetylcholine. Tracheal smooth muscle responded more considerably in comparison with the smooth muscle of the lung tissue. Both NOS inhibitors increased tracheal smooth muscle reactivity to histamine. MSG administration decreased this increased response. Aminoguanidine showed the effect on the lung tissue smooth muscle as well and its reactivity decreased. Aminoguanidine showed on the whole more significant effect compared with L-NAME indicating a role of iNOS for these conditions. The activation of NMDA receptor with MSG increased eNO levels. The simultaneous administration of NOS inhibitors with MSG decreased the eNO level. The results refer to the possibility of interaction of glutamatergic and nitrergic neurotransmission in experimental airway hyperreactivity.