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The Use of efocaine in the control of episiorrhaphy pain

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INTRODUCTION

Perineal pain following episiorrhaphy is a frequent postpartum complaint and a source of annoyance to both the patient and the obstetrician. The rationale and indications for episiotomy are well founded, and the advantages of both mother and infant widely recognized (1).

The operation may be carried out with either a median or mediolateral incision, the mediolateral being used most commonly as it best protects the anal sphincter. The type of repair carried out has been postulated as a possible cause for the persistent postpartum perineal discomfort, but the results achieved by the various suggested episorrhaphies have not been highly successful (2-4).

Local infiltration of an anesthetic-oil solution for the control of episiorrhaphy pain was suggested by Hunter in 1939 (5). However, Kelly (6) proved the failure of the anesthetic-oil solution and demonstrated that any prolonged anesthetic effect observed was due to neurodegeneration caused by the benzyl alcohol which was combined with the oil solvent. The period of anesthetic action was limited to the period of regeneration of the nerve fibers instead of being due to the pharmacologic

activity of the preparation.

Recent reports have described a newly developed long-acting local anesthetic, efocaine, which has been used with a high degree of success in the control of postepisiotomy pain and other postoperative wound pain. The purpose of this report is to review toxicity studies (7), anesthetic properties (7-8), histiopathologic studies (7-10) and to present sufficient clinical evidence to evaluate the efficiency and desirability of efocaine as a long acting local anesthetic for use in control of episiorrhaphy pain.

LABORATORY INVESTIGATION

Chemical and physical properties of efocaine.

The active ingredients of efocaine are procaine (1 per cent), procaine hydrochloride (0.25 per cent), and butyl-p-aminobenzoate (5 per cent). The solvent is a mixture of polyethylene glycol-300 (2 per cent) and propylene glycol (78 per cent), with sodium metabisulfite (0.1 per cent) and phenyl mercuric borate (1:25,000) added for preservative action.

This anesthetic solution has been shown (11) to produce effective anesthesia for from 6 to 12 days. The rationale for the prolonged effect of efocaine is based upon the pharmacological fact that water-insoluble and slowly absorbed agents produce a sustained effect. This has been demonstrated by the well known use of the hormone implants and the suspension of certain antibiotics. The anesthetic bases are insoluble in water and are slowly absorbed. Efocaine contains two of these bases, namely 5 per cent butyl-p-aminobenzoate and 1 per cent procaine base. These are soluble in the non-toxic aqueous miscible solvents, propylene glycol and polyethylene-glycol 300 (12-14). The latter acts a protective polymer to stop decomposition (15). When this solution is diluted with aqueous fluids (serum, lymph

or extracellular fluid) the anesthetic agents deposit in a crystalline form. After injection of efocaine a drug depot is formed which is then slowly absorbed to elaborate the anesthetic action over an extended period (16).

Toxicity

The mouse toxicity of efocaine can not be entirely determined on the basis of the 1 per cent procaine base and 0.25 per cent procaine hydrochloride present, since according to the formula, 5 per cent butyl-p-amminobenzoate is also present. The toxicity of butyl-p-aminobenzoate has been found to be quite high when compared to procaine hydrochloride (17). The amount of procaine base and procaine hydrochloride contained in efocaine is far below the MLD_{50} found in toxicity studies for these two compounds.

A determination of the toxicity of several of the long acting local anesthetics was made by Downing (7).

Mouse toxicity test.

The MLD_{50} was determined by using test groups of 30 mice until a dosage was found that would consistently kill 50 per cent of the animals. The MLD_{50} is defined as the number of mgs. of a compound per kilogram that when injected subcutaneously, will kill half of the test

group. The toxicity ratios were determined according to the following formula:

$$\text{Ratio} = \frac{\text{M.L.D. of drug}}{\text{M.L.D. of Procaine HCL}}$$

The MLD_{50} with efocaine was found to be 11 mgs. procaine, 44 mgs. butyl-p-aminobenzoate as compared to a MLD_{50} of 700 mgs. of procaine HCL. The approximate toxicity ratio was found to be 0.015 when compared with procaine hydrochloride.

Intravenous toxicity.

