SPINAL ANALGESIA WITH SOLUTIONS OF PROCAINE AND EPINEPHRINE

A PRELIMINARY REPORT OF 108 CASES *

MAHLON D. PRICKETT, M.D., E. G. GROSS, M.D., AND STUART C. CULLEN, M.D.

Iowa City, Iowa

ONE of the significant disadvantages of procaine for spinal anesthesia is its relatively short duration of action. Repeated injections of procaine or the use of longer acting and more toxic agents is necessary to insure anesthesia for extended procedures. It is a well established fact that epinephrine prolongs the action of procaine used for infiltration and regional anesthesia. It seemed worth while to investigate the possibilities of epinephrine-procaine combinations introduced intrathecally as a means of prolonging spinal analgesia.

In 1911 Owen Richards (1) reported the use of suprarenin borate with procaine in normal saline solution intraspinally in three cases. He stated that the anesthesia lasted one and one-half hours. The mixture was:

Suprarenin borate	0.000325 Gm.
Procaine	0.15 Gm.
Normal saline	3.0 Gm.

He also reported 381 cases in which he used a similar vehicle for stovaine. It was his belief that the suprarenin prolonged and intensified the spinal anesthesia. Freeman Allen (2), in 1911, reported before the New York Society of Anesthesia that intrathecal adrenalin made the spinal anesthesia of his day safe. Pitkin (3), in a paper presented at a joint meeting of anesthesia societies in Philadelphia in 1939, offered a new solution to prolong spinal anesthesia. This new solution contained a "non-oxidizing epinephrine with a subarachnoid capacity control." Each ampule of the solution contained:

Suprarenin	0.00036 Gm.
Ephedrine HCl	0.050 Gm.
Gliadin acetate	0.010 Gm.
Procaine	0.3 Gm.
Alcohol	0.7 Gm.
Aqua dist. q.s.	6.0 Gm.

The specific gravity of this mixture was 0.983. A heavy solution with a specific gravity of 1.025 was made by partial substitution of water by glucose. Pitkin stated that the gliadin acetate had glue-like properties.

* From the Division of Anesthesiology, Department of Surgery and the Department of Pharmacology, State University of Iowa College of Medicine, Iowa City, Iowa.

and when it came in contact with the spinal fluid, it precipitated and formed a semipermeable osmotic membrane between the spinal anesthetic mixture and the spinal fluid. This viscous property of the gliadin acetate furnished a molecular protection for the suprarenin against systemic oxidation. The membrane synchronized the liberation of the suprarenin, ephedrine, and the anesthetic drug. The ephedrine was used to synergize the suprarenin. Pitkin claimed that the epinephrine would be oxidized as readily as if it were injected into the blood stream if the "subarachnoid capacity control" with the membrane was not present. de la Pena (4) reported lengthening of duration of procaine spinal anesthesia with intrathecal epinephrine in 1–10,000 dilution. Barker (5) believes that it is inadvisable to inject epinephrine intrathecally because it causes ischemia of the nerve roots.

This experimental study was begun in 1940 by Weir * and one of us (E. G. G.). A solution of 1 per cent procaine with epinephrine in a dilution of 1–100,000 was introduced intrathecally in a number of rabbits. The procaine-epinephrine combination produced a 60 per cent increase in length of action of the spinal anesthesia. In the current project, dogs were selected in preference to rabbits for the experimental animals because it is difficult to secure spinal fluid from the rabbit's spinal dural sac and damage to the cord from the needle is more frequent in the rabbit than in the dog. Twelve dogs were given spinal anesthesia with procaine-normal saline and procaine-epinephrine-normal saline combinations in an attempt to determine the duration of anesthesia and the effect of the epinephrine on the spinal fluid cell count and protein level. Five milligrams per kilogram of a 5 per cent solution was used and the anesthesia was considered terminated when the animal could stand unsupported. The dogs were injected with procaine in normal saline and a week later were reinjected with procaine in normal saline solution to which was added epinephrine in dilutions of 1–30,000 and 1–50,000. There was a 60 per cent average increase in the duration of the spinal analgesia with the solutions containing epinephrine. There was no evidence of permanent or temporary damage to the spinal cord or nerve roots in any of the animals. Cell counts and protein determinations gave no indication of untoward response to the solutions containing the epinephrine.

Clinical Results

The clinical cases were unselected, and ranged in age from 15 to 8[illegible] years. Sixty-seven patients were given the procaine-epinephrine mixture in normal saline solution. Procaine crystals, sufficient to make a 10 per cent solution, were dissolved in normal saline solution containing epinephrine in a dilution of 1–30,000. Ringer's solution was used instead of saline in a few cases. In 38 patients, the procaine and epinephrine were mixed directly with the spinal fluid. Enough spinal fluid was

* Now Director Anesthesia, Baylor Hospital, Dallas, Texas.

withdrawn to make a 10 per cent procaine solution to which was added a quantity of epinephrine sufficient to make a dilution of 1–10,000. The normal saline was omitted from the latter solution and the epinephrine concentration increased because it was felt that the 1–10,000 epinephrine dilution was safe and it was more convenient to make this dilution directly in the spinal fluid.

