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A Double-Blind Assessment of Segmental Sensory Changes with Epidural Fentanyl Versus *Epidural Saline in Patients Undergoing Extracorporeal Shock-Wave Lithotripsy*

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Segmental changes to pin prick and cold stimuli were tested in a double-blind manner in pain-free patients scheduled for extracorporeal shockwave lithotripsy (ESWL). Fifty patients were randomly allocated to receive either epidural fentanyl (100 μg in 10 ml normal saline) or 10 ml epidural normal saline. In a further 25 patients an epidural catheter was inserted but no solution injected. In contrast to this latter group, epidural fentanyl and normal saline both produced segmental sensory changes. There were no significant differences between fentanyl and normal saline groups in the number of patients reporting sensory changes to pin prick, rate of onset of these changes, or segmental level. For cold stimuli, more patients in the fentanyl group than the normal saline group reported a change (16 *vs.* 8; $P = 0.02$) but the segmental level was similar. The effect of normal saline as a diluent in epidurally administered opioids may be of clinical importance. (Key words: Analgesics, opioid: Fentanyl. Anesthetic techniques, epidural. Lithotripsy.)

SINCE THE FIRST description of epidural and intrathecal opioids acting upon the spinal cord[1] a number of studies have demonstrated that opioids given by these routes can produce segmental hypalgesia.[2–5] Other studies have not demonstrated such an effect.[6,7] Many of these studies can be criticized on the basis of lack of controls, small study groups, use of test doses with local anesthetics, and failure to employ double-blind design.

Most of the anesthesia for extracorporeal shock wave lithotripsy (ESWL) at our institution is performed using epidural fentanyl in combination with epidural lidocaine. By administering the fentanyl before the lidocaine it is possible to assess the presence or absence of segmental hypalgesia in these patients. Using pin prick and ice as stimuli we sought segmental sensory changes in patients administered either epidural fentanyl diluted in normal saline or epidural normal saline alone. A third group was used as a control and assessed after epidural catheter insertion but without injection of any solution.

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Materials and Methods

The study protocol was approved by the Hospital Research Ethics Committee and informed consent was obtained from all patients. Fifty unpremedicated ASA physical status 1 or 2 patients scheduled for ESWL and with no contraindications to epidural anesthesia were randomly allocated to one of two groups. Twenty-five patients received epidural fentanyl (group F) and 25 patients received epidural normal saline (group NS). A further 25 patients were included in a control group in which an epidural catheter was inserted but no solution injected (group C).

On arrival in the ESWL suite an iv cannula was inserted, EKG monitoring established, and blood pressure measured with an automated blood pressure cuff (Dinamap™, Critikon). The epidural space was located at L1-2 by loss of resistance to air using a 16-G Tuohy needle and an epidural catheter was inserted 3 cm into the space. No test dose of local anesthetic was administered. Blood pressure, pulse rate, and respiratory rate were recorded at baseline and at 1, 5, 10, 15, and 20 min following injection of the study drug.

The study drug, either 100 μg fentanyl diluted in 10 ml of preservative-free normal saline or 10 ml of preservative-free normal saline alone was prepared at room temperature (20–23° C), by an independent anesthesiologist and injected slowly into the epidural catheter by the administering anesthesiologist who remained blind to the identity of the study drug. In group C the anesthesiologist making the assessments was unaware that no drug had been injected into the epidural catheter.