In dogs it was reported that with intravenous injection of increasing dosage of efocaine there was usually a slight increase in the amplitude of respiration which was then followed by a decrease in amplitude and rate. Blood pressure was depressed. Four ml. had a marked effect on both respiration and blood pressure, while 5 ml. caused respiratory arrest and drop in blood pressure followed shortly by cardiac arrest and death of the dog. On the basis of the 3 component anesthetic drugs contained in efocaine, toxic doses were found to be as follows: 21 mgm. per kilogram of butyl-p-aminobenzoate, 5 mgm. per kilogram of procaine base, and 1.5 mgm. per kilogram of procaine hydrochloride.

Efocaine was also injected into the ear veins of 2 Kg. rabbits. Intravenous injections of one and one-

half ml. resulted in respiratory paralysis, collapse and death before convulsions had time to develop. The convulsive dose of procaine hydrochloride was in the range of 60 mg. per kilogram of body weight in the rabbits. Procaine base suspension was relatively non-toxic in that 410 mg. per kilogram were necessary to produce convulsions.

The high toxicity of efocaine as compared to procaine hydrochloride and procaine base is apparently due to the 5 per cent butyl-p-aminobenzoate present.

ANESTHETIC PROPERTIES

Conduction anesthesia involves the penetration of a nerve sheath by an anesthetic followed by paralysis of a nerve trunk. Immersion of the nerve in anesthetic solution followed by stimulation by means of a faradic current results in a motor reflex if the anesthetic is ineffective. Downing (7) found that efocaine caused prompt interruption of conduction in a minimum effective dose of 0.1 per cent of the butyl-p-aminobenzoate present as compared to a minimum effective dose of 0.75 per cent procaine hydrochloride. Preparations used were the gastrocneumius muscle of the frog immersed in a frog ringer preparation with the sciatic nerve suspended in the anesthetic solution in a separate chamber for 1 to 2 minutes.

Anesthesia of the rabbit's eye lid as a method of testing anesthetic activity of injected anesthetics was used by Downing (7). This method is also useful in studying the tissue reactions grossly by observing the conjunctival reactions. One half ml. of efocaine was injected into each lid using the other eye as a control. Approximate duration of anesthesia with efocaine as measured by eye lid reflex was found to be 32 hours as compared to 35 minutes with procaine HCL 2 per cent.

There was hyperemia and edema of the conjuctiva 24 hours after injection with efocaine which cleared in all cases in 2 to 3 days. No tissue slough was seen up to 3 weeks time.

Comparison of the duration of action of efocaine and procaine hydrochloride was made by Downing by subcutaneous injection of one ml. of efocaine into the volar aspect of one forearm and injection of one ml. of 1 per cent procaine hydrochloride into the corresponding area of the other arm on a series of 10 cases. It was reported that with the injection of efocaine there was a short period of burning of 2 to 3 minutes duration, and anesthesia occurred in a few seconds. No burning occurred with the injection of procaine hydrochloride.

Hyperemia occurred after injection of efocaine, being maximal at 24 hours and clearing by 48 hours. The injection of procaine hydrochloride caused little or no reaction.

The mean duration of anesthesia with efocaine was 14 days, maximal being 17 days and minimal duration of 4 days. The mean duration of anesthesia with 1 per cent procaine hydrochloride was 25 minutes, maximal being 40 minutes and minimal duration of 20 minutes.

Ansbro (8) and his associates reported the duration

of anesthesia with efocaine with similar results. The mean duration of anesthesia being 14.6 days, with maximal duration of 18 days and minimal duration of 6 days. Two ml. of efocaine was injected in the inner aspect of the forearm.

TISSUE STUDIES

A study of the effects of efocaine upon nerves, muscle, skin and subcutaneous tissues of rabbits, guinea pigs and rats was made by Weinberg (9). Efocaine, 0.5 cc., was injected into the following sites: The lower lip, the skin of the sternal region, the triceps muscle and the brachial plexus. The animals were autoposied at various intervals up to ninety-eight days after injection. Gross autopsy findings up to 13 days were reported as showing some degree of fibrous reaction about the brachial plexus and the muscles showed evidence of necrosis in the line of injection. Multiple sectioning of muscle in the animals sacrificed after 89 to 98 days showed no gross abnormalities, the brachial plexus showed no evidence of perineural fibrosis and the sections through lip and sternal skin showed no abnormalities. Miscroscopic studies of the animals autopsied up to 13 days were reported as showing no definite evidence of histiologic alterations in the nerve fiber bundles, muscle sections showed necrosis and partial disappearance of muscle fibers with little or no inflammatory reaction. The section of skin and subcutaneous showed very little alteration. Microscopic studies after 89 to 98 days of nerve sections through the

brachial plexus showed no inflammatory reaction or perineural fibrosis. Only one muscle section showed a small local area of fibrous replacement of muscle fibers, the rest of the muscle sections showing no histiopathology. Sections through skins and subcutaneous tissue showed no histiopathology. There was no evidence in any of the microscopic examinations of foreign body giant cell reaction or any apparent permanent storage of efocaine at the site of injection.

