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EFFECT OF THYROXINE ON EXPERIMENTAL BRONCHOSPASM IN GUINEAPIGS

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Abstract: Effect of Thyroxine was studied in histamine induced bronchospasam in guineapigs. Chronic treatment with the drug significantly protected against experimental bronchospasm. Thyroxine also potentiated salbutamol evoked bronchodilation in this experimental model. Up-regulation of beta-2 adrenoceptors in bronchial smooth muscle may be the probable mechanism of action of thyroxine.

Key words: thyroxine salbutamol guineapig bronchospasm Beta-2 receptors.

INTRODUCTION

Tri-iodothyronine potentiates the chronotropic effect of norepinephrine in rat atria (1), but no such effect is reported on bronchial smooth muscle. Therefore, the present work is envisaged to study the acute and chronic effect of thyroxine on histamine induced bronchospasm and bronchodilator effect of salbutamol in guineapigs.

METHODS

The study was conducted in guineapigs of either sex weighing 300-400 g. Animals were kept on standard diet (Hindusthan Lever Ltd. India) and water *ad libitum*.

Animals were divided into four groups i.e. two control groups and two treated groups. Each group composed of six animals. One treatment group (T_1) received thyroxine (Eltroxin, Glaxo) in a daily dose of 90 µg/kg, P.O. (2) and the other treatment group (T_2) received the same dose of thyroxine and salbutamol 0.2 mg/kg, P.O. which was administered only on the day of experiment, 30 min before administration of histamine aerosol. One control group (C_1) received equivalent volume of normal saline and the other one (C_2) was administered salbutamol (0.2 mg/kg) in the same volume of water just 30 min before the administration of histamine aerosol.

Bronchospasm was induced by histamine aerosol (0.1 mg/ml) according to the method described by Turner (3). Bronchospasm was recognised by dilatation of nostrils, working up of alae nasi and fall of the animal on its side. The fall of the animal on its side was considered as the end point. Bronchospasm and the latent period for its onset was noted at day 0, 7, 14 and 21 in each group of animals. The animals that did not show sign of bronchospasm within 10 min were considered to be completely protected.

Statistical analysis of latent period and bonchospasm were done by unpaired 't' test and 'Chi square' test respectively.

RESULTS

Thyroxine failed to protect guineapigs against histamine induced bronchospasm on the first day of administration (Day '0'). The average latent period for bronchospasm was 2 min in

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TABLE I : Effect of thyroxine on histamine induced bronchospasm in guineapigs. (n=6 in each group).

	No. of animals producing bronchospasm within 10 min							
	Day - 0		*Day - 7*		*Day - 14*		*Day - 21*	
Group	*Broncho-spasm*	*Latent period in sec. (Mean±SE)*	*Broncho-spasm*	*Latent period in sec. (Mean±SE)*	*Broncho-spasm*	*Latent period in sec. (Mean±SE)*	*Broncho-spasm*	*Latent period in sec. (Mean±SE)*
C_1	6/6	110 ± 35	6/6	80 ± 30	6/6	84 ± 20	6/6	60 ± 24
T_1	6/6	130 ± 42	3/6	150 ± 37	1/6*	220	1/6*	240
C_2	6/6	220 ± 65	6/6	224 ± 61	6/6	106 ± 24	6/6	100 ± 35
T_2	6/6	240 ± 62	1/6*	274	0/6**	--	0/6**	--

*P < .01 and **P < .001 compared to control.

both the control (C_1) and the treatment group (T_1). Protection against bronchospasm was observed (though not statistically significant) when histamine aerosol was administered after 7 days of treatment with thyroxine. The degree of protection gradually increased and became statistically significant after 14 (P<.01) and 21 days (P<.01).

Salbutamol did not prevent bronchospasm but increased the latency by 2 min. Salbutamol when administered on day-7 (P<.01), 14 (P<.001) and 21 (P<.001) days of treatment with thyroxine (T_2) offered a significant degree of protection compared to group C_2. Though not statistically significant, a higher degree of protection was observed in Group T_2 when compared to Group T_1. In Gr. T_1 and T_2, the animals that did not prevent bronchospasm on day-7, day-14, and day-21, increased the latency by 2-4 min. The latent periods were widely variable with high standard deviations and their differences between the control and the treatment groups were never significant.

DISCUSSION

Only chronic treatment with thyroxine prevented histamine induced bronchospasm in guineapigs. Thyroxine also enhanced the protective action of salbutamol against experimental bronchospasm. The exact mechanism of bronchodilatation by thyroxine can not be ascertained from the present investigation. It is reported that the secretion rates of epinephrine and norephinephrine as well as their plasma concentrations are normal in thyrotoxicosis (4, 5). So, the protective effect of thyroxine may not be mediated through increased secretion of endogenous catecholamines. Chronic administration of thyroid hormone increased the number and not the affinity of beta-1 receptors (6, 7) in rat heart. Similarly up-regulation of beta-2 receptors in bronchial smooth muscle may be responsible for the bronchodilatation. Genesis of a new protein takes a latent period of several days (8), and that's why perhaps acute administration of thyroxine failed to provide protection in the experiment.

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