

## MYANESIN®: A STUDY IN POSTOPERATIVE PAIN RELIEF \* †

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PATIENTS subjected to spinal fusion operations appear to experience an uncomfortable early postoperative convalescence. Several factors could conceivably contribute to the unpleasant nature of this period. Among them are a constrained posture in a heavy plaster jacket, wound and bone pain, the psychological elements concerned with an anticipated prolonged period of hospitalization, and the pain of paraspinal muscle spasm. It is readily apparent that there is great difficulty in evaluating these factors quantitatively. It seemed possible, however, to gather reasonably precise information on the last of these elements, the role of muscle spasm in the total picture of postoperative distress. The limitations and difficulties of a study on postoperative pain have been demonstrated amply and were appreciated as a problem of magnitude in this study (1, 2, 3).

In considering methods of observation directed toward the evaluation of the role of muscle spasm in postoperative distress after spinal fusion operations, the reported ability of myanesin® to relax skeletal muscles was attractive as a first approach to the problem. It is of interest to summarize the behavior of this drug in order to establish a background for evaluation of the findings to be described.

As early as 1909 it was known that alpha esters of glycerol would cause muscular paralysis. Berger and Bradley in 1946 were the first to report on the pharmacological properties of myanesin (4). Mallinson described its clinical usage in anesthesia two years later (5). Myanesin is distributed widely in body tissues and fluids (6). This distribution is conditioned both by lipoid and water solubility. The brain and pancreas contain the highest concentration after equilibration of distribution. Its destruction is rapidly accomplished in the body probably by detoxification in the liver (7). In the dog from 0.1 to 2.0 per cent of administered dose is excreted as free myanesin: from 32 to 42 per cent as conjugated myanesin in twenty-four hours (8).

The exact mode of action of the drug is not settled completely. The site of action is believed to be the internuncial cell (9). Gammon and

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Churchill (10) believe that its action is differentially selective for the clusters of subcortical nuclei which make up the basal ganglia, thalamus and brain stem. Larger doses, it is believed, block the conducting mechanisms of the spinal cord (motor and sensory). Experiments on mice have demonstrated that myanesin will antagonize strychnine without any other effects (11). This seems to indicate that the drug decreases reflex hyperexcitability and prevents the passage of abnormal excitatory impulses through the spinal reflex arc. According to Magoun's studies, spasticity results from the hyperaction or unopposed facilitation of stretch reflexes (12). The absolute numbers of facilitory and inhibitory impulses reaching the anterior horn cells are more important in determining muscle tone than the ratio between them. Any drug which reduces the total number of facilitory impulses, even if it also diminishes the residue of inhibition, will relieve spasticity. Myanesin apparently establishes a new balance at a lower level of activity (9).

When myanesin is given to a conscious patient, muscular and emotional relaxation is produced without loss of consciousness. As dosage is increased, analgesia, ataxia, and light sleep progressing to complete paralysis are said to occur (10). Paralysis occurs first in the muscles of the posterior half of the body, then the peripheral and intercostal muscles followed by the cranial muscles and lastly the diaphragm (11).

The site of action of the sedative effect is obscure as this action outlasts the paralyzing effect. By inducing mental or emotional relaxation, myanesin may indirectly decrease the outflow from higher centers.

#### METHODS

Patients who were to have two or more spinal fusions were selected for study so that they could act as their own controls. Two grams of 1 per cent solution of myanesin in 0.9 per cent saline solution was administered as an intravenous drip during the course of operation which lasted from one to three hours. The "blind testing" method was used. The observers evaluating postoperative pain were not aware of the nature of the injected solution. Each patient received 0.9 per cent saline solution on another occasion for a similar but staged spinal fusion operation. No evaluation of psychological factors in the patient's complaints of pain was attempted. Complaints of pain were treated promptly by administration of 30 mg. of codeine parenterally. If relief was not obtained in thirty minutes, morphine or meperidine was injected. The only patients who were not considered suitable for the study were those who had kidney or myocardial damage. Of a total of 21 patients and 45 operations 17 had scoliosis and 4 had reoperations for pseudoarthrodiesis. The anesthetics in all cases were intravenous thiopental given fractionally and nitrous oxide-oxygen in concentrations of at least 25 per cent oxygen by a circle semiclosed technique with

the absorber in the circuit. The course of each patient was then followed for forty-eight hours to ascertain the amount of narcotics required. The need for narcotics was determined only by complaints of pain by the patients and was considered a useful guide to the presence of pain.