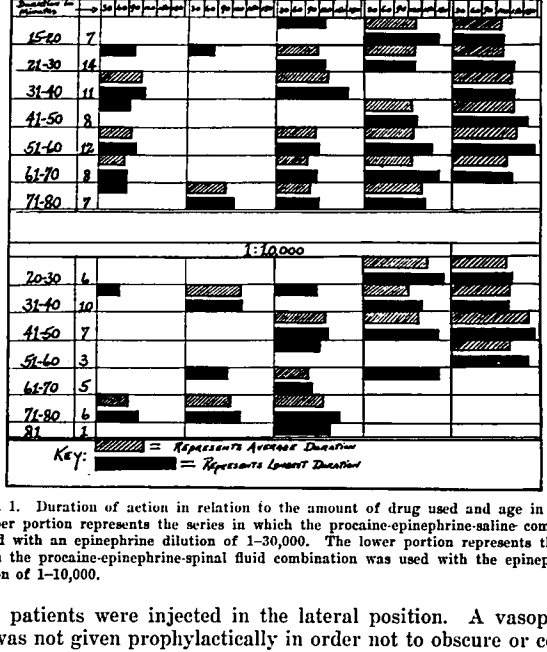

FIG. 1. Duration of action in relation to the amount of drug used and age in decades. The upper portion represents the series in which the procaine-epinephrine-saline combination was used with an epinephrine dilution of 1–30,000. The lower portion represents the series in which the procaine-epinephrine-spinal fluid combination was used with the epinephrine in a dilution of 1–10,000.

All patients were injected in the lateral position. A vasopressor drug was not given prophylactically in order not to obscure or confuse any such action of epinephrine injected intrathecally. The patient was turned to the supine position immediately after injection. Frequent blood pressure readings were taken and the dermatome level determined. In those cases in which the procaine and epinephrine were dissolved in normal saline or Ringer's solution, it was usually necessary to lower the head of the table 10 degrees in order to facilitate cephalad distribution of the anesthetic. The table was left in this position until the desired level was obtained. It was unnecessary to lower the head

when the procaine-spinal fluid-epinephrine combinations were used. The rate of injection with either combination was faster than that used with procaine alone in spinal fluid, and barbotage was not employed. The continuous technic was not used. The amount of procaine used depended on the estimated time of anesthesia required. It was anticipated that the epinephrine would add 60–70 per cent time to the action of the procaine. Sensory paresis was judged to have terminated if

	1:30,000				
Amount of Drug (Mg.)	50	75	100	150	200
Sensory Level Above T6	2	0	3	7	11
Region of Operation	Perineum Thigh Leg	Thigh Leg	Lower Abdomen Thigh	Lower Abdomen	Lower Abdomen
Hypotension During Anesthesia Moderate	0	1	4	7	6
Severe	0	0	0	1	0
Nausea and Emesis During Anesthesia	0	0	1	8	6
Post-Operative Complications					
Headache	0	0	0	0	1
Retention	1	0	6*	6	3
Parasthesias	1	0	1	0	0
Paralyses	0	0	0	0	0
Pulmonary Edema	0	0	0	0	0
Deaths					
Respiratory	0	0	0	0	0
Circulatory	0	0	0	0	0

FIG. 2. The sensory levels obtained, the site of the operation, the hypotension during anesthesia, and the complications during and after anesthesia are shown in the series in which the procaine-epinephrine-saline mixture was used with the epinephrine in a dilution of 1–30,000.

* Patient was 75 years old. Had prostatic hypertrophy. Was catheterized for 33 days.

during surgery it was necessary to supplement the spinal anesthesia with some other agent and technic or at that time after the surgical procedure when the patient could feel pin pricks in the leg.

The onset of anesthesia was observed to be longer and the ascent of the analgesia was more gradual with the procaine-epinephrine mixtures than with procaine alone. Eighteen of the 67 patients in whom the procaine-epinephrine-saline mixture was used received supplemental

anesthesia either because of failure to obtain sufficient height of the analgesia or because the analgesia had terminated. Only 3 patients in whom the procaine-epinephrine-spinal fluid mixture was used required supplemental anesthesia. Figure 1 reveals the duration of the analgesia in relation to the amount of procaine used and to the ages in decades. Figures 2 and 3 show the sensory levels obtained, the site of the operations, and the anesthetic and postanesthetic complications with

