

INTRAVENOUS PROCAINE: ITS EFFECT ON LIVER FUNCTION IN MAN AS DETERMINED BY THE CEPHALIN FLOCCULATION TEST *

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Received for publication January 13, 1949

INTRAVENOUS procaine is rapidly assuming a commonplace role in medical therapy owing to its safety and simplicity of administration. It has been used in a variety of conditions, such as tinnitus aurium (1), pruritus associated with jaundice (2), postoperative embolism (3), burns (4), postoperative pain (5), epinephrine-induced ventricular fibrillation occurring during cyclopropane anesthesia (6), asthma (7), serum sickness (8), obstetrics (9), acute trauma, arthritis (10), anesthesia (11) and in combination with sodium pentothal for anesthesia (12).

Serious toxic effects are conspicuous by their absence. McLachlin (5) mentioned a rare idiosyncrasy which may give rise to toxic symptoms of two types: a nervous convulsive type which is easily controlled by intravenous barbiturates, and a respiratory asthmatic type that can be relieved by 2 minims of 1 to 1000 epinephrine subcutaneously. Waldbott (13) warned against the danger of sensitization to procaine. He also mentioned a near fatality, allergic in nature (14). Tetany (12), the preconvulsive stage of procaine toxicity, has been produced, but in all of these cases a 1 per cent solution was used. Graubard (10) saw two instances of momentary unconsciousness. Some hazard (15) does exist to patients who receive repeated injections.

LIVER FUNCTION

Jacoby et al. (16), in an extensive review of the literature, found that the liver was the principal organ involved in the detoxification of procaine. Their study on rats, dogs, and human beings indicated that liver function is not altered by procaine as determined by the brom-sulfalein and hippuric acid excretion methods. Graubard (10), who gave over 2000 multiple intravenous infusions with procaine, submitted 5 of his patients to Bruger of the Post-Graduate Hospital, New York,

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for a study of the blood chemistry in patients receiving intravenous procaine. Their conclusions were, "no significant alteration in any of the chemical constituents of the blood were noted. . . . It would appear safe to state at this time that procaine administered intravenously twice weekly over a period of one month in the doses indicated has no measurable effect on renal or hepatic function, nor does it alter the sugar or cholesterol content of the blood or the rate of sedimentation of the red cells."

A study of the effect of multiple intravenous procaine infusions on liver function in man as determined by the cephalin flocculation test was undertaken by me. The results will be reported in this paper.

METHOD OF STUDY

Ambulatory and bed patients on the orthopedic ward who were constantly complaining of pain were given a cephalin flocculation test (Hanger flocculation test) and a phenolsulfonphthalein test prior to receiving a course in intravenous procaine therapy. It was my plan to determine kidney function as well as liver function, but the determination of the kidney function by the phenolsulfonphthalein method proved unsatisfactory. As soon as the above tests were completed the patients either walked or were brought to the operating room at 2 p.m.

TABLE I
EFFECT OF REPEATED INTRAVENOUS INJECTIONS OF PROCAINE HYDROCHLORIDE ON THE LIVER FUNCTION IN MAN AS DETERMINED BY THE CEPHALIN FLOCCULATION TEST AND CLINICAL RESULTS

Patient	Age, years	Disease	Cephalin Flocculation Test Before Therapy	Cephalin Flocculation Test After First Course of Therapy	Cephalin Flocculation Test After Second Course of Therapy	Results
1. E. H.	50	Rheumatoid Arthritis	Negative	Negative	Second Course 2 wks. Negative	Marked Improvement. Discharged from hospital.
2. R. S.	40	Rheumatoid Arthritis	Negative	Negative	Second Course 3 wks. Negative	Marked Improvement. Discharged from hospital.
3. H. B.	40	Herniated Intravertebral Disk	Negative	Negative	Second Course 3 wks. Negative	Marked Improvement. Discharged from hospital.
4. G. J.	60	Acute Bursitis Iliopsoas Muscle	Negative	Negative	Second Course 4 wks. Negative	Marked Improvement. Discharged from hospital.
5. E. D.	59	Rheumatoid Arthritis	Negative	Negative	Second Course 4 wks. Negative	Improved.
6. F. B.	58	Osteoarthritis of Spine	Negative	Negative	Second Course 2 wks. Negative	Failed to Improve.

twice weekly. They were permitted to lie quietly and as comfortably as they could for fifteen to thirty minutes. The blood pressure and the pulse were recorded. They were recorded again every ten minutes during therapy and ten minutes after the treatment. The amount of procaine employed was based on the procaine unit set forth by Graubard et al. (17). At the end of eight infusions, the liver and kidney tests were repeated. Since the patients manifested neither ill-effects nor improvement clinically and by laboratory tests, it was considered safe to double the dose of procaine. The patients were given 8 mg. of procaine per kilogram of body weight in twenty minutes. The infusions were given twice weekly and continued for two to four weeks.

Liver and kidney tests were repeated. An attempt was made to observe objectively mild and severe response during the flow of procaine.

