obstructive hypertrophic cardiomyopathy and discrete subaortic stenosis, since this abnormality is seen commonly in both conditions. As pointed out by Dr. Claser, a recent article by Krajez et al describes a consistent difference in the timing of midystolic closure of the aortic valve: in each of 22 patients with obstructive hypertrophic cardiomyopathy, midystolic aortic closure occurred at least 0.07 sec after aortic valve opening (mean 0.14 sec ± 0.04 SD) and in each of nine patients with discrete subaortic stenosis midystolic aortic closure occurred no later than 0.06 sec after aortic valve opening (mean 0.05 sec ± 0.01). Each of the patients with discrete subaortic stenosis had severe subvalve gradients; no "mild cases" were described by these authors. If these data are confirmed by further experience, the timing of midystolic closure would appear to offer a useful means of discriminating between obstructive hypertrophic cardiomyopathy and discrete subaortic stenosis.

In the same article, Krajez et al point out that flouting of the aortic leaflets can be seen either in obstructive hypertrophic cardiomyopathy or in discrete subaortic stenosis, that this flouting can be seen both before and after operative treatment, and, indeed, that such flouting is occasionally seen in normal persons. Our experience has been similar. For this reason, we are reluctant to ascribe pathologic significance to flouting of the aortic leaflets.

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Ventilatory Effects of Metoprolol in Asthmatic Patients after Administration of Ordinary and Slow-Release Tablets

To the Editor:

In the treatment of essential hypertension with the selective β₁-receptor blocking agent metoprolol no difference in the reduction of blood pressure has been found between a single daily dosage schedule and a three times a day regimen of the same amount. During a single daily dose regimen, higher peak plasma levels of the drug are to be expected. One might wonder whether these higher plasma levels reduce the relative β₁-selectivity of metoprolol, which might increase the risk of pulmonary side effects.

Therefore, in ten patients with chronic obstructive lung disease we investigated the ventilatory effects of metoprolol using placebo and 200 mg metoprolol, after double-blind administration either as ordinary or as slow-release tablets; for administration of metoprolol in slow-release durules lowers considerably the peak plasma level in comparison with the ordinary tablets about two hours after ingestion of the drug. The study was performed on different days, separated by one or two days.

Vital capacity (VC), forced expiratory volume in one second (FEV₁) and expiratory peak flow rate (PFR) were measured before and two hours after ingestion of the tablets. Next, these measurements were repeated half an hour after the selective β₁-receptor stimulating agent terbutaline was given in a dose of 0.25 mg subcutaneously.

Blood samples for the determination of the plasma level of metoprolol, were taken two hours after ingestion of the drugs. All patients had discontinued bronchodilator treatment at least four days before the study.

The results are shown in the accompanying table. According to other studies in asthmatic patients, metoprolol induced a slight decrease in ventilatory function. The reduction seems to be more pronounced after administration of ordinary tablets. The plasma levels after ingestion of ordinary tablets were about twice as high as after ingestion of the durules. The ventilatory variables measured after stimulation with terbutaline during metoprolol medication were not statistically lower than the basic values before ingestion of the drug. Thus, the bronchoconstriction resulting from metoprolol can be reversed by terbutaline.

This study indicates that using a single daily dosage regimen in patients with chronic obstructive lung disease, slow-release metoprolol is preferred over ordinary tablets. As slow-release tablets avoid high peak plasma levels, the relative β₁-selectivity of metoprolol appears to be higher. When bronchospasm is present, metoprolol can be used in combination with a β₂-stimulating agent.

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REFERENCES


Table 1—Changes in VC, FEV₁ and PFR

<table>
<thead>
<tr>
<th></th>
<th>Placebo (p)</th>
<th>MOT (p)*</th>
<th>MSR (p)</th>
<th>Comparison between the periods</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>VC (L)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Δ 0±0.1 (NS**)</td>
<td>-0.3±0.1 (&lt;0.05)</td>
<td>0±0.1 (NS)</td>
<td>NS &lt;0.05</td>
</tr>
<tr>
<td></td>
<td>Δ FEF₅₁ (L)</td>
<td>+0.14±0.1 (NS)</td>
<td>-0.23±0.1 (&lt;0.05)</td>
<td>-0.16±0.1 (&lt;0.05)</td>
</tr>
<tr>
<td></td>
<td>Δ PFR (L/min)</td>
<td>+24±12 (NS)</td>
<td>-55±10 (&lt;0.01)</td>
<td>-12±8 (NS)</td>
</tr>
<tr>
<td></td>
<td>Plasma-level (nmol/L)</td>
<td>871±146</td>
<td>351±63</td>
<td>NS &lt;0.001</td>
</tr>
</tbody>
</table>

*MOT = Metoprolol ordinary tablets; MSR = Metoprolol slow release; **NS = P > 0.10

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