### DISCUSSION

No reasonable evidence is available concerning the duration of action of myanesin. It was thought, however, that any sedative, analgesia, or relaxant effect of myanesin if observed at all, should be obvious in a period of twenty-four hours. The patients were observed for an additional period of forty-eight hours to make sure that any delayed action would be noted. In a total of 21 patients, 14 demonstrated no appreciable difference in their postoperative narcotic requirements and 7 showed a moderate reduction in the requirement for narcotics (table 1) in the first twenty-four hours. There were instances in which narcotics were given for relief of pain from abdominal distress or dis-

TABLE I

		Dose in Mg. for 1-12 Hrs.	Dose in Mg. for 12-24 Hrs.	Dose in Mg. for 24-36 Hrs.	Dose in Mg. for 36-48 Hrs.
A. D.	Control Myanesin	M 24 My 24	M 36 M 24	M 36 M 24	M 24 M 12 C 30
J. N.	Control Myanesin	M 18 e	M 27 C 30	M 9 C 30	M 18 e
P. R.	Control Myanesin	M 36 M 27	M 27 M 36	M 18 M 18	M 27 M 36
R. S.	Control Myanesin	M 18 M 9 C 9	M 27 C 6	M 9 M 18	M 9 M 36
G. B.	Myanesin Control	D 200 D 200	D 200 D 200	D 200 D 300	D 200 D 200
M. Mu.	Control Myanesin	M 12 M 24	M 24 M 12	M 12 M 12	M 12 M 12
B. P.	Myanesin Control	M 8 C 30 M 24	M 16 M 16	M 16 M 16	M 16 C 30
C. V.	Myanesin Control	C 90 M 30	C 90 M 45	C 60 M 30	C 60 M 30
M. Y.	Myanesin Control	D 150 D 75 M 24	D 200 M 24	D 100 M 24	D 100 M 12
J. B.	Myanesin Control	D 200 D 200	D 400 D 400	D 200 D 200	D 300 D 200
E. B.	Control Myanesin	M 45 M 45	M 45 M 60	M 30 M 45	M 30 M 30

TABLE I—Continued

		Dose in Mg. for 1-12 Hrs.	Dose in Mg. for 12-24 Hrs.	Dose in Mg. for 24-36 Hrs.	Dose in Mg. for 36-48 Hrs.
G. Bl.	Myanesin Control Myanesin	M 9 M 27 D 100	M 18 M 18 D 50	M 9 M 18 D 50	M 9 M 9 D 50
I. G.	Myanesin Control	D 75 C 30 D 75 C 30	C 90 D 225	D 75 C 30 D 225	C 60 D 150
D. V.	Myanesin Control	D 50 M 15	D 50 M 18	D 25 M 9	Ø M 9
M. Mi.	Control Myanesin	D 75 D 250	D 225 D 300	D 75 D 200	D 150 D 400
J. No.	Control Myanesin	M 30 C 90	M 45 M 30 C 30	M 45 M 30	M 30 M 45
V. P.	Control Myanesin	D 150 C 60	D 100 D 100 C 30	D 50 D 50 C 30	D 150 D 150
S. B.	Control Myanesin	M 20 D 150	M 20 D 150	M 10 D 150	M 20 D 150
B. M.	Myanesin Control Myanesin	D 225 D 225 D 225	D 150 D 225 D 150	D 225 D 225 D 225	D 150 D 225 D 150
R. F.	Myanesin Control	Ø M 9 C 30	M 12 C 30 C 30	C 30 M 9	Ø Ø
M. D.	Myanesin Control Control	M 24 C 30 M 24 M 12	M 12 M 24 M 12	M 24 M 36 M 12 C 60	M 12 M 12 C 60 C 60

C = Codeine, M = Morphine, D = Demerol.

Dosage variation: Codeine = 30 mg.

Morphine = 6-15 mg.

Demerol = 25-100 mg.

comfort of the Risser jacket in both control and drug treated cases. In general, it is apparent that myanesin administered in the manner described is not an important adjuvant to postoperative analgesia and sedation in spine fusion operations. It is impossible to determine from these data whether the myanesin effect is dissipated quickly or muscle spasm is not a significant factor in postoperative pain after spinal fusion.

There were no serious complications during anesthesia. A few instances of respiratory depression, attributable to lowered tidal exchange and not intercostal paralysis, were noted. These were expeditiously corrected by assisted respirations and slowing of the myanesin drip. There have been reports of rapid intravenous administration causing decerebrate rigidity, and also cardiac arrest owing to depression of the SA node or a quinidine-like reaction causing pro-

longed refractory period of the cardiac cycle (13). None of these complications were noted.

In the immediate postoperative period, patients given myanesin frequently appeared to be more lethargic; they would react when stimulated but fall asleep again. The postoperative course revealed no unusual complications, no increased evidence of abdominal distention, urinary retention, nausea or vomiting and no indication of hemoglobinuria.

#### SUMMARY

A controlled method for evaluating the postoperative analgesic effect of myanesin in spine fusion operations is described.

There appeared to be little analgesic effect with myanesin used under the conditions of this study in the immediate postoperative period.

No important complications were noted consequent to the use of myanesin.

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