Sensory changes to pin prick and ice were noted by the assessing anesthesiologist at 2-cm intervals, 8–10 cm from the midline bilaterally on the trunk, legs and, if necessary, perineum and head. After initial identification of the stimuli in the cervical dermatomes, assessment was made commencing on the lower abdomen and then moving at first cranially and subsequently caudally. This was performed at 1, 5, 10, 15, and 20 min following injection of the study drug or after catheter placement (group C). Motor blockade was assessed by the Bromage scale for motor blockade[8] and any side effects, specifically nausea, vomiting, drowsiness, pruritis, or respiratory depression

TABLE 1. Patient Data

	Fentanyl n = 25	Normal Saline n = 25	No Drug n = 25
Age (yr)	54.10 ± 2.76	50.20 ± 2.49	45.76 ± 3.10
Weight (kg)	75.56 ± 2.59	75.44 ± 3.15	76.71 ± 3.13
Height (cm)	168.68 ± 1.73	168.21 ± 1.47	170.46 ± 1.60

Mean ± SE.

(rate less than 10 breaths per min) were noted. Patients were assessed and questioned as to whether they felt certain or hesitant about the sensory changes they reported. Intravenous sedation was avoided until testing was complete at which time an appropriate dose of local anesthetic was administered for ESWL. Anesthesia was satisfactory for ESWL in all cases, confirming the correct placement of the catheter.

Parametric data were analyzed by Student's *t* test and nonparametric data by chi-square test (Statview II™, Abacus Concepts Inc.).

Results

There were no significant differences in age, weight, and height between group F, group NS, and group C (table 1). There were also no significant differences in blood pressures, pulse rates, and respiratory rates between or within groups at any time. Twenty patients in group F, 17 patients in group NS and 21 patients in group C felt certain of their assessment of sensory changes (no significant difference).

Between groups F and NS there was no significant difference in the total number of patients reporting sensory changes to pin prick. Nineteen patients in group F and 16 patients in group NS reported such a change. The incidence of these changes increased with time and was similar in both groups (fig. 1). Among the patients who reported a sensory change to pin prick, the level of block also increased with time and was similar in both groups (fig. 2). The range of upper block level for both groups varied from T2-T10.

Sixteen patients in group F and eight in group NS reported sensory changes to cold. This difference was significant ($P = 0.02$, chi-square test). The number of pa-

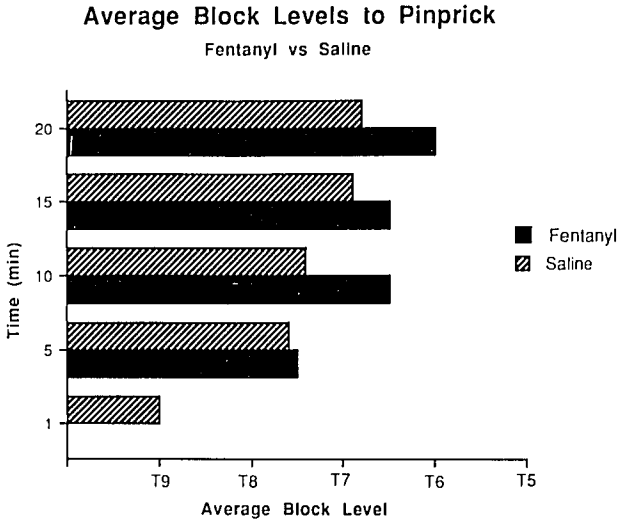

FIG. 2. Thoracic dermatomal level for pin prick *versus* time for fentanyl and normal saline groups.

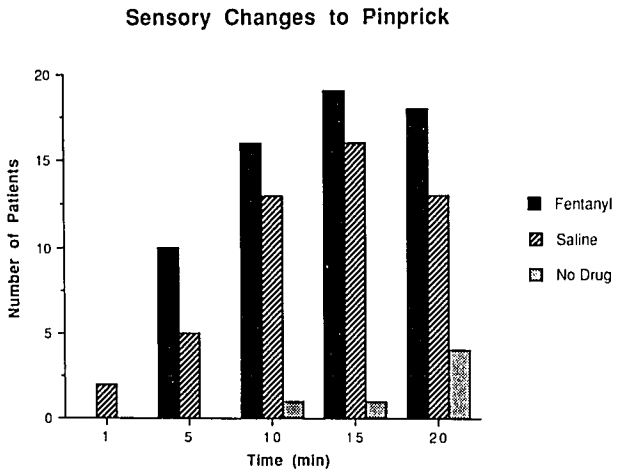

FIG. 1. Frequency of sensory changes to pin prick *versus* time for fentanyl, normal saline, and control (no drug) groups. At all time intervals the number of patients in the control group with sensory changes to pin prick was significantly less than the fentanyl and normal saline groups.

