Postoperative Pain Relief and Respiratory Function in Man:

Comparison Between Intermittent Intravenous Injections of Meperidine and Continuous Lumbar Epidural Analgesia

Mannosuke Muneyuki, M.D., Yutaka Ueda, M.D.,† Nobukata Urabe, M.D.,† Hiroshi Takeshita, M.D.,‡ Akira Inamoto, M.D.§*

The effect of postoperative pain relief on cardiopulmonary function was examined quantitatively in 36 patients who underwent upper abdominal surgery. Postoperative pain relief was obtained by intravenous meperidine or by mepivacaine epidurally. Expiratory volumes increased during analgesia, despite decreases in respiratory rate and minute volume, especially in the epidural group. The reduction of respiratory rate and minute volume did not result in respiratory acidosis. A reduction of 7 or 8 per cent in oxygen consumption was observed in both groups during analgesia without significant changes in metabolic factors. Differences between decreased $\dot{Q}_E/\dot{Q}_T$ in the epidural group and increased $\dot{Q}_E/\dot{Q}_T$ in the meperidine group were statistically significant. After the establishment of analgesia, arterial oxygen tension increased in the epidural group and decreased in the meperidine group. The implications of these findings for the problems of postoperative pain relief are discussed.

SEVERAL INVESTIGATORS[1,2] have reported that narcotics in doses ordinarily used for postoperative pain relief may exert a suppressive effect upon respiratory function. These studies, however, have been based mostly upon classical but now relatively crude measurements of vital capacity[1] or estimation of respiratory patterns[2] without precise quantitation. There is no doubt that excessive doses of narcotics can cause respiratory depression, but there have been no data to quantify the action upon cardiopulmonary function of narcotics used in minimal effective dosage. The favorable influence of pain relief upon metabolism and respiratory activity must be taken into consideration also. Recent advances in the methodology of blood gas analysis have made it possible to detect minute changes in respiratory function by direct measurement of arterial blood gas tensions.

The present study was undertaken to compare the effects on respiratory function of two methods of postoperative pain relief: intermittent intravenous administration of meperidine (Demerol) and continuous lumbar epidural analgesia with mepivacaine (Carbocaine).

Subjects and Methods

Thirty-six adult patients of both sexes scheduled for upper abdominal surgery (cholecystectomy for cholelithiasis or gastrectomy for peptic ulcer) were chosen for this study. They were divided into two groups, the first consisting of 24 patients (Study I) and the second, 12 patients (Study II). No patient had clinical evidence of cardiac or respiratory disease preoperatively; all were classified as physical status I on a five-point scale.

Premedication consisted of atropine, 0.5 mg. subcutaneously, one hour prior to induction of anesthesia. No narcotic drug was given. Anesthesia was induced with thiamylal (Surital), followed by succinylcholine, 40 mg., to facilitate endotracheal intubatoin with a cuffed tube. Anesthesia was maintained with nitrous oxide and halothane, supplemented with succinylcholine as needed for muscle relaxation.

* Lecturer.
† Postgraduate Course.
‡ Associate Professor.
§ Professor.

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After recovery from anesthesia, no special treatments other than routine postoperative measures were instituted. All patients lay supine and breathed room air throughout the period of study. Rectal temperatures were recorded electrically.

Study I: Preliminary Study

The 24-patient-group was divided into two subgroups, 11 "epidural" patients and 13 "meperidine" patients.

Arterial oxygen and carbon dioxide tensions and *p*H were measured before analgesia and 30 minutes after analgesia had been obtained. In the epidural group, a polyethylene catheter introduced into the epidural space between the eighth or ninth intervertebral space prior to induction of general anesthesia was retained in place for postoperative analgesia with mepivacaine 1 per cent solution. In the meperidine group, the drug was administered intravenously in intermittent doses of 10 mg. until almost complete analgesia [3] was obtained. No other analgesics were used. P_{O_2}, P_{CO_2} and pH were determined in arterial blood at 37° C. by means of an I.L. Electrode System. Measurements were made in duplicate. Statistical significance was determined with Student's *t* test.

Study II: Long-term Study

Twelve patients were divided equally into an epidural group and a meperidine group. In the epidural group the first series of measurements was performed at an average of 235 (±24.4 S.E.) minutes after the end of operation, and in the meperidine group at an average of 231 ± 19.9 minutes, when the residual effects of the general anesthetic had disappeared and the patients were beginning to complain of abdominal incisional pain.

