

each patient's effective prophylactic and therapeutic doses are related to the penetrance of his MH gene and vary with the precipitating factors of each episode.

In summary, a case is presented in which the patient was diagnosed as malignant hyperthermia-susceptible following trismus with succinylcholine and an elevated CPK. Despite preoperative oral administration of dantrolene and neurolept-anesthesia, MH was triggered during the second exposure to anesthesia. Following successful treatment, the patient had a recrudescence of symptoms and was again treated successfully, this time with intravenously administered dantrolene only.

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Segmental Effect of Morphine Injected into the Epidural Space in Man

HARUKA ASARI, M.D.,* KAZUJEI INOUE, M.D.,† TOSHINARI SHIBATA, M.D.,‡ TAKEHISA SOGA, M.D.‡

Although narcotics have injected into the epidural and subarachnoid spaces to produce analgesia,¹⁻⁶ there is no documentation whether the narcotic analgesics applied in that fashion exert any segmental effect clinically, as occurs with local anesthetic-induced epidural or spinal anesthesia. This report presents the results of a clinical study we have performed to clarify the segmental effect of morphine injected into the epidural space.

* Assistant Professor of Anesthesiology.

† Clinical Associate of Anesthesiology.

‡ Assistant in Anesthesiology.

Received from the Department of Anesthesiology, Yokohama City University, School of Medicine, Mail Code: 232, 3-46 Urafunecho, Minamiku, Yokohama, Japan. Accepted for publication July 22, 1980.

Address reprint requests to Dr. Asari.

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MATERIALS AND METHODS

Fifty patients undergoing upper abdominal surgical procedures, including 36 gastrectomies and 14 cholecystectomies, were selected for this study. In all cases, skin incisions were made in sixth to eleventh thoracic segments on the sensory dermatome. Before the operation, every patient consented to receive epidural injection for pain relief immediately after termination of the operative procedure. Premedication consisted of atropine sulfate and diazepam, and anesthesia was maintained by use of halothane, nitrous oxide, and pancuronium. After conclusion of the surgical procedure and extubation of trachea, an experimental solution was injected epidurally. The patients were divided into two groups. They received the epidural injections either at the level of the tenth to eleventh thoracic interspace (Group I, high level) or at the level of the fifth lumbar and

TABLE 1. Evaluation of Analgesic Effects in the Patients Studied

	Number of Patients	Age (Years) Mean \pm SD	Score			
			2	1	0	Mean
Group I						
High-level morphine	25	54.5 \pm 13.6	10	2	1	1.69
High-level saline solution			2	5	5	0.75
Group II						
Low-level morphine	25	53.2 \pm 13.1	2	5	6	0.69
Low-level saline solution			0	1	11	0.08

first sacral interspace (Group II, low level). The solution injected was either 2 mg morphine in 10 ml physiologic saline solution or 10 ml of saline solution alone. The analgesic effect was evaluated an hour after injection; neither the anesthesiologist performing injection nor the person evaluating the effect was aware of the identity of the solution injected. The analgesic effect was rated on a three-point scale (0 to 2) by the criteria that the patient was: capable of deep breathing without pain (score 2); capable of deep breathing with pain (score 1); or incapable of deep breathing when so directed by the evaluating personnel (score 0). After analgesic effects in all patients had been assessed, the data were collated with the solutions and levels of injection. Then the initial two groups were divided into four subgroups. The χ^2 test was conducted for each pair among the four subgroups to assure significant differences as to scores of 2 and 0.

RESULTS

Data from the two groups of patients were statistically analyzed by the four subgroups, designated according to the solution employed for epidural injection: high-level morphine injection; high-level saline solution injection; low-level morphine injection; low-level saline solution injection. The high-level morphine injection group showed a mean score of 1.69; the high-level saline solution injection group, 0.75; the low-level morphine injection group, 0.69; the low-level saline solution injection group, 0.08 (table 1). Hence, there was a significant difference between the high-level and low-level morphine injection groups ($P < 0.01$). All three of the other groups had significantly higher scores than did the

low-level saline solution injection group ($P < 0.05$). Results of the statistical testing conducted for assurance as to scores of 2 and 0 among the four subgroups are summarized in table 2.

