

Relief of Pain by Oral Medications

A Controlled Evaluation of Analgesic Combinations

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• A double-blind study of analgesic drug combinations was conducted, involving 100 patients with pain due to cancer. The combinations of 650 mg of aspirin plus either 65 mg of codeine, 9.76 mg of oxycodone, or 25 mg of pentazocine hydrochloride each produced significantly greater pain relief than aspirin alone. Side effects for a single dose of these effective combinations were essentially equal and clinically tolerable. The combinations of 650 mg of aspirin plus either 65 mg of caffeine, 32 mg of pentobarbital sodium, 25 mg of promazine hydrochloride, 75 mg of ethoheptazine citrate, or 100 mg of propoxyphene napsylate did not show significant advantage in analgesic effect over aspirin alone.

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BY FAR the most common pharmacologic challenge encountered by the physician today is relief of pain. The demand for oral analgesics dominates both the prescription and nonprescription drug markets. The 1973 *Physicians' Desk Reference* lists 113 different brand-name drugs promoted for pain relief by oral administration; to this list must be added perhaps an even larger number of nonpromoted, generic prescription drugs and heavily promoted over-the-counter preparations.

Although several analgesics and narcotics have been demonstrated to produce significant relief of pain when given alone, the modern trend among pharmaceutical industry, physician, and patient seems clearly to be in favor of analgesic combinations. Of oral analgesics listed in the *Physicians' Desk Reference*, 83% are combinations. The largest-selling prescription drug in this country, Darvon Compound-65, and the two largest-

selling brand name over-the-counter drugs, Anacin and Excedrin, are all combination analgesic drugs. Whether this great popularity of analgesic drug combinations is the result of true therapeutic superiority or superiority in promotional efforts becomes a difficult point to resolve on the basis of scientific evidence. Although the need for well-designed programs of clinical evaluation of analgesic drug combinations is great, investigators have seemed reluctant to enter this sensitive arena, and controlled trials of analgesic combinations have been recorded only infrequently in the literature.

In a previous double-blind evaluation of single analgesics,¹ we found aspirin at a dosage of 650 mg to be significantly superior to placebo and to be unexcelled in analgesic effect by any of the other single-entity medications we tested at manufacturers' recommended dosages.

Aspirin also has proved to have consistent analgesic activity in controlled studies conducted by numerous other investigators,² and 650 mg probably approximates the ideal dos-

age. The purpose of this study was to compare the analgesic effectiveness of 650 mg of aspirin used alone with the analgesic effectiveness of the same dose of aspirin in combination with other drugs of the type commonly incorporated into marketed analgesic combinations.

Materials and Methods

One hundred patients were chosen for study, each of whom had chronic or recurring pain problems resulting from unresectable cancer. All were ambulatory outpatients, and all could reliably tolerate oral medications. The patients did not have appreciable systemic symptoms related to their malignant disease, and they were not receiving any antitumor treatment (eg, chemotherapy or radiation therapy) that could confuse observation of analgesic side effects. The pain that the patients experienced was assumed to be related to intra-abdominal, retroperitoneal, pelvic, or osseous malignant tumors. The degree of pain was classified as mild or moderate. Patients were excluded from study if they gave a history of an allergic reaction to any of the studied drugs. Patients also were not accepted for study if they had previously been on a schedule of narcotic drugs that was judged capable of producing any degree of physiologic dependence. Particularly, patients were chosen who in our opinion were intelligent, dependable observers. They were informed they were participating in a randomized type of study. Patients were not allowed any other analgesics, narcotics, sedatives, stimulants, anti-

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