1:10,000					
AMOUNT of DRUG (MG.)	50	75	100	150	200
SENSORY LEVEL ABOVE T6	0	0	0	4	2
REGION of OPERATION	THROUGH THIGH LEG	THIGH LEG	LOWER ABDOMEN THIGH	LOWER ABDOMEN	LOWER ABDOMEN
HYPOTENSION DURING ANESTHESIA, MODERATE	1	0	3	3	3
SEVERE	0	0	0	0	0
NAUSEA AND EMESIS DURING ANESTHESIA	1	0	3	5	4
POST-OPERATIVE COMPLICATIONS					
HEADACHE	0	0	0	0	0
RETENTION	0	0	3*	7	3
PARASTHESIAS	0	0	0	0	0
PARALYSES	0	0	0	0	0
PULMONARY EDEMA	0	0	1	0	0
DEATHS					
RESPIRATORY	0	0	1**	0	0
CIRCULATORY	0	0	0	0	0

FIG. 3. The sensory levels obtained, the site of the operation, the hypotension during anesthesia, and the complications during and after anesthesia are shown in the series in which the procaine-epinephrine-spinal fluid mixture was used with the epinephrine in a dilution of 1–10,000.

* Patient was 80 years old. Had prostatic hypertrophy. Was catheterized for 2 weeks.

** Patient was given blood transfusion 24 hrs. postoperatively. Died immediately following.

the different dilutions of epinephrine. The few patients in whom Ringer's solution was substituted for saline showed no prolongation in duration of action of procaine over that obtained with procaine-saline-epinephrine mixtures.

Figure 2 shows that in 18 patients in the series in whom procaine-epinephrine-saline solutions were used moderate hypotension developed

(20–30 per cent below the mean pressure). Two patients exhibited a drop after five minutes, 8 developed the hypotension after fifteen minutes, 3 showed drops in pressure after twenty-five minutes, and 3 showed no drop in pressure until after thirty-five minutes. One severe drop in pressure (40 per cent below the mean pressure) occurred fifteen minutes after the introduction of the drugs.

Figure 3 shows that in 10 patients in the series in whom procaine-spinal fluid-epinephrine mixtures were used moderate hypotension developed after the introduction of the agents. In 1, hypotension developed after five minutes, in 5 after fifteen minutes, in 2 after twenty-five minutes, and in 1 it did not develop until after thirty-five minutes. The hypotension was satisfactorily controlled in both series by the intravenous administration of ephedrine. In neither series was there a pronounced elevation in blood pressure following the introduction of the epinephrine.

Twenty-eight patients suffered nausea during anesthesia and there appeared to be no appreciable difference in its incidence between the two series. The nausea was successfully controlled by treating the hypotension and administering 100 per cent oxygen. Significant intercostal paralysis did not develop in any case.

Moderate headache occurred after anesthesia in one case. The headache disappeared after two days of conservative treatment. Fifteen patients in the series in which a 1–30,000 dilution was used had to be catheterized for approximately forty-eight hours after anesthesia. Severe retention occurred in a man 75 years old and it was necessary to catheterize him for thirty-three days. Thirteen patients in whom the 1–10,000 dilution was used had retention postoperatively and were catheterized once or twice. One man, 80 years old, had retention requiring catheterization for fourteen days.

Paresthesia, consisting of burning and itching of the skin, appeared in one case. It was of short duration and required no therapy. No temporary or permanent paralysis was found. There were no major or minor respiratory complications in these series. One death occurred in the postoperative period after a transfusion which precipitated pulmonary edema.

SUMMARY

Epinephrine added to the procaine solution injected intrathecally does not seem to be absorbed into the blood stream in sufficient concentration to exert its vasopressor effect but it apparently acts to delay the systemic absorption of procaine. In the concentrations used, epinephrine does not seem to cause any temporary or permanent spinal cord or nerve root damage. It does, however, produce definite and impressive prolongation of the analgesia when introduced intrathecally in combination with procaine.

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3. Pitkin, Geo. P.: A Nonoxidizable Epinephrine to Prolong Spinal Anesthesia with a Sub-arachnoid Capacity Control, Anesth. & Analg. 19: 241–260 (Sept.–Oct.); 19: 315–335 (Nov.–Dec.) 1940.
4. de la Pena, Adalberto: Personal communication.
5. Barker, Arthur: Experiments with Spinal Analgesia in Reference to 2,354 Cases, British M. J. 1: 597–602 (Mar. 16) 1912.

MEETING OF THE AMERICAN SOCIETY OF ANESTHESIOLOGISTS, INC.

NEW YORK ACADEMY OF MEDICINE

FIFTH AVENUE AT 102ND STREET, NEW YORK CITY

OCTOBER 11, 1945

Business Session: 8:15 P.M.

Scientific Session: 8:30 P.M.

"Postmortem Examination in Deaths Attributed to Anesthetics." 20 minutes.

By George Kendall Higgins, M.D., Ph.D., Professor of Pathology, New York Medical College.

"Operating Room Deaths: Case Reports." 30 minutes.

By Harold F. Bishop, Major, M.C., Halloran General Hospital, New York.

Film: "The Upright Operating Position Using the "Craig Head Rest' and Inhalation Anesthesia." 25 minutes.

Harold F. Bishop, Major, M.C.