DISCUSSION

Local anesthetics administered epidurally have been known to diffuse partially into the subarachnoid space and act directly on the spinal cord.⁷ Recently, an abundant distribution of opiate receptors has been identified in substantia gelatinosa of the cord by case of an autoradiographic technique.⁸ Yaksh and Rudy, in animal experiments,⁹ and Wang *et al.*, in clinical observations,⁵ have demonstrated that a small dose of morphine applied intrathecally produces analgesia. Perhaps morphine injected into the epidural space diffuses into the subarachnoid space and acts directly upon the spinal cord. Supporting this hypothesis is the work of Magora *et al.*, who found morphine in the cerebrospinal fluid 10–20 min after epidural injection by radioimmunoassay tests.²

The only objective of present study was to ascertain whether morphine injected epidurally might exert any segmental effect. There exists, however, no established method for measurement of pain, especially for those who are just recovering from anesthesia and are still confused. We tried to apply a three-point scale to the evaluation of analgesic effects in our patients on the basis that patients subjected to upper abdominal surgical procedures are usually less capable of deep breathing because of pain from the surgical wounds compared with those whose operations involve other regions. The severity of pain with deep breathing seems to depend mainly upon increasing muscle tone in the

TABLE 2. Statistical Analyses as to Score 2 (above the oblique line) and Score 0 (below the oblique line) among Four Subgroups, by χ^2 Test

Score 0	Score 2	High-level Morphine Injection	High-level Saline Solution Injection	Low-level Morphine Injection	Low-level Saline Solution Injection
High-level morphine injection			$P < 0.01$	$P < 0.01$	$P < 0.005$
High-level saline solution injection		NS		NS	NS
Low-level morphine injection		NS	NS		NS
Low-level saline solution injection		$P < 0.005$	$P < 0.05$	$P < 0.05$	

regions of skin incision, because intercostal nerve block, as well as epidural block, performed in the wound-involving segments, has been recommended for pain relief in rib-fractured or postoperative patients who have respiratory difficulties.^{10,11}

A local anesthetic applied epidurally is said to diffuse into the subarachnoid space in amounts ranging from 1/130 to 1/14 of the dose.⁷ Applying this ratio to the present study, the amounts of morphine estimated to have acted directly upon the spinal cord are approximately 15–140 μg , which may be a helpful guide to use of morphine for direct injection into the subarachnoid space. Wang *et al.* stated that increasing the dose of morphine from 0.5 to 1.0 mg did not prolong pain relief proportionately.⁵ Yagishita *et al.* reported that a decrease in respiratory rate and a slight increase in PaCO_2 , as well as euphoria, nausea, vomiting, and retention of urine, were observed in the patients who received intrathecal injections 0.1–1.0 mg morphine; all these symptoms were antagonized by naloxone given systemically.⁶ Obviously, further studies are needed to determine the optimal doses of morphine for the use by both epidural injection and subarachnoid injection.

Finally, it is noteworthy that the high-level saline solution injection group experienced an analgesic effect comparable to that in the low-level morphine injection group. This is similar to the effect of subarachnoid saline irrigation employed for the treatment of intractable pain^{12,13} and, at the same time, appears to suggest some segmental effect in light of the fact that no such effect was observed in the low-level saline solution injection group. Urban and McKain demonstrated that 5–10 ml of physiologic saline solution injected intrathecally produced segmental hypesthesia, as well as partial sympathetic block.¹⁴ It is, however, worthy of further investigation whether the neural mechanism to modulate

pain perception elicited by the injection of saline solution into the epidural space might be exactly the same event as that occurring in the subarachnoid space.

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