RESULTS

Table 1 shows that liver function, as determined by the cephalin flocculation test in 6 patients, was not affected by intravenous procaine after two courses of therapy. Clinical improvement was noted in 5 patients and 4 of these patients were discharged as markedly improved. Nine other patients were to be included, but they left the hospital before the studies were completed.

COMMENT

A plan was devised to study the liver and kidney function of 15 ambulatory, wheelchair, and bed-ridden patients. Nine patients left the hospital before the studies were completed. The kidney function test, as determined by the phenolsulfonphthalein method, proved unsatisfactory. Six patients who completed the major portion of the study proved to have normal liver function after the therapy, as determined by the cephalin flocculation test. The blood pressure and the pulse were not affected at any time in any patient receiving treatment.

Toxic manifestations were noticeably absent. Patients often felt warm and were slightly flushed. They looked comfortable and dozed off to sleep. The patients complained of dizziness if the rate of flow was increased rapidly. I could not distinguish between mild and severe responses. I was guided by the voluntary remark of "dizziness" as a warning sign to slow the rate of flow. No infusion was discontinued, although I have given only 100 injections.

In order to give procaine intravenously, it is mandatory that patients have good veins for venipuncture. I have found the 19-gauge needle well suited for my purpose. On one occasion it was necessary to use a 20-gauge needle and to preserve carefully two small veins on the dorsum of the hand.

The patients were despondent, because of the length of their illness, the constant pain, and the lack of ability to move about in comfort.

They had been subjected to many forms of treatment previously without much help. They were sceptical of this new treatment. They soon noticed, however, that they could withstand physical therapy if intravenous procaine was given immediately preceding manipulations. This ability to withstand physiotherapy led to rapid improvement in motion, and they were able to get about in comfort. The psychological effect was dramatic and permitted patients to leave the hospital.

SUMMARY

Six patients received two courses of intravenous procaine therapy and showed no evidence of impaired liver function as determined by the cephalin flocculation test.

REFERENCES

1. Lewy, R. B.: Treatment of Tinnitus Aurium by the Intravenous Use of Local Anesthetic Agents, *Arch. Otolaryng* **25**: 178-183 (Feb.) 1937.
2. Lundy, John S.: *Clinical Anesthesia*, Philadelphia, W. B. Saunders Co., 1942, chap. 10, pp. 365-393; chap. 21, pp. 560-586.
3. Funck-Brentano, P.; Bourdin, J., and dos Gholl, J.: Intravenous Novocaine for Post-operative Embolism, *Mem. Acad. de chir.* **68**: 438-456 (Nov.-Dec.) 1942.
4. Gordon, R. A.: Intravenous Novocaine for Analgesia in Burns, *Canad. M. A. J.* **49**: 478-481 (Dec.) 1943.
5. McLachlin, J. A.: The Intravenous Use of Novocaine as a Substitute for Morphine in Postoperative Care, *Canad. M. A. J.* **52**: 383-386 (April) 1945.
6. Burstein, C. L.: Treatment of Acute Arrhythmias during Anesthesia by Intravenous Procaine, *Anesthesiology* **7**: 113-121 (March) 1946.
7. Durieu, H. F.; DeClereq, F., and Duprez, A.: Treatment of Asthma with Intravenous Administration of Procaine Hydrochloride, *J. A. M. A.* **133**: 729 (March 8) 1947.
8. State, D., and Wangenstein, O. H.: Procaine Intravenously in Treatment of Delayed Serum Sickness, *J. A. M. A.* **130**: 990-995 (April 13) 1946.
9. Allen, F. M.: Intravenous Obstetrical Anesthesia, *Am. J. Surg.* **70**: 283 (Dec.) 1945.
10. Graubard, D. J.; Robertazzi, R. W., and Peterson, M. D.: Intravenous Procaine: A Preliminary Report, *New York State J. Med.* **47**: 20 (Oct. 15) 1947.
11. Allen, F. M.; Crossman, L. W., and Lyons, L. V.: Intravenous Procaine Analgesia, *Anesth. & Analg.* **25**: 1-9 (Jan.-Feb.) 1946.
12. Fraser, R. J.: Intravenous Procaine Analgesia, *Anesth. & Analg.* **27**: 159-163 (May-June) 1948.
13. Waldbott, G. L.: So-Called Thymic Death. V. Respiratory Sensitization to General and Local Anesthetics, *Arch. Otolaryng* **17**: 547 (April) 1933.
14. Waldbott, G. L.: Procaine for Urticaria from Penicillin, *J. A. M. A.* **133**: 1301 (April 26) 1947.
15. Queries and Minor Notes, *J. A. M. A.* **137**: 1568 (Aug. 21) 1948.
16. Jacoby, J. J.; Coon, J. M.; Woolf, M. P.; Salerno, P. R., and Livingstone, M. D.: Effect of Procaine on Liver Function: An Experimental and Clinical Study, *Anesthesiology* **9**: 481-489 (Sept.) 1948.
17. Graubard, D. J.; Robertazzi, R. W., and Peterson, M. D.: Microdetermination of Blood Levels of Procaine Hydrochloride after Intravenous Injection, *Anesthesiology* **8**: 236-240 (May) 1947.