INTRODUCTION

Beta receptor blockers are one of the most effective drugs in treatment of cardiovascular as well as non-cardiovascular diseases. However controversies exist regarding the ability of these agents to induce bronchospasm in patients with COAD. Previous studies show that no β blocker is absolutely safe for asthmatic patients, but β1-selective blockers may have better respiratory tolerability though even they are not completely free of this adverse effect. Celiprolol is cardioselective β receptor antagonist with uniquely strong partial agonist activity at β2 receptors and can exert a direct vasodilating and bronchodilating effect. Recent studies have shown that vasodilation is due to its ability to cause release of nitric oxide from endothelial cells. However the ability of celiprolol to cause bronchodilation is still controversial since in some studies it worsened spirometric indices in patients with asthma. So the present study was aimed to determine the effect of celiprolol on histamine-induced contraction in isolated sensitized tracheal muscle of guinea pigs.

MATERIAL AND METHODS

The present study was conducted on the isolated tracheal smooth muscle of guinea pigs of Dunkin Hartley variety weighing 500–600 gm. Ethics Committee approval of the protocol was obtained. The animals were given tap water ad libitum and were fed with a standard diet. Guinea pigs were sensitised to ovalbumin so as to create animal model of asthma and divided randomly into two groups. Development of sensitivity was confirmed by demonstration of Schultz-Dale reaction. Krebs Henseleit solution was used as the nutrient solution the composition of which per 1,000 ml was: NaCl 118.2 mM, KCl 4.7 mM, MgSO4.7H2O 1.2 mM, CaCl2 2.5 mM, KH2PO4 1.3 mM, NaHCO3 25.0 mM, Dextrose 11.7 mM. The trachea was obtained from guinea pigs and preserved in Kreb’s solution. Rings, 2–3 mm wide were formed from it and cut into strips by a longitudinal cut on the ventral side opposite to the smooth muscle. The strip was then suspended in a tissue bath of 50 ml capacity, containing Kreb’s solution at 37 °C and was aerated with oxygen continuously. Its one end was attached to the oxygen tube while the other end was connected to an isometric force displacement transducer. The tissue was equilibrated for 45 minutes against an imposed tension of two grams. A tension of one gram was applied to the tracheal strip continuously throughout the experiments. The trachealis muscle activity was recorded through the transducer on a 4-channel oscillograph by adding different concentrations of histamine with an interval of ten minutes between each concentration. Six experiments were performed and the mean response for each concentration was worked out. A concentration response curve was obtained by plotting the percent contraction against the logarithm of concentrations. In the second group tracheal muscle strips were pre-treated with fixed dose of celiprolol, i.e., 10⁻⁴ M for 15 minutes. Same procedure was followed for different concentrations of histamine. The results have been expressed as Mean±SEM using Microsoft Excel. The differences between the observations were considered significant if the p-value was less than 0.05 by using Student’s t-test.

RESULTS

Mean±SEM values of the responses and the percent responses to different concentrations of histamine are shown in the tables. Percent response with 10⁻¹ M of histamine was taken as 100%.
The difference in mean values of responses between Group 1 and Group 2 were found significant (p<0.05). The mean percent deviations for each dose of histamine used in Group 1 and Group 2 were 35.48, 19.10, 13.92, 8.82, and 9.38% respectively.

**Table-1: Effect of histamine and celiprolol on ovalbumin sensitised isolated tracheal muscle of guinea pig (Group 1 & 2)**

<table>
<thead>
<tr>
<th>Histamine Concentration (M)</th>
<th>Group 1</th>
<th>Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Amplitude of Contraction (Mean±SEM)</td>
<td>Percent Response</td>
</tr>
<tr>
<td>10⁻⁴</td>
<td>12.50±1.76</td>
<td>15.63</td>
</tr>
<tr>
<td>10⁻³</td>
<td>33.16±1.57</td>
<td>41.46</td>
</tr>
<tr>
<td>10⁻²</td>
<td>52.66±1.60</td>
<td>65.83</td>
</tr>
<tr>
<td>10⁻¹</td>
<td>68.0±2.78</td>
<td>85</td>
</tr>
<tr>
<td>10⁰</td>
<td>80.0±2.56</td>
<td>100</td>
</tr>
</tbody>
</table>

The mechanism underlying the effect of celiprolol on tracheal smooth muscle is still unclear. It may involve its β₁ selectivity but studies on highly cardio-selective beta blocker, bisoprolol, indicate that this selectivity does not contribute to bronchodilation. Isolated tissue studies suggest that weak α₂ blocking effect may also contribute to this bronchodilation but this property is not significant at therapeutic doses. The partial agonist activity of celiprolol at β₂ receptors has also been implicated which seems plausible. Also according to recent studies modulation of nitric oxide by celiprolol may have some role in its property of bronchodilation.

**CONCLUSION**

Celiprolol decreased the tone of sensitised tracheal muscle. Thus it may be considered a potential option for asthma patients when beta blockers are considered to be essential treatment. However additional clinical studies are required to verify the pulmonary effects of celiprolol.

**REFERENCES**


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