Downing (7) made a similar study of the effects of efocaine upon nerves, muscles and subcutaneous tissues of rabbits, rats and dogs. One half of the rabbits and rats were sacrificed at 24 hours and the others at 7 to 14 days following injection. The dogs were sacrificed two to three weeks after injection. Dr. Morton Kulesh of the Pathology Department of the University of Nebraska College of Medicine did the microscopic studies of the tissues.

It was reported that 21 days following the perineural injection of efocaine that the nerve fiber bundles showed no histiological changes. Muscle sections 24 hours following efocaine injection showed no inflammatory reaction and the muscle sections from animals autopsied 21 days after injection showed no foreign body re-

action, but did show a few areas of chronic inflammatory infiltration in the fibrous septa between muscle bundles. Subcutaneous sections made 24 hours after efocaine injections were reported as showing several large areas of coagulation necrosis surrounded by inflammatory reaction with primarily chronic inflammatory cells. Sections of skin and subcutaneous tissues 14 days following efocaine injection were reported as showing an area of granulomatous inflammation with this area also involving the muscle layer.

Efocaine, 2 cc., was injected subcutaneously and pooled in a group of eight dogs to observe the gross effects of pooled efocaine. Ulceration at the site of injection occurred in all these animals within a few days following injection (18).

A recent report by Mannheimer and associates (10) on the effects of efocaine injection in laboratory animals is in almost direct contradiction to the above reports. It was reported that two days following the perineural injection of efocaine there was coagulation necrosis of nerve fibers, deterioration of the myelin sheath and infiltration of lymphocytes. Eleven days after intranerual injection of efocaine extreme dissociation in the nerve fibers were noted and the neurilemma

sheaths were empty. Sixty-eight days after the intraneural injection of efocaine regeneration of axis cylinders was noted. Also in contrast to former reports on the effects of proplyene glycol and polyethylene glycol (12-15) Mannheimer et al (10) reported that these agents alone, and also the mixture, caused nerve changes identical to the changes caused by efocaine.

CLINICAL INVESTIGATION

There are reports in the literature of the clinical use of efocaine to control postoperative pain following tonsillectomy, surgery of head and neck, thoracic surgery, abdominal surgery, herniorrhaphy, ano-rectal work, and in minor surgical procedures.

Allen (19) injected 3 cc. of efocaine into each tonsillar fossa on 20 tonsillectomy cases. Local pain was greatly reduced with also a decrease in the referred pain to the ears. There was no increase in the normal number of postoperative hemmorrhages and no instance of infection or abscess formation in his series.

Penn (20) reports a series of 45 tonsillectomy cases in which efocaine was injected into the anterior and posterior pillars (1 to 1.5 cc.) immediately following surgery. He reported a high degree of local pain control with anesthesia lasting from five to six days. The patients had no difficulty in swallowing and none of the usual sequelae, such as earaches. There was no interference with wound healing, no post-tonsillectomy hemmorrhages or other untoward reactions.

Iason and Shaftel (11) reported on a series of 100 patients in which efocaine was used. Their series included thyroidectomies, upper and lower abdominal surgery,

ano-rectal and vaginal surgery. Local infiltration was used for thyroidectomy, ano-rectal and vaginal surgery. Intercostal block was used for upper abdominal and para-vertebral block for lower abdominal surgery. Local anesthesia was produced for an average of 12 days. Efficient postoperative pain control was accomplished which resulted in greatly diminished narcotic requirements. There were no local reactions observed nor were there any systemic toxicities noted. Wound healing was not interferred with and the drug was well tolerated in all instances.