The first set of samples was taken at this time to obtain control values. The second set was obtained approximately 30 minutes later when analgesia was almost complete. These two sets of samples constitute "the first series of measurements" (tables 3–7). The examinations were repeated early the next morning, when analgesia was temporarily discontinued and pain began to return, *i.e.*, 943 ± 42.2 minutes after the end of operation in the epidural group; 863 ± 12.4 minutes in the meperidine group ("the second series of measurements," tables 3–7). In each series, the procedures were almost the same as in the first study except that several additional parameters of cardiopulmonary function were measured.

Since each patient received the minimal dosage of meperidine required for adequate and sustained analgesia of Grade 3,[3] the amount varied from patient to patient. The average dose was 0.61 mg./kg. Details of age, body weight, body surface area and duration of operation are shown in table 3.

In each case, a Cutter "Cathalet" intravenous catheter was inserted via the right basilic vein into the superior vena cava and another via the right or left femoral vein into the inferior vena cava.

When the first (control) samples were taken, heart rate, blood pressure, body temperature (rectal), respiratory volume, carbon dioxide fraction of end-expired gas, respiratory rate and oxygen uptake were measured also. Arterial blood samples were taken from a femoral artery, and venous blood samples were obtained simultaneously from the catheters in the superior and inferior venae cavae. The blood samples, withdrawn anaerobically into 10-ml. syringes whose deadspaces were filled with heparin solution, were stored in ice water until analyzed. All blood gas analyses were completed within three hours after sampling. Arterial oxygen tension was measured by means of modified Clark electrodes. Carbon dioxide tension was determined using a Severinghaus electrode at 37° C. The *p*H, standard bicarbonate, buffer base and base excess were measured using the micro-Astrup electrode for whole blood and the Siggaard-Andersen nomogram.[4] No temperature correction was needed since, in all cases, the shift of rectal temperature was less than 1° C. during the experiment.

Respiratory rate was counted and respiratory volume measured by means of a Wright respirometer which previously had been calibrated against a Benedict-Roth respirometer. An infrared carbon dioxide analyzer (Beckman Medical Gas Analyzer LB-1) was used to monitor the end-expiratory carbon dioxide fraction. The gas emerging from the expiratory limb of a nonrebreathing valve was collected in a polyvinyl Douglas bag. The vol-

TABLE 1. Average Values for Age, Weight and Time of Measurement for Epidural and Meperidine Groups (Study I)

Group	Patients				Time of Measurement (min.) after Termination of Operation	Mean Dose
	Number	Males	Age (years)	Weight (kg.)		
Epidural (±S.E.)	11	8	49 ±10.8	53.8±11.8	99.5±10.3	1% Mepivacaine 5 ml.
Meperidine (±SE)	13	11	48.9±11.1	47.5±10.3	88.5± 8.4	0.78 mg./kg.±0.09
P			NS	NS	NS	

NS = $P > 0.05$.

ume of the bag was measured by expelling its contents through the Wright respirometer after first taking a sample of mixed expired gas for analysis in a Beckman Medical Gas Analyzer LB-1. The bag was washed out twice with expired gas before each measurement. Oxygen uptake was measured with a Benedict-Roth spirometer. Spirometric measurements were recorded at S.T.P.D. (standard temperature pressure dry). During spirometry the nasal airway was closed by means of a nose clip and the patient was allowed to breathe air via a mouthpiece; he was encouraged to relax and breathe naturally.

Calculations

Physiological deadspace was calculated from the following form of the Bohr equation:

$$V_D = V_E \frac{Paco_2 - Peco_2}{Paco_2} - V_D \text{ app.}$$

with subtraction of apparatus deadspace (V_D app.). Apparatus deadspace was determined by water displacement. Physiological deadspace also was expressed as a percentage of tidal volume (V_D/V_T). Alveolar oxygen tension (P_{AO_2}) during breathing of air was estimated by applying the alveolar air equation[5]:

$$P_{AO_2} = P_{IO_2} - P_{ACO_2}\left[F_{IO_2} + \frac{1 - F_{IO_2}}{R}\right]$$

R was measured and F_{IO_2} equalled 0.21. P_{ACO_2} was assumed to be equal to $Paco_2$. The alveolar-arterial oxygen tension difference (AaD_{O_2}) was obtained by subtraction.