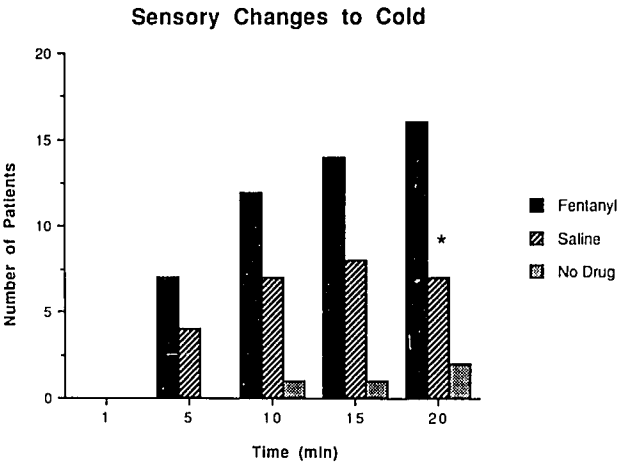

FIG. 3. Frequency of sensory changes to cold *versus* time for fentanyl, normal saline, and control (no drug) groups. At all time intervals the number of patients in the control group with sensory changes to cold was significantly less than the fentanyl and normal saline groups.

*At 20 min the number of patients reporting sensory changes to cold was significantly less in the normal saline group compared with the fentanyl group.

tients with sensory changes to cold increased with time for both groups (fig. 3) but was significantly different at 20 min ($P = 0.01$, chi-square test). Among the patients who reported a sensory change to cold, the average level of block increased with time for both groups and was similar in both groups (fig. 4). The range of upper block level for both groups was T1-T10.

In group C, four patients experienced sensory changes. This is significantly less than for both group F and group NS ($P = 0.0001$ and $P = 0.0005$, respectively, chi-square test). Three of these four were not confident of the change. Also, in three of the four patients, sensory change was not reported until 20 min after catheter insertion, the remaining patient reporting a change after 10 min. Two of the four patients experienced a segmental sensory change to pin prick but not to cold. The remaining 21 patients were certain that they experienced no sensory changes after catheter insertion.

The side effects are shown in table 2. The incidence in the fentanyl group of pruritus (16%) and drowsiness (16%) was significantly more frequent than that in patients receiving normal saline. No side effects required treatment. No side effects were identified in group C.

TABLE 2. Side Effects

	Fentanyl n = 25	Normal Saline n = 25	No Drug n = 25
Nausea	2	1	0
Pruritus*	4	0	0
Drowsiness*	4	0	0
Shivering	1	0	0
Respiration depression	0	0	0
Motor blockade	0	0	0

* $P = 0.04$ (chi-square test).

Discussion

Dermatomal levels of hypalgesia to pin prick and ice have been demonstrated following epidural administration of various opioids.[2-4,9] Most of these studies have been carried out on postoperative patients in pain or with small numbers of pain-free volunteers. In a double-blind study comparing the effects of epidural morphine and normal saline, Asari *et al.*,[10] using a three-point pain scale in patients undergoing abdominal surgery, demonstrated a significant difference between high-level (interspace between T10 and T11) and low-level (interspace between L5 and S1) epidural morphine injection and between epidural morphine and epidural saline. Although demonstrating a segmental effect, they did not clearly identify dermatomal sensory levels. Decreased sensitivity to pin prick in a dermatomal distribution has, however, been demonstrated following the administration of epidural meperidine for hip surgery.[9]