Deaton and Bradshaw (21) used efocaine for intercostal block on 84 thoracotomy patients with an average duration of anesthesia of approximately 15 days. Good relief of postoperative pain was obtained with a 50 per cent reduction in narcotic requirements. No complications in any way were observed. Cotton and Paulsen (22) have shown that in series of 100 patients, in which efocaine was used for intercostal block, that postoperative pain was reduced as compared to a control series of 100 patients who underwent thoracotomy but did not receive the drug. The incidence of atelectasis was much lower in patients receiving efocaine than in the control series, since postoperative pain discourages coughing which is

necessary to keep the respiratory tract open. There were no reported complications.

Bartlett and Eastwood (23) reported on a series of 38 cases in which efocaine was used for intercostal nerve block preceding upper abdominal surgery. They reported excellent relaxation of the upper abdominal muscles during surgery and subsequent anesthesia in the region of the wound, to pinprick, for a period of one to two weeks following surgery. The patients were active, turning in bed during the first few hours after leaving the operating room, and were able to get out of bed the evening of operation or the next day. Narcotic requirements during the postoperative period were greatly reduced, and less nursing care needed. The only complication reported was local pain postoperatively at the site of injection when a 3 cc. injection was used, with a dosage of 1 to 1½ cc. of the anesthetic solution there was no sebsequent pain. Puderback and Shafter (24) used efocaine for intercostal block following upper abdominal surgery. In a series of 30 cases they reported a high degree of pain relief permitting freedom of movement, deeper breathing and coughing. These patients required an average of 0.7 doses of postoperative medication as compared to 5.2 doses required by the control group.

Local anesthesia was present for a duration of from 8 to 21 days. They reported no interference with wound healing or any evidence of local or systemic toxic manifestations.

Tucker (25) reported on a series of 40 patients in which efocaine was used for local infiltration for ano-rectal surgery. The patients were followed for presence of pain, development of any local tissue reactions, presence of anesthesia and effects of wound healing throughout the convalescence. A dramatic relief of postoperative pain was reported, postoperative narcotic requirements being virtually eliminated. Local anesthesia was present for 10 days or more. Sphincter control was normal in all instances. No untoward reactions were observed. There were no local tissue reactions, sloughs or abscesses. Raicus (26) made a comparison study of efocaine and an oil anesthetic mixture on a series of 30 ano-rectal cases. He reported very little pain relief with the oil anesthetic but the efocaine gave marked relief of pain and postoperative narcotic requirements were practically nil in the efocaine group. In the efocaine group sphincter control was normal in all cases, average duration of anesthesia by skin-prick technique was approximately 13 days, and there were no tissue

reactions noted. Gross and Shaftel (27) have reported on a series of 65 cases of ano-rectal surgery and 15 cases of pruritus ani in which efocaine was used. Post-operative medication requirements of the treated group were 0.6 dose as compared to 4.63 doses required by a control group undergoing similar surgery. Local anesthesia was observed for a period of from ten days to three weeks. There were no local tissue reactions or interference with wound healing. All the patients with pruritus ani were benefited by the use of efocaine. Perrin (28) has reported on a series of 42 patients with pruritic dermatoses who were treated by local efocaine injections. Among these were 18 cases of pruritus ani, 14 cases of pruritus ani and vulvae, 8 cases of lichen simplex chronicus and 2 cases of hypertrophic lichen planus. He reported 78.6 per cent obtained complete relief, 11.9 per cent temporary relief, and 9.5 per cent had no relief. No local or systemic toxic reactions were reported.

A recent report by Turell (29) in which efocaine was used in a series of 39 hemmorrhoidectomies is not in accordance with earlier reports of its effectiveness in pain relief following ano-rectal surgery. He reports no significant decrease in the narcotic requirements be-

tween the treated group and the controls. He also reported fecal incontinence in 3 of the 39 treated cases lasting from 16 to 30 days and delay in wound healing in 10 cases. However, the delay in wound healing was not marked and he stated that "once healed the wounds remained well healed and were indistinguishable from those of the controls". He reported no instances of tissue slough or other untoward reactions in his series, but did include in his report, communications from colleagues who had witnessed instances of suppuration and necrosis in patients following the injection of efocaine.

Ansbro and associates (8) used efocaine for 25 minor surgical procedures for which local anesthesia was required. Such procedures as excision of sebaceous cysts and lipomas, excision of toe nail, parenchyma, infiltration for trauma and sprains were included. The patients were observed at regular intervals and an average of 8-9 days of anesthesia was reported. No tissue slough, abscesses, systemic toxicity or local tissue reactions were observed.

