

randomized sequences according to the latin-square method. One drug was directly followed by another, and there was not a planned-placebo or no-treatment interval between active drugs. Each patient received only one test sequence of each of the study drugs. The oral form of pentazocine was not available to us when our investigation was initiated; this was added to the study after the initial 27 patients (three latin square) had been entered.

Patients were instructed to take the planned single dose whenever definite pain was present but no more often than every six hours. The intervals between doses were therefore variable, depending on the requirement of the patient for analgesia, but none were shorter than six hours. There was a corresponding variability in the total period required for each patient study. With each dose, patients were asked to record the time of administration, the time when the onset of definite relief of pain was noted, and the time when pain returned; they were also asked to record the estimated maximum degree of pain relief on a percentage basis. Specific inquiry was made regarding the following side effects: stomach upset, nausea, vomiting, sleepiness, dizziness, impaired thinking and excitement. Patients were also asked to volunteer any additional side effects that they experienced. This information was recorded on a separate form for each drug dose.

It should be emphasized that these observations were recorded by the patient and not by medical observers. It should also be emphasized that this was a study only of single-dose administration and not of chronic administration.

RESULTS

To avoid any possible statistical distortion and to make full use of data, analgesic effects were evaluated by three methods of analysis.

The first method used the proportion of patients treated with each analgesic agent and placebo who claimed greater than 50 per cent relief of pain at any time during six hours after drug administration. This approach seemed to be the best in selection of patients who obtained a truly useful therapeutic effect. The results (Fig. 1) showed that 650 mg of aspirin quite clearly led the pack. Both aspirin and mefenamic acid showed a significant advantage over placebo. In addition, aspirin was significantly superior (p less than 0.05) to ethoheptazine, promazine, codeine and propoxyphene. None of the other drug differences were at statistically significant levels.

The second means of analysis (Table 1) employed the mean percentage of analgesia claimed by patients with each study drug and placebo. This method allows a relative crediting of all degrees of analgesic effect from very minor to complete relief of pain. Again, aspirin leads, but pentazocine, acetaminophen, phenacetin, mefenamic acid, and codeine all show a significant advantage over the placebo. Propoxyphene, ethoheptazine and promazine remain significantly inferior to aspirin.

The third method of analysis (Table 2), perhaps most important from a comparative standpoint, employed the relative ranking method of analgesic effect assigned by each patient to each of the test drugs—i.e., the drug to which an individual patient attributed the greatest percentage relief of pain was given the rank of one, and that with the lowest percentage a rank of 10. The figures recorded in Table 2 are the sums of ranks accorded to each drug by the 57 patients. Still, aspirin is the leader, showing a highly significant superiority over the placebo as well as over propoxyphene, ethoheptazine and promazine.