Physiological shunt was calculated from the following equation:

$$\frac{\dot{Q}s}{\dot{Q}T} = \frac{C\acute{c}o_2 - Cao_2}{C\acute{c}o_2 - C\bar{v}o_2}$$

Mixed venous blood was not sampled but oxygen content ($C\bar{v}o_2$) was assumed by averag-

TABLE 2. Values for Pao_2, $Paco_2$ and pH During Postoperative Period (Study I)

	Epidural Group			Meperidine Group		
	Pao_2 (mm. Hg)	$Paco_2$ (mm. Hg)	pH	Pao_2 (mm. Hg)	$Paco_2$ (mm. Hg)	pH
Before Analgesia (Mean)	83.6	36.5	7.404	84.4	35.8	7.389
During analgesia (Mean)	83.0	36.4	7.412	82.9	36.6	7.378
Mean of Differences	−0.62	−0.12	0.008	−1.51*	0.83*	−0.01*
S.E.	±2.54	±1.34	±0.014	±1.83	±0.61	±0.006
P	NS	NS	NS	NS	NS	NS

* No significant intergroup difference.
NS = $P > 0.05$.

TABLE 3. Mean Values for Epidural and Meperidine Groups (Study II)

Group	Patients					Duration of Operation (min.)	First Series of Measurements Time (min.) after the End of Operation	Second Series of Measurements Time (min.) after the End of Operation
	Number	Males	Age (years)	Weight (kg.)	Body Surface ($m.^2$)			
Epidural	6	4	46.7	54.2	1.56	140	235	943
(±S.E.)			±3.66	±6.1	±0.43	±22.5	±24.4	±42.2
Meperidine	6	5	29.2	52.5	1.57	273	231	863
(±S.E.)			±2.5	±3.7	±0.42	±36.0	±19.9	±12.4
P			<0.01	NS	NS	NS	NS	NS
						0.05 < *P* < 0.1		0.1 < *P* < 0.2

NS = $P > 0.05$.

ing arithmetically the oxygen contents of inferior vena cav and superior vena cav blood.[6] End-pulmonary capillary oxygen content (Cc'_{O_2}) was calculated from the following equation:

$$Cc'_{O_2} = S_{O_2}P_{A_{O_2}} \times 1.34\ Hb + 0.0031\ P_{A_{O_2}}$$

where 0.0031 is the solubility coefficient for dissolved oxygen and end-pulmonary capillary blood was assumed to have the same P_{O_2} as the calculated alveolar oxygen tension ($P_{A_{O_2}}$). Oxygen saturation ($S_{O_2}P_{A_{O_2}}$) was calculated from the nomogram of Severinghaus[7] after correcting arterial oxygen tension for pH.

Results

STUDY I

This study was designed to measure a relatively short-term effect of postoperative pain relief upon respiratory function. Therefore, both methods of analgesia were instituted early in the postoperative period.

Sex, age and weight of patients and the average doses of analgesic drugs (meperidine or mepivacaine) are shown in table 1, together with the time intervals between the end of operation and the start of the study, 99.5 ± 10.3 (S.E.) minutes in the epidural group, and 88.5 ± 8.4 minutes in the meperidine group. The difference between the two time intervals was not significant.

Mean values for blood gas analyses in both groups are presented in table 2, together with P values representing significance of the differences between the results obtained before and during analgesia.

There was no significant difference in Pa_{O_2}, Pa_{CO_2} or *p*H before and during analgesia in either group, nor did the values in both groups during analgesia show any significant differences.

STUDY II

In this study, the first series of measurements of blood gas tension were carried out approximately four hours after the end of operation (235 ± 24.4 minutes in the epidural group; 231 ± 19.9 minutes in the meperidine group) and the second series of measurements approximately 15 hours after the end of operation in order to determine the long-term effects of each method of analgesia (table 3).

The average duration of operation was longer in the meperidine group (273 ± 36.0 minutes) than in the epidural group (140 ± 22.5 minutes), but the difference was not significant (table 3). Mean age in the epidural group was significantly higher than in the meperidine group ($P < 0.01$).