Wilson (18) carried out a research project, using several of the long-acting local anesthetics in the department of surgery at U.N.H. this past year. The local anesthetics used were efocaine, 2 per cent procaine base

and 5 per cent procaine base. A total of 119 cases were included, the following points being recorded: objective wound pain as observed by the examiner, subjective wound pain as complained of by the patient, narcotic requirements, ease of deep breathing and coughing, ease of ambulation, first day of voluntary urination and first day walking.

The floor nurses and surgical residents were not aware of which patients received the different anesthetics. The intensity of wound pain was graded by the degree of tenderness or pain to palpation in the region of the incision and the freedom with which the patient moved and coughed. This was observed daily and recorded either 4, 3, 2 or 1 plus.

TABLE I

	Efocaine	Procaine base 2%	Procaine base 5%	Control
Objective wound pain	1.36	1.25	1.38	1.32
Subjective wound pain	1.56	1.54	1.56	1.56
Ease of ambulation	2.06	2.50	2.16	2.25
Ease of deep breathing and coughing	1.81	2.54	2.39	2.40
Narcotic hypodermics	5.53	4.59	5.82	5.83
1st day of vol. urination	1.71	2.26	1.45	1.93
1st day walking	2.65	2.74	2.52	3.10

No attempt was made to select patients for any group. The operations and incisions used were nearly the same in each group.

TABLE II

Type of Incision	Efocaine	Procaine base 2%	Procaine base 5%	Control
Upper abdominal	19	11	17	20
Lower abdominal	4	2	3	3
McBurney	2	2	3	1
Inguinal	2	3	3	3
Thoracic	7	0	2	0
Hemorrhoidectomy	2	0	2	0
Lumbar Sympathectomy	2	0	1	0
Thyroidectomy	0	1	0	0

Results.

On the basis of narcotic requirements the 2 per cent procaine base patients received the least number of postoperative hypodermic injections, the efocaine patients required next lease, and there was essentially no difference between the 5 per cent procaine base patient and the control patient. Two per cent procaine base also gave the best objective and subjective pain relief, there being little or no difference between the other three groups. The ease of deep breathing and coughing and ease of ambulation was best in the efocaine group. The first day of voluntary urination was prolonged most in the 2 per cent procaine base patient. The first day of walking being prolonged most in the control group.

USE OF EFOCAINE IN CONTROL OF PAIN FOLLOWING EPISIORRHAPHY

Crisp and McDonald (30) used efocaine (6 to 8 cc.) for local infiltration to control post-episiotomy pain on a series of 74 patients and ran a control of 88 untreated patients. The effects of the drug as a means of perineal pain control are apparent from the data reported in Table III.

TABLE III

Effect of Efocaine on Postepisiotomy Pain

No. patients complaining of pain during the period of observation	Duration of perineal pain experienced (in days)	Type of episiotomy	
		Median	Medio-lateral
	TEST SERIES		
29	0	16	13
20	1	6	14
18	2	7	11
7	3	0	7
	CONTROL SERIES		
4	0	3	1
11	1	7	4
36	2	8	28
29	3	5	24
8	4	0	8

Twenty-nine of the treated patients had no pain during their hospital stay in contrast to only 4 patients in the control group who had no pain. The treated patients were ambulatory 12 to 24 hours earlier than the untreated controls and the multipara patients volun-

teered the information that the present episiotomy was not as painful as previous ones. They reported that one break down occurred in their series, but stated that it was due to the drug being placed superficially, almost directly into the incision. With the exception of the one mentioned case, they reported no evidence of gross tissue necrosis, acute inflammatory or foreign body reaction. They reported return of sensation within the expected time limits which they felt indicated no neuro-degeneration.

Cappe and Pallin (16) reported a high degree of episiotomy pain relief, with local infiltration of 6 to 12 cc. of efocaine, in a series of 94 patients. Out of this group 21 patients were injected 24 to 36 hours postpartum, these patients were incapacitated by local pain of the episiotomy, being either unable to move without severe distress or so uncomfortable as to interfere with normal nursing care. Complete and immediate pain relief followed efocaine infiltration in all these patients. In the total group anesthesia was reported present in 96 per cent of the patients for at least 3 days, 63.8 per cent for more than 5 days. They reported no local tissue reaction, systemic toxicity or interference with wound healing.