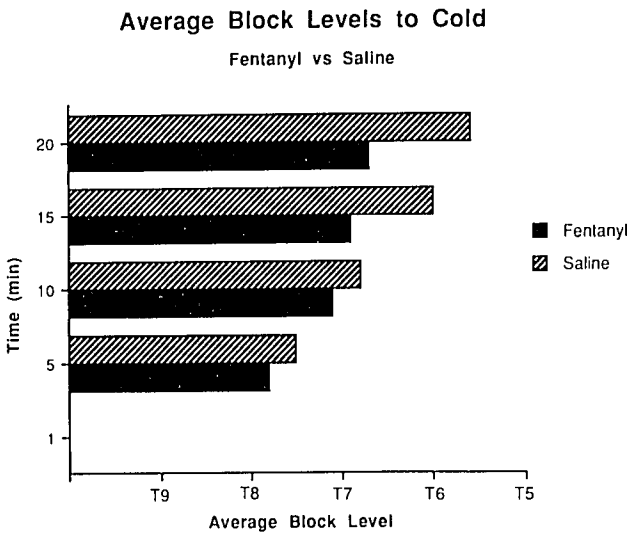

FIG. 4. Thoracic dermatomal level for cold *versus* time for fentanyl and normal saline groups.

In contrast to these studies in postoperative patients, several authors have used pain-free volunteers to demonstrate segmental analgesic effects of epidural opioids, with or without sensory levels.[3,4] Invariably, small numbers of subjects have been employed and the studies were not performed in a double-blind manner. Although there are many reports of the use of epidural fentanyl for analgesia, we could find no reports investigating a cutaneous sensory change with this particular drug in either patients suffering pain or in volunteers.

We were able to demonstrate segmental sensory changes with epidurally administered fentanyl but the finding that normal saline produced similar changes is also of interest. The local anesthetic effects of intrathecally administered normal saline were first suggested by Urban and McKain in their study of graduated spinal anesthesia in chronic pain patients.[11] MacMurdo *et al.*, also demonstrated "hypesthesia" with large volumes (10 ml) of intrathecal normal saline.¶ These results have been questioned, however, by subsequent studies.[12]

The temperature of the injectate may be of importance for the local anesthetic action of normal saline when given intrathecally. Cold (2–4° C) normal saline is said to have an effect on pain carrying C fibers.[13] Our injections were at room temperature and given *via* the epidural route so this effect of cold should not have been evident. It is interesting to note that a recent report indicates that the analgesic activity of epidural fentanyl (100 μg in 10 ml of

¶ MacMurdo SD, Barsa J, Ready LB: Placebo injection in diagnostic subarachnoid block (abstract). ANESTHESIOLOGY 55:A143, 1981.

normal saline) may in fact be reduced by injection at low (4° C) temperatures.[14]

We have found no previous study looking at the segmental sensory effects of epidurally rather than intrathecally administered normal saline. We did not anticipate finding any sensory change with epidural normal saline and as a result the third group in which a catheter was inserted but no solution injected was subsequently introduced to form a true control. There could be no random assignment of patients to this group; however, the observer performing the sensory assessment was blinded to the nature of the study. We were thus able to exclude a placebo effect from the epidural catheter alone.

In our study, the time of onset and height of block in both fentanyl and normal saline groups were similar for the pin prick stimulus. Although there was a statistically significant difference between groups in response to cold, the clinical meaning of this is unclear. The effect of normal saline used as a diluent in the administration of epidural opioids may be of clinical relevance. The action of normal saline at a spinal level may explain, for example, the observed improvement in sensory blockade with larger volumes of less-concentrated epidural fentanyl.[15]

In conclusion, the majority of patients demonstrated segmental sensory changes, increasing with time, in response to both epidurally administered normal saline and fentanyl diluted in normal saline. A spinal effect of epidural normal saline is suggested. The relevance of this to clinical experience in patients with pain requires further study.

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