Long-term Continuous Infusion of Labetalol

To the Editor:

We read with interest the report by Gonzalez and Ram1 on the treatment of hypertensive urgencies and emergencies and the letter by Mitchell and Sirgo2 regarding recommended rates and cumulative doses of intravenous (IV) labetalol (Normodyne or Trandate). Most experience has focused on short-term intermittent or continuous IV infusion with adequate response attained below the 300-mg maximum cumulative dose.3,4

We report the usage of long-term continuous infusion of labetalol in controlling the hypertension of a 40-year-old, 80-kg black man, who was admitted to our medical intensive care unit after cardiac and respiratory arrest with hypoxic encephalopathy. His blood pressure of 320/156 mm Hg on admission was controlled initially with nitroprusside, 0.5 μg/kg/min, and then replaced after 36 hours with a continuous infusion of labetalol. A continuous infusion of labetalol was used for 5 days at a rate of 20 to 30 mg/h, with blood pressure controlled between 154/94 and 134/77 mm Hg. No adverse effects on heart rate or resolving acute renal failure were noted. The patient was transferred to a nursing ward on a regimen of 200 mg of oral labetalol every 6 h via nasogastic tube.

The patient required a daily dose of 450 to 720 mg of IV labetalol. While dosage guidelines suggest that some patients may require 1.2 to 2.4 g of oral labetalol daily, the same guidelines recommend stopping IV labetalol at the 300-mg cumulative dose.3 No controlled trials exist to guide the clinician in long-term continuous labetalol infusion; however, a recent case report summarizes experience to date and documents usage of 120 to 180 mg/h for 14 days in a trauma patient.5

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Use of Pleural Alkaline Phosphatase Content to Diagnose Tuberculous Effusions

To the Editor:

Pleural effusion may evolve from a variety of pleuropulmonary and systemic diseases.1,2 According to Light's criteria,1 pleural effusions may be classified as either transudates or exudates. An exudative effusion is one with a fluid-serum protein ratio >0.5; LDH ratio ≥0.6, and/or pleural LDH concentration ≥200 IU. It also has a higher cholesterol level (>60 mg/dl).3 Pulmonary tuberculosis (PTB) is the most common cause of exudative effusion and the most common cause of effusions in our country. On the other hand, transudative effusions are mostly due to congestive heart failure (CHF).

There have been attempts to differentiate tuberculous effusions
Table 1—Biochemistry of Pleural Effusion in Tuberculous and Congestive Heart Failure Effusions

<table>
<thead>
<tr>
<th></th>
<th>TB Effusion</th>
<th>CHF Effusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>SG</td>
<td>1.4</td>
<td>1.3*</td>
</tr>
<tr>
<td>Protein (g/dl)</td>
<td>4.9 ± 0.7</td>
<td>1.2 ± 0.6*</td>
</tr>
<tr>
<td>Cholesterol (mg/dl)</td>
<td>73.3 ± 19.6</td>
<td>15.0 ± 5.5†</td>
</tr>
<tr>
<td>LDH (IU)</td>
<td>367.7 ± 228.1</td>
<td>53.8 ± 25.4</td>
</tr>
<tr>
<td>Alkaline phosphatase (IU)</td>
<td>118.5 ± 45.7</td>
<td>45.9 ± 33.2*</td>
</tr>
</tbody>
</table>

Values are mean ± standard deviation.
*p<0.001. †p<0.005 for TB effusion compared with CHF effusion.

Nebulized Ipratropium in the Treatment of Acute Asthma

To the Editor:

Summers and Tarala recently reported a study comparing nebulized ipratropium and beta agonist therapy in acute asthma, and concluded that there was no advantage to be gained from combination treatment.1

However, the data show the opposite. This was not apparent in the initial analysis due to type II statistical error, but the results seem to be consistent with those of all other similar trials, as compared by meta-analysis.2

The immediate practical question that should be addressed by the study is: "Should this patient who has just arrived in the emergency room be treated with nebulized beta agonist or with beta agonist and ipratropium bromide together?" Thus, we should compare only groups A and C in the study by Summers and Tarala, lest the data be confounded by treatment crossover. We see that the beta agonist-only group experienced a mean percentage increase in peak flow rate of about 55 percent at 60 min, compared with about 64 percent after combination treatment. The difference was therefore 9 percent, within the 95 percent confidence interval (CI) we calculated from previous trials (mean difference, 12.5 percent; 95 percent CI, +1.2 percent to +23.9 percent). The difference in the study by Summers and Tarala rises to about 14 percent if patients receiving additional intravenous treatment are excluded. O’Driscoll et al have reported results of a similar trial, differing in that preservative-free ipratropium was used.3 There was a difference between mean percentage change in peak flow of 44 percent (95 percent CI, +8 percent to +84 percent) in favor of combination treatment.

Thus, five published, randomized trials have all produced very similar results indicating that combination treatment is better than beta agonist treatment alone in acute asthma. I am not aware of any unpublished trials with negative results that might affect this conclusion. The degree of homogeneity in the results of these five trials is remarkable, compared to the results of various trials in acute asthma which have addressed other aspects of management. The advantage gained from combination treatment does however seem to be modest, and is most apparent in the first hour or two of treatment: whether combination treatment is of benefit after the first four hours, or whether it affects mortality or the duration of hospital stay, has not been determined in these trials.

REFERENCES

4. Ward MJ. Clinical trials in acute severe asthma: are type II errors important? Thorax 1986; 41:824-29

To the Editor:

We thank Mr Higgins for his interesting comments. Although we do not dispute the general points raised regarding meta-analysis, we do not agree that a type II error is the only reason for failing to