Cosgreve and Bradley (31) reported on a similar study on 200 patients, efocaine (5 to 10 cc.) used on 100 patients and the other 100 being used as a control group. The treated patients were all injected while still on the delivery table immediately following episiotomy repair. They reported that 85 per cent of the treated group experienced satisfactory relief from local pain, 67 of those treated being pain-free on the first postpartum day, as opposed to 29 of the control group, with this same pattern continuing throughout the period of observation. They reported no significant local or systemic toxic effects or interference with wound healing in the efocaine group.

Greshenfeld and Savel (32) made a study of 61 patients using efocaine for control of postepisiotomy pain. In their study they included the effects of superficial injection of efocaine to determine what might occur if the drug was inadvertently injected too superficially. In their first group of 19 patients 8 to 10 cc. of efocaine was injected subcutaneously near the skin surface and along the edges of the episiotomy. Two cases of tissue slough and one case of late suppuration occurred in this group. In the second group 5 to 9 cc. of efocaine was injected about 2 cm. from the edges of the episiotomy,

but still close to the skin surface, One tissue slough occurred in this series. In the third group of 38 patients 4 to 6 cc. of efocaine was injected about 1 to 2 cm. from the edges of the wound and deep in the perineal tissues. Three cases of induration and sloughing was reported in this group. They reported that of the total of 61 patients, 53 (87 per cent) exhibited no tenderness at all, or to deep pressure only. Only 8 patients were tender to slight pressure during the postpartum period. Except for the mentioned cases and one case where the patient exhibited a procaine allergy there were no local or systemic toxic effects.

In view of the favorable reports in the literature of the use of efocaine, it was thought worthy of trial for use in control of local pain following episiorrhaphy.

Method of study.

The majority of the patients studied were consecutive cases, half of the patients were injected and the other half followed for a control. The injections were all made immediately following the repair of the episiotomy. The episiotomy was performed by different operators and both mediolateral and median incisions were made. There were different types of episiorrhaphies conducted,

no attempt being made to keep this factor constant, since the local infiltration procedure is independent of the type of surgery. In the treated group the skin was prepared in the usual manner and an aseptic technic was carefully observed. The efocaine solution was drawn into a dry syringe to avoid precipitation of the procaine base. A long 22 gauge needle was inserted at approximately 2 cm. from the lower angle of the episiotomy and advanced at a depth of 0.25 to 0.5 inch through the subcutaneous tissue and parallel to the incision, up to the mucocutaneous junction. As the needle was withdrawn 1.5 to 2.5 cc. of the solution was slowly injected, creating a fine anesthetic line. The infiltration was repeated on the opposite side in an identical manner to completely block the episiotomy area. Care was taken to avoid too superficial or intradermal injection of the drug and to avoid pooling of the agent. In no case were any of the patients made aware of the treatment with efocaine.

A number of things have to be taken into consideration in dealing with pain. Temperament of the patient is important, some patients are stoic individuals who stand pain without too much complaint. Others are nervous individuals who complain readily of very little pain.

With this in mind the following things were taken into consideration in following patients postoperatively: subjective wound pain as complained of by the patient, objective wound pain as observed by the examiner, return of sensation (through pin prick technique) to the anesthetized area, ease of ambulation and any complications.

Results.

The total number of patients in this series was 49, the number treated with efocaine being 21 with 28 cases for a control. Patients in both groups were observed daily throughout the post partum course. The intensity of wound pain was graded by the degree of tenderness or pain to palpation in the region of the incision and the freedom with which the patient moved, and was recorded either 4, 3, 2, 1 plus, or 0 if no pain. The effects of the drug as a means of perineal pain control are apparent from the data presented in Table IV.

TABLE IV

	Efocaine	Control
Objective wound pain	0.54	1.44
Subjective wound pain	0.71	1.59
Ease of ambulation	1.28	1.79
Number patients with no complaints of pain throughout postpartum period	8	1

Eight of the treated patients had no pain during their hospital stay as compared to only 1 patient in the control group who had no pain. The treated patients also had less discomfort on ambulation than those in the control group.

Anesthesia of the episiotomy area in the efocaine group was not as prolonged as was to be expected from previous reports in the literature. One patient, who developed a hematoma 6 hours after delivery, had pain throughout her hospital stay. Return of sensation, determined by pin prick technique, occurred on the third day with four patients. Three patients had return of sensation on the fourth day, two on the fifth day, and one on the sixth day. Ten patients still had anesthesia when they left the hospital.