Mean values for circulatory signs and respiratory volume in both groups before and during postoperative pain relief are presented in table 4. Compared with the preanalgesic period, the significant changes were: an increase from 297 ml. to 325 ml. ($P < 0.05$) in expiratory volume (V_E) in the epidural group; in the meperidine group decreases from 23 to 18 ($P < 0.05$) in respiratory rate and from 7,565 ml. to 6,057 ml. in minute volume (M.V.); in turn, an increase from 331 to 339 ml. ($P < 0.05$) was observed in expiratory volume in the second series of measurements. Systolic blood pressure (B.P.) and heart rate

TABLE 4. Values for Systolic Blood Pressure, Heart Rate, Respiratory Ratio, Minute Volume and Tidal Volume Before and During Postoperative Pain Relief (Study II)

		Epidural						Meperidine					
		No. of Obser-vations	B.P. (mm. Hg)	H.R.	(b.p.m.)	M.V. (ml./ (BTPD)	Vs (ml./ (BTPD)	No. of Obser-vations	D.P. (mm. Hg)	H.R.	f (b.p.m.)	M.V. (ml./ (BTPD)	Vs (ml./ (BTPD)
The First Series of Measurements	Before Analgesia (Mean)	0	110	70.5	24.4	6,313	293	0	110	84	21	6,023	310
	During Analgesia (mean)	0	115	82.5	21.0	6,310	303	0	126	87	19.0	6,703	290
	Mean of Differences		−1.0	3.0	−3.4	100	10.0		7.0	3.0	−1.1	−801	−20.0
	± S.E.		4.2	4.0	1.6	694	37.7		3.1	2.7	1.2	447	22.0
	P		NS	NS	NS	NS	NS		NS	NS	NS	NS	NS
					0.05 < P < 0.1				0.05 < P < 0.1			0.1 < P < 0.2	
The Second Series of Measurements	Before Analgesia (mean)	0	124	84	21.8	6,904	207	0	128	93	23	7505	331
	During Analgesia (mean)	0	110	80	22.9	6,883	325	0	127	90	18	6,057	339
	Mean of Differences		−5.0	5	−0.9	−111	28		−1.0	−3.0	−5.0**	−1508*	8**
	± S.E.		3.0	4.4	0.5	396	10.3		2.2	3.0	1.4	481	2.5
	P		NS	NS	NS	NS	<0.05		NS	NS	<0.05	<0.05	<0.05

* Significant intergroup difference ($P < 0.05$).
** Highly significant intergroup difference ($P < 0.01$).
B.P. = systolic blood pressure; H.R. = heart rate, f = respiratory rate; M.V. = minute volume; Vs = expiratory volume.

(H.R.) remained at normal levels throughout the study in both groups (table 4).

Concerning the significance of intergroup differences, the decrease in respiratory rate in the meperidine group was highly significant compared with the rate in the epidural group. The increase in expiratory volume in the epidural group was also highly significant ($P < 0.01$) compared with that in the meperidine group, whereas the decrease in minute volume in the meperidine group was significant ($P < 0.05$) compared with that in the epidural group. Thus, the increase in expiratory volume was greater in the epidural group ($P < 0.01$), whereas the decreases in both respiratory rate and minute volume were greater in the meperidine group ($P < 0.01$, $P < 0.05$, respectively).

In the second series of measurements in Study II (table 5), a reduction of approximately 7 or 8 per cent in oxygen uptake was observed after establishment of analgesia. In both groups this was highly significant ($P < 0.01$).

The values for respiratory exchange ratio (R) were generally low in both groups, with no statistically significant changes, except that a highly significant increase appeared during analgesia in the second series of measurements of the epidural group (table 5).

Respiratory deadspace showed no significant alteration associated with postoperative pain relief, except that in the first series of measurements physiological deadspace decreased significantly with analgesia in the meperidine group ($P < 0.05$).

The ratio of physiological deadspace to tidal volume (V_D/V_T) showed no significant change except for a fall with meperidine in the second series. Nor did the intergroup values differ significantly. This evidence is compatible with the finding that no statistical significance was observed in arterial-end-tidal (a-ET) difference of carbon dioxide tension (table 6).

