EFFECT OF DEMEROL ON THE CEREBROSPINAL FLUID PRESSURE *

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SINCE Eisleb and Schauman (1) introduced the synthetic compound 1-methyl-4-phenylpiperidine-4-carboxylate (demerol, dolantin, meperidine, D-140, and so forth) in 1938, the drug has become popular and is widely used for its analgesic, spasmolytic and sedative properties. Rovenstine and Batterman (2) used demerol in 1942 as a substitute for morphine in the preoperative medication of patients, and Brotman and Cullen (3) suggested that it be employed as a supplement to nitrous oxide anesthesia.

The purpose of this investigation was to find out the suitability of demerol as a preoperative and supplemental agent in anesthesia for cranial operations or for traumatic surgical procedures on patients who have cranial injuries, and for patients in whom a change in intracranial pressure is undesirable. Morphine and barbiturates (amytal and luminal) have been investigated by Finesinger and Cobb (4). Their results showed that in 25 cats given morphine intravenously, the cerebrospinal fluid pressure increased from 4 to 34 per cent of the initial figure; in 15 cats given amytal, the pressure increased from 9 to 52 per cent, and in 14 cats given luminal, the elevation ranged from 4 to 33 per cent. Guttman (5) administered demerol to 20 patients with intracranial lesions of various kinds. In 7 of the 20 patients the respiratory rate fell to 12 or less per minute. He pointed out that the drug should be administered with caution, if at all. No measurements of intracranial pressure, however, were mentioned.

METHOD OF INVESTIGATION

Thirty-two unselected consecutive patients, who had various surgical disorders and who were scheduled for spinal anesthesia, received no medication on the day of operation. There were 5 women and 27 men. The ages ranged from 32 to 82 years. A spinal puncture was performed in the third or fourth lumbar intervertebral space with a 20-gauge needle, the patient lying in the lateral recumbent position with

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the head at the same level as the lumbar spine. A spinal water manometer was attached. When the fluid reached a constant level, the initial control reading was made. Systolic and diastolic blood pressure readings were taken throughout. Morphine sulfate, 6.4, 10.6 or 16 mg., was given to 5 patients. Demerol 50, 75 or 100 mg. was given to 27 patients. Each drug was slowly injected intravenously. The dose was selected according to the age of the patients. Cerebrospinal fluid pressure and blood pressure readings were made every two or three minutes for ten to twenty minutes, depending on the time available in a busy operating

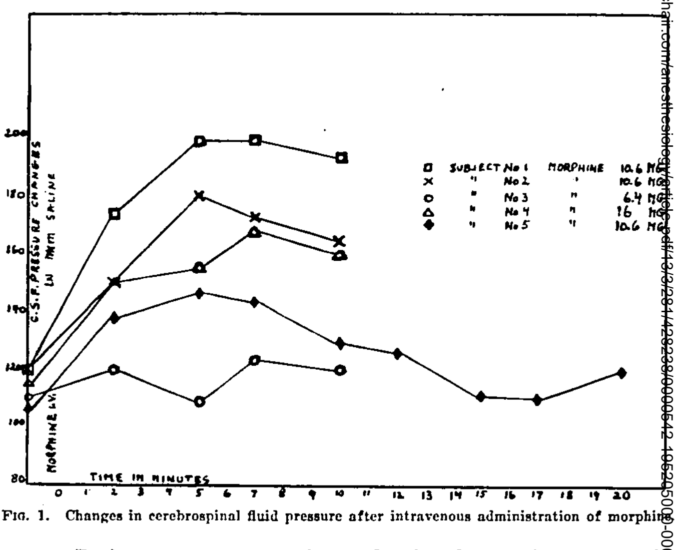

FIG. 1. Changes in cerebrospinal fluid pressure after intravenous administration of morphine.

room. Patients were cooperative and relaxed, especially after the morphine or demerol had taken effect.

RESULTS

Figure 1 shows the results obtained in the 5 patients given intravenous injections of morphine sulfate. Case 3, a 77 year old man, received 6.4 mg. of morphine. The rise of cerebrospinal fluid pressure was only 12 mm. of water. In the other 4 cases, in which 10.6 to 16 mg. was given, a rise of 40 to 82 mm. of water occurred.

In table 1 the data on the 27 patients who were given demerol are summarized.