Considerable more tissue reaction was noted in the patients treated with efocaine than has been reported in similar studies in the literature. Interference with wound healing occurred in six (28 per cent) of the treated patients. Two tissue sloughs were observed, edema at the episiotomy site occurring the day following delivery in both cases, with wound separation occurring on the third and fourth day and definite evidence of tissue slough by the sixth day. One of these patients was seen in clinic

two weeks following delivery at which time she complained of perineal pain and discomfort on sitting or walking. There was an area of tissue slough at the inferior margin of the episiotomy site approximately 1 x 1 cm. She was seen again at the clinic one week later, at that time the pain had subsided and the slough area was filling in with granulation tissue. The second case of tissue slough occurred along the medial aspect of the inferior margin of the episiotomy site and was approximately 1 x 2 cm. in size. This patient has not been seen since dismissal from the hospital. Two patients developed edema and discoloration at the episiotomy site and along the line of the efocaine injection on the second day after delivery. Slight separation of the distal portion of the episiotomy occurred in both these cases but there was no tissue slough. Two other patients developed edema and discoloration along the episiotomy site but had no wound separation or tissue slough. There were no signs of systemic toxicity in any of the patients.

In the control group two patients developed edema and discoloration at the episiotomy site which cleared up by the time the patients left the hospital. There were no instances of wound separation or tissue slough in this group.

COMPLICATIONS

Three cases of neurological complications following the use of efocaine has been reported by Shapiro and Norman (33). In case 1, after intercostal block a transverse myelitis developed; in case 2, a lumbosacral neuritis developed following an injection into the lumbosacral plexus; and in case 3, involvement of the sympathetic nervous system as manifested by unilateral anhidrosis followed after an intercostal block.

Brittingham, Berlin and Wolff (34) reported on 3 cases of nervous system damage following paravertebral block with efocaine. Case 1 was a patient who was given a paravertebral block with efocaine from the fifth to the eighth dorsal segments because of chest pain associated with widespread inoperable thoracic carcinoma. Two hours after the block the patient was unable to move his left leg and developed weakness of right leg and fecal incontinence. Examination the next day showed an incomplete transverse myelitis at the fourth dorsal level. His neurological condition was reported as essentially unchanged at time of death approximately three months later. Autopsy findings revealed carcinoma of the pancreas with widespread metastases but none affecting the spinal cord. Examination of the cord was reported

as showing "striking degeneration of the gracilis column and to a lesser extent of the peripheral layers of the cord." These changes were present in the thoracic region and extended to the cervical level. The second case reported was a patient who developed weakness of both legs two days following paravertebral block with efocaine at the conclusion of thoracic surgery. Five days postoperatively the patient was reported as having severe weakness of the left leg, slight weakness of the right leg, slight diminution of position sense in the toes of the left foot and inability to void spontaneously. It was reported that the neurological changes slowly improved and when the patient was last seen one month later she had regained sphincter control and could walk with only slight difficulty. Position and vibration sense was intact. The third case was a patient who received an intercostal nerve block with efocaine following thoracic surgery. Complete paralysis of the right leg, marked paresis of the left leg, and loss of anal, rectal and bladder control and sensation developed a few days after surgery. The patient began to show improvement after one week, and two and one-half months after operation had regained anal and rectal sensations and control and was aware of bladder fullness.

Bonica (35) reports on a series of over 100 patients on which efocaine was used for nerve block, post injection and neuritis and pain were encountered in six cases.

Eastwood and Bartlett (36) have reported that on late postoperative examination of patients who had received nerve blocks with efocaine "a not infrequent incidence of pain at the site of injection and, occasionally, in the nerve distribution". They had reported favorably on efocaine in an earlier paper.

In a recent report by Moore (37) on complications following the use of efocaine there were 9 cases of intercostal neuritis described, 4 cases of transverse myelitis, three cases of cellulitis and one case of tissue slough. The 9 cases of intercostal neuritis followed intercostal nerve block where from 2 to 5 cc. of efocaine was injected in each intercostal space in a series of 45 cases. It was reported that the majority of these patients were free or partially relieved of pain and required little sedation. The 9 cases that developed neuritis were free of pain for the first two weeks following operation and then noticed pain at the site of injection radiating to the abdominal wall, the duration of the neuritis was from 2 to 6 weeks. The other complications listed in Moore's report were ob-

tained through personal communications with colleagues at medical meetings. One of the cases of transverse myelitis he obtained resulted from an injection of 3 cc. of efocaine at the level of the second lumbar vertebrae for a paravertebral lumbar sympathetic block. The other three cases of transverse myelitis occurred after injection of 2 to 3 cc. of efocaine into the intercostal nerves under direct surgical exposure either at the transverse processes of the thoracic vertebrae or within 2 or 3 inches from the intervertebral foramina. The 3 cases of cellulitis following efocaine injection, that he obtained for his report, were of 7 to 10 days duration. The one case of tissue slough occurred around the anus following efocaine injection for control of pain following hemorrhoidectomy.