As demonstrated in table 6, mean values for $Paco_2$ varied insignificantly with both methods of analgesia. On the other hand, in the second series of Study II Pa_{O_2} increased significantly from 82.6 to 86.6 mm. Hg in the epidural group but decreased significantly (from 93.3 to 88.3 mm. Hg) in the meperidine group

TABLE 5. Values for Oxygen Uptake, Respiratory Exchange Ratio, Respiratory Deadspace and V_D/V_T Before and During Postoperative Pain Relief (Study II)

	Epidural						Meperidine					
	$\dot{V}_{O_2}$ ml./m.²/m²p.s. (STPD)	R	V_D			V_{DP}.	$\dot{V}_{O_2}$ ml./m.²/m²p.s. (STPD)	R	V_D			V_{DP}.
			Anat.	Physiol.	Alv.	V_T			Anat.	Physiol.	Alv.	V_T
Before Analgesia (Mean)	156	0.67	108	121	13	0.428	169	0.63	134	150	16	0.479
During Analgesia (Mean)	142	0.71	121	130	8.5	0.431	160	0.66	114	129	14	0.434
		NS						NS				
Mean of Differences	−14	0.04	13.0	9.0	−4.5	0.003	−9.0	0.03	−20.0	−21.0	−2.0	−0.045
±S.E.	9.4	0.11	14.1	15.6	7.8	0.02	5.3	0.028	14.7	7.0	9.1	0.023
P	NS	NS	NS	NS	NS	NS	NS	NS	NS	<0.05	NS	NS
Before Analgesia (Mean)	150	0.64	126	140	14	0.478	159	0.78	130	150	9.3	0.461
During Analgesia (Mean)	144	0.73	133	147	15	0.461	147	0.72	135	139	4.3	0.412
		NS						NS				NS
Mean of Differences	−12.0	0.09	7.0	7.0	1.0	−0.017	−12.0	−0.06	−4.0	−11	−5.0	−0.049
±S.E.	1.9	0.14	10.7	9.2	8.3	0.02	2.8	0.057	10.2	7.4	7.2	0.018
P	<0.01	<0.01	NS	NS	NS	NS	<0.01	NS	NS	NS	NS	<0.05

NS = $P > 0.05$. Vo_2 = oxygen uptake; R = respiratory exchange ratio; V_D = respiratory deadspace.

($P < 0.05$). Consequently, the intergroup difference in Pa_{O_2} was highly significant ($P < 0.01$) (table 6).

It is of interest that no significant changes in alveolar-arterial P_{O_2} difference (AaD_{O_2}) or venous admixture ($\dot{Q}_S/\dot{Q}_T$) were observed in association with postoperative analgesia. The only statistically significant difference noted was in the intergroup differences of $\dot{Q}_S/\dot{Q}_T$ in the second series of Study II.

Table 7 shows the values of *p*H, buffer base, base excess and standard bicarbonate during postoperative analgesia. In the first series of Study II, patients in the epidural group showed a definite increase in arterial *p*H (0.013 ± 0.005, $P < 0.05$), but in the meperidine group, *p*H decreased significantly (0.027 ± 0.007, $P < 0.05$) and the difference between the two groups was highly significant ($P < 0.01$) (table 7). In the second series of Study II, however, the changes in *p*H during analgesia were minimal in both epidural and meperidine groups. No significant differences in other metabolic factors were encountered.

Discussion

In analyzing the data obtained, the degree of significant change seemed higher in the second series of Study II than in the first series. Although the reason for this is not clear, it may have been due to the residual effects of the general anesthetic (halothane), not yet completely eliminated at the time of the first series of measurements.

Fletcher[8] reported that respiratory tidal volume was reduced and arterial carbon dioxide tension increased within a few minutes after administration of morphine sulfate 0.1 mg./kg. to normal subjects. On the other hand, Egbert[2] reported that neither respiratory rate nor volume was greatly affected by morphine. In the present study, respiratory minute volume and rate both were reduced significantly after meperidine administration, but a striking finding was an increase in expiratory volume in both groups, especially the epidural series. After laparotomy, postoperative incisional pain is likely to render respiration rapid and shallow with constant tidal volume, or at least to diminish effective sighing. Such patients are unwilling to breathe deeply because of incisional pain and fear of rupturing the wound.[9] This concept is supported by our findings of increased expiratory volume during analgesia in spite of decreased respiratory rate and minute volume.