TABLE 1

Cerebrospinal Fluid Pressure and Blood Pressure After Injection of Demerol

Expt. No.	Sex	Age	‖Demerol, mg.	Control Values		After 2 Min.		After 5 Min.		After 7 Min.		After 10 Min.		Percentage Elevation, Per Cent
				CSF, mm. H_2O	BP, mm. Hg	CSF, mm. H_2O	BP, mm. Hg	CSF, mm. H_2O	BP, mm. Hg	CSF, mm. H_2O	BP, mm. Hg	CSF, mm. H_2O	BP, mm. Hg	
1	M	71	50	64	184	70	200	82	200	90	200	86	200	40.6
2	M	77	50	82	170	104	168	102	160	94	144	94	144	26.8
3	M	75	50	96	160	96	160	86	150	106	150	118	140	23.9
4	M	66	50	120	170	100	—	110	190	118	—	120	170	0.0
5	M	77	75	76	160	68	160	66	165	78	155	87	140	14.4
6	M	66	75	160	120	164	130	162	150	162	150	168	150	5.0
7	M	71	75	105	130	100	130	106	120	110	—	106	130	4.7
8	M	62	75	204	140	228	130	216	130	220	—	226	120	23.0
9	F	76	75	176	150	220	154	260	170	290	170	250	170	64.2
10	F	66	75	158	135	144	120	170	130	180	120	200	125	26.5
11	M	65	75	146	150	170	150	202	150	240	144	230	138	64.3
12	M	75	75	152	240	166	240	196	240	158	220	172	220	28.9
13	M	82	75	40	120	33	120	64	105	68	105	64	120	70.0
14	M	77	75	62	175	52	185	56	180	56	168	53	170	Decrease
15*	M	76	75	140	170	178	120	190	160	220	145	208	150	57.0
16*	M	77	75	145	120	140	120	160	120	180	120	182	130	28.9
17	M	49	100	152	130	150	145	230	150	290	160	260	155	90.7
18	M	46	100	206	190	218	185	242	185	249	170	244	160	20.8
19	M	66	100	120	140	126	134	134	136	168	140	166	138	40.0
20	F	33	100	140	115	164	112	220	112	260	108	258	110	85.7
21	M	33	100	218	140	238	136	266	136	264	130	262	130	22.0
22	M	74	100	134	130	190	125	214	125	158	125	138	125	59.7
23	M	60	100	68	110	52	125	66	120	90	—	82	105	32.3
24	F	40	100	185	180	220	175	200	180	235	185	236	175	27.5
25**	M	63	100	108	120	162	120	164	120	194	120	192	120	79.6
26**	F	47	100	90	100	110	120	140	120	142	120	130	120	57.7
27**	M	40	100	130	110	136	110	154	110	170	110	170	110	30.7

* In Cases 15 and 16, twenty minutes after injection of 75 mg. of demerol, the cerebrospinal fluid pressure had decreased to 148 mm. and 174 mm. of water and the blood pressure to 140 mm. and 120 mm. of mercury, respectively.

** In Cases 25, 26 and 27, twenty minutes after injection of 100 mg. of demerol, the cerebrospinal fluid pressure was 132 mm., 100 mm. and 170 mm. of water and the blood pressure reading was 120 mm., 120 mm. and 110 mm. of mercury, respectively.

Four patients were given 50 mg. of demerol. In 3 cases, the cerebrospinal fluid pressure increased from 22 to 26 mm. of water, with an average of 25.3 per cent.

Twelve patients were given 75 mg. of demerol. In one case the cerebrospinal fluid pressure decreased 10 mm. of water. In the other 11 cases the pressure rose from 1 to 114 mm. of water. In 3 cases the rise was over 80 mm. of water. The average rise was 31.4 per cent.

Eleven patients were given 100 mg. of demerol. In all 11 cases, the cerebrospinal fluid pressure rose from 22 to 120 mm. of water. In 4 cases the rise was over 80 mm. of water. The average rise was 49.8 per cent.

Figure 2 demonstrates that the average pressure rise of the cerebrospinal fluid is directly related to the dose administered.

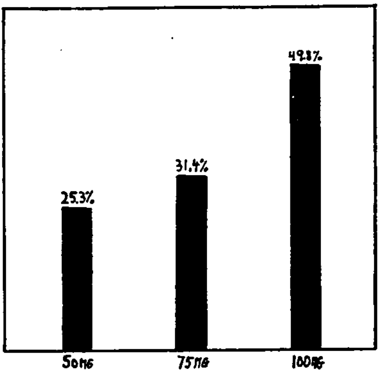

FIG. 2. Average changes of cerebrospinal fluid pressure after injection of demerol.