A case of death following the use of efocaine in intercostal nerve block has been reported by Angerer, Su and Head (38). Autopsy disclosed thrombophlebitis of the intercostal vein at the site of injection and marked necrosis and inflammation of the spinal cord. A spinal fluid test for procaine was positive.

SUMMARY AND CONCLUSIONS

The laboratory and clinical investigation of a newly developed long-acting local anesthetic, efocaine, is presented in this paper. The active ingredients of efocaine are procaine and butyl-p-aminobenzoate in a solvent of propylene glycol and polyethylene glycol-300. This anesthetic solution has been reported as producing effective anesthesia for from 6 to 12 days. The rationale for the mechanism of this prolonged duration is that water insoluble anesthetic agents when injected into tissues come in contact with body fluids resulting in the deposition of the anesthetic agents in a crystalline form producing an anesthetic depot which is slowly absorbed.

Toxicity studies (7) have shown that efocaine injected into laboratory animals proved to be approximately sixty times as toxic as procaine hydrochloride and intravenous injection of 5 ml. of efocaine resulted in cardiac arrest and death in the dog. The high toxicity of efocaine is apparently due to the butyl-p-aminobenzoate present.

Histiopathological reports on the effects of efocaine upon tissues have not been consistent. Early reports (9) stated that subcutaneous intramuscular and

perineural injection of efocaine produced no significant damage to the tissues involved. A recent report (10) stated that efocaine and the vehicle in efocaine produces severe nerve destruction in animals, similar to that produced by injection of alcohol or phenol.

Early reports on the clinical use of efocaine were very favorable. Several investigators reporting a marked relief of postoperative pain and decrease in the narcotic requirements of patients who received nerve blocks or local infiltration with the drug. However, a review of 119 general surgical cases at this hospital in which efocaine, procaine base 2 percent and procaine base 5 per cent were used for control of postoperative pain, failed to show that efocaine was of any marked value in control of pain. No local tissue reaction or systemic effects were noted in these reports on the use of efocaine.

In view of these reports a study of the clinical effectiveness of efocaine in the control of episiorrhaphy pain was carried out on a series of 21 patients. A marked decrease in pain was observed as compared to a similar group of controls. However, local anesthesia was not as prolonged as was expected from reports in the literature, 48 per cent of the patients having a

return of sensation before the sixth postoperative day.

Due to the engorgement of the pelvic area during the puerperal period, and vasodilatation as well as edema in the immediate episiotomy area, more rapid absorption of the anesthetic depot than in other areas of the body may take place.

More tissue reaction was observed than has been reported in similar studies in the literature. Interference with wound healing occurred in six (28 per cent) of the treated patients. Tissue sloughing was observed in two cases, separation of the episiotomy in two cases, and marked edema and discoloration in two other cases. There were no significant wound complications in the control group.

Within the past several months the literature has contained several reports of complications from the use of efocaine. Over 10 cases of nervous system damage following intercostal or paravertebral nerve block with efocaine have been reported. Transverse myelitis developed in several of these cases and there was one case of death due to efocaine. The development of intercostal neuritis has been reported following intercostal nerve block. A few cases of cellulitis and tissue slough following the local infiltration of efocaine have been

reported.

Following animal experiments one investigator (37) reports that the drug may travel along the perineural spaces to the spinal cord after intraneural injection. Others (38) postulate that the pathway may be through the intercostal artery or intercostal vein after intravascular injection.

In view of these serious complications efocaine is absolutely contraindicated in the intercostal region or for use proximal to the spine or for blockade of nerves communicating directly with spine. With the local reaction observed in the study made at this hospital in regard to the use of this drug, although a good degree of pain relief was obtained, the continued use of any agent capable of producing such untoward reactions is to be condemned until further study of histiopathological effects are made.

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