The reduction of respiratory rate and minute volume did not result in respiratory acidosis; the shift of Pa_{CO_2} during analgesia was minor and not significant. The absence of hypercarbia in the postoperative period coincides with the report of Hamilton *et al.*,[10] and the suggestion of Bendixen *et al.*[11] that a pattern of slow, deep breathing may maintain normal arterial tensions of both oxygen and carbon dioxide by preventing atelectasis and shunting. The increased expiratory volume noted might be a logical explanation for the lack of change in arterial carbon dioxide tension despite significant decreases in respiratory rate and minute volume during analgesia.

Again, considering the decreases observed in respiratory rate and minute volume, it is interesting that decresaes in oxygen uptake following analgesia were consistently observed in both groups in the second series of measurements of Study II (table 5).

The reasons for the rise in Pa_{O_2} in the epidural group and the fall in the meperidine group during analgesia, especially in the second series of Study II, are not immediately apparent. Possible causes under the conditions of this study include hypoventilation, impaired diffusing capacity, maldistribution, and shunting.[12] Since the expiratory volume in the patients of both groups was increased significantly, especially in the epidural group, while carbon dioxide tensions exhibited no significant change, the changes in Pa_{O_2} clearly were not due to hypoventilation.

It might be that the relatively large increase in tidal volume in patients of the epidural group could more effectively prevent alveolar collapse than would be the case in the meperidine group; this might also account for the increased Pa_{O_2} in the patients of the epidural group. Moreover, since the alveolar oxygen tensions (PA_{O_2}) were close to the normal value of 100 mm. Hg in the second series of measurements, the decrease in Pa_{O_2} in the meperidine group cannot be explained by a reduction of diffusing capacity.[13]

TABLE 6. Values for P_{ACO_2}, ($\bar{a}$-ET)D_{CO_2}, P_{AO_2}, P_{aO_2}, AnD_{O_2} and $\dot{Q}_S/\dot{Q}_T$ Before and During Postoperative Pain Relief (Study II)

	Epidural						Meperidine					
	P_{ACO_2} (mm. Hg)	($\bar{a}$-ET)D_{CO_2} (mm. Hg)	P_{AO_2} (mm. Hg)	P_{aO_2} (mm. Hg)	AnD_{O_2} (mm. Hg)	$\dot{Q}_S/\dot{Q}_T$ (%)	P_{AO_2} (mm. Hg)	($\bar{a}$-ET)D_{CO_2} (mm. Hg)	P_{AO_2} (mm. Hg)	P_{aO_2} (mm. Hg)	AnD_{O_2} (mm. Hg)	$\dot{Q}_S/\dot{Q}_T$ (%)
Before Analgesia (mean)	34.6	3.2	98.5	81.5	17.1	0.1	36.8	4.1	94.5	90.2	4.3	0.6
During Analgesia (mean)	34.5	2.8	100.8	80.6	20.1	11.5	37.6	2.2	94.8	90.8	3.0	7.2
Mean of Differences	−0.1	−0.4	2.3	−0.9	3.0	2.4	0.8	−1.9	0.3	0.6	−0.4	0.6
±S.E.	0.3	1.5	5.5	3.2	7.1	2.5	1.2	1.1	1.6	3.7	3.0	1.4
P	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	—
Before Analgesia (mean)	34.9	3.8	100.2	82.6	17.6	7.1	36.8	2.9	103.0	93.3	9.7	5.8
During Analgesia (mean)	35.0	3.2	104.5	80.6	17.9	0.1	38.0	1.8	98.0	88.3	9.7	7.2
Mean of Differences	0.1	−0.6	4.3*	4.0	0.3	−1.0	1.2	−1.1	−5.0	−5.0**	0	1.4*
±S.E.	1.3	1.2	1.8	1.6	2.0	0.8	1.2	1.6	3.6	1.7	5.0	0.7
P	NS	NS	NS $0.05 < P < 0.1$	+0.05	NS	NS	NS	NS	NS	<0.05	NS	NS

* Significant intergroup difference ($P < 0.05$).
** Highly significant intergroup difference ($P < 0.01$).