Figure 3 shows measurements of cerebrospinal fluid pressure up to twenty minutes after the administration of demerol. The peak of the rise occurred five to seven minutes after its administration. After this time an adjustment took place and, although the pressure did not return to its original level after twenty minutes, a tendency to return to the original level was observed.

Another observation of interest is that there was no correlation between the blood pressure readings and changes in the cerebrospinal fluid pressure. In the doses of demerol and morphine employed in this investigation, the systemic blood pressure remained unchanged, rose or fell slightly. This supports the view of Browder and Meyers (6), who have shown clinically and experimentally that there is no relationship between the cerebrospinal fluid pressure and systemic blood pressure unless the level of the former reaches the diastolic or mean blood pres-

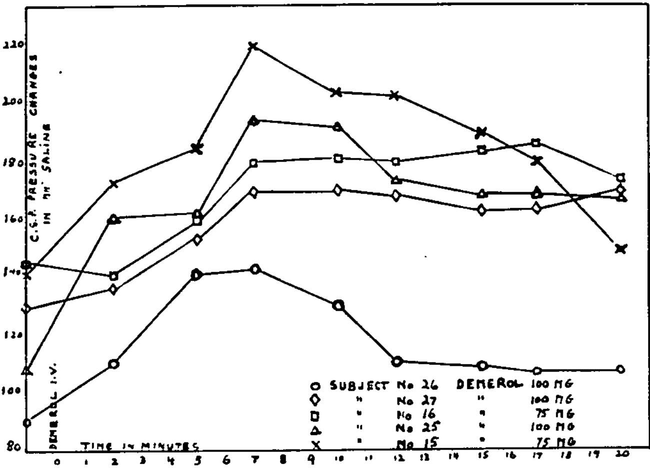

FIG. 3. Changes in cerebrospinal fluid pressure after intravenous administration of demerol.

sure, and of Evans et al. (7), who recently stated that intracranial pressure rise does not increase the blood pressure but that cerebral blood flow becomes adjusted through reflex dilatation of intracranial vessels.

DISCUSSION

From the preceding investigation it can be seen that the cerebrospinal fluid pressure became elevated after administration of demerol. Of the 27 cases investigated there was a rise in 25. If small doses were used, the pressure rise was not impressive. Textbooks on anesthesiology (8) warn against the use of morphine in intracranial diseases accompanied by increased intracranial pressure. From the results shown, demerol may be added to this list. It may also be concluded that the amount injected is directly related to the rise of the cerebrospinal fluid pressure. Further investigations on a larger scale are warranted in view of the wide usage of the drug, the increasing scope of neurosurgery, and the large number of head injuries treated in combat zones.

SUMMARY

After demerol was injected intravenously into 27 human subjects, cerebrospinal fluid pressure and blood pressure readings were taken for ten to twenty minutes.

The cerebrospinal fluid pressure rose in 25 of 27 cases. There was no significant influence on the blood pressure with the dosage employed

and during the time investigated. The amount of demerol injected was directly related to the rise of cerebrospinal fluid pressure.

Morphine used in a like manner gave results similar to those with demerol.

This property of demerol of raising the cerebrospinal fluid pressure should be considered and the drug used with caution or avoided altogether in patients who have intracranial diseases which are accompanied by elevation of intracranial pressure or in which a rise in cerebrospinal fluid pressure is undesirable.

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ANNUAL MEETING OF THE AMERICAN MEDICAL ASSOCIATION

CHICAGO, ILLINOIS—JUNE 9–13, 1952

SCIENTIFIC EXHIBITS

The Scientific Exhibits on anesthesiological subjects which will be presented at the Annual Meeting of the AMA in Chicago are listed below:

Continuous Measurement of CO_2 Concentrations During Anesthesia.
James O. Elam, Raymond H. Ten Pas, Elwyn S. Brown, and Douglas W. Eastwood, Washington University School of Medicine and Barnes Hospital, St. Louis.

Mobile Anesthesia Unit for Field Use.
Lieut. Col. Fred C. Dye, USAF (MC), Sampson Air Force Base, Geneva, N. Y.

Accidents and Complications of Local Anesthesia.
John Adriani and John Parmley, Louisiana State University Medical School and Charity Hospital, New Orleans, La.

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