TABLE 7. Values for pH, Buffer Base, Base Excess and Standard Bicarbonate Before and During Postoperative Pain Relief (Study II)

	Epidural				Meperidine			
	pH	B.B. (m.Eq./L)	B.E. (m.Eq./L)	S.B. (m.Eq./L)	pH	B.B. (m.Eq./L)	B.E. (m.Eq./L)	S.B. (m.Eq./L)
Before Analgesia (Mean)	7.391	47.6	−3.8	21.1	7.385	48.3	−2.9	21.7
During Analgesia (mean)	7.404	48.6	−3.2	21.6	7.358	47.7	−4.0	20.9
Mean of Differences	0.013	1.0	0.6	0.5	−0.027**	−0.6	−1.1	−0.8
±S.E.	0.005	0.6	0.28	0.2	0.007	1.6	0.6	0.6
P	<0.05	NS	NS	NS (0.05<P<0.1)	<0.05	NS	NS	NS
Before Analgesia (mean)	7.422	51.8	−0.33	23.7	7.381	47.3	−3.0	21.8
During Analgesia (mean)	7.420	50.6	−0.93	23.2	7.381	50.1	−1.82	22.8
Mean of Differences	−0.002	−1.2	−0.60	−0.5	−0.0002	2.80	1.18	1.0
±S.E.	0.033	1.6	0.73	0.7	0.008	1.56	0.89	0.8
P	NS	NS	NS	NS	NS	NS	NS	NS

** Highly significant intergroup difference.
B.B = buffer base; B.E. = base excess; S.B. = standard bicarbonate.

Since hypoventilation and impaired diffusing capacity are not responsible for the findings observed, the only remaining possibilities are the existence of shunts and maldistribution within the lungs.[10,12,14] Unfortunately, it is not easy to distinguish between these disturbances in this study; it is difficult to estimate the degree of contribution of ventilation-perfusion abnormalities to the total shunt without additional blood gas values obtained while permitting the patients to breathe a high concentration of oxygen.

The significant difference in $\dot{Q}s/\dot{Q}T$ between the mean of differences of the two groups might account for the significant changes in Pa_{O_2} in the second series of Study II.

Generally, values for respiratory exchange ratio were low, especially in the first series of measurements in Study II. The reason for this is not apparent but, as may be seen in table 5, an increase (as in the epidural group) or a decrease (as in the meperidine group in the second series of measurements) in respiratory exchange ratio would cause a corresponding increase in calculated PA_{O_2}. This explanation also may account for the lack of change in (A-a) oxygen tension difference even though Pa_{O_2} increased in the epidural group and decreased in the meperidine group in the second series of Study II.

Larger values in (A-a) difference of oxygen tension and lower mean values in Pa_{O_2} were observed in the epidural group than in the meperidine group in Study II. This coincides with the fact that the average age of patients in the epidural group was higher than in the meperidine group, which may be regarded as a cause of low oxygen tension in arterial blood.[15,16]

The clinical significance of the postoperative fall of Pa_{O_2} in the meperidine group is difficult to assess, but this sort of decrease in arterial oxygen tension serves to emphasize the fallacy of relying upon clinical observation to detect moderate degrees of hypoxemia: no patient in the present study was suspected of being hypoxic. No patient in either group developed serious pulmonary complications, but it does not seem wholly justified to suggest that absence of complications in patients in

the meperidine group indicates that change in oxygen tension is unimportant. Although probably of minor significance in most good-risk patients, under unfavorable circumstances cardiopulmonary complications may develop. This possibility in geriatric cases is now under investigation in this laboratory.

Another striking feature appeared in the determinations of metabolic factors (table 7). Postoperative analgesia with either intravenous meperidine or epidural block produced no significant alteration in the nonrespiratory components of acid-base balance.

Summary

The effect of postoperative pain relief upon respiratory function was studied in 36 patients who underwent upper abdominal surgery. The first 24 patients participated in a preliminary study on short-term effects of intravenously-administered meperidine or mepivacaine epidurally. In the other 12 patients, who received long-term postoperative pain relief (Study II), arterial blood gas tensions and spirometric measurements were made four and 15 hours postoperatively, and before and during the two methods of analgesia, respectively.

During analgesia, arterial oxygen tension decreased significantly in patients of the meperidine group and increased significantly in patients of the epidural group, especially in the second series of measurements 15 hours after operation.

Hypercapnea did not occur in either the early or the late series. This was attributed to increased expiratory volume during analgesia in spite of decreases in respiratory rate and minute volume.

The implications of these findings for the problems of postoperative pain relief were discussed.

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