

TRENDS IN REGIONAL ANESTHESIA * †

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WITHIN the past twenty years, the clinical practice of anesthesiology has progressed remarkably owing to the introduction of new anesthetic agents and improved methods of administration of standard drugs. In parallel manner, there has been a manifold increase in the number of physicians seeking enlightenment in both the clinical and basic scientific aspects of anesthesia. In no small measure, the rapid strides in this field have been the result of this broadening interest. World War II demonstrated clearly the need for more thoroughly trained medical anesthetists; it afforded invaluable opportunities for further evaluation of standard methods of anesthesia and for critical appraisal of some concepts lately introduced.

The availability of proven anesthetic drugs in recent years has strengthened the tendency to use selected agents in suitable combinations. The term "balanced anesthesia" has been coined to designate the supplementation of one agent by one or more additional agents (1). The introduction of cyclopropane and pentothal increased the possibilities for balanced anesthesia. Within the past ten years new preparations and methods have come into common use, resulting in further sweeping changes in anesthetic practice. Numerous concepts concerning management of the anesthetic period have been revised. "Trial and error" has been replaced by well directed clinical and laboratory investigation. Regional anesthesia has been profoundly affected by these changes. It is now frequently combined with other methods to meet the needs of patient, surgeon and anesthetist.

SPINAL ANESTHESIA

Early enthusiasm for this form of anesthesia led to its indiscriminate use. Unwarranted application of the method with poorly standardized agents and technics produced a high incidence of untoward results. The introduction of balanced anesthesia contributed to a renewal of interest in the method. The administration of "light" general anesthesia following the induction of spinal anesthesia made pos-

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sible the use of smaller doses by the latter route (2, 3, 4). Adequate relaxation and more favorable operating conditions can be provided at greatly decreased expense in terms of toxicity. Several of the disquieting features attending the employment of spinal anesthesia were thus more easily controlled. A factor contributing to the renewed popularity of spinal anesthesia was the introduction of ephedrine (5, 6, 7). Preliminary injection of suitable doses of this drug either maintained values for blood pressure close to normal levels or reduced the incidence of severe decrease in blood pressure. A number of pharmacologically similar drugs have been synthesized and employed to support blood pressure during spinal anesthesia—neosynephrin, parendrine, propadrine, methedrine (8); ephedrine has also been combined with other agents (9), but without marked added benefit. Methods for maintenance of blood pressure are as numerous as the drugs used. The intramuscular route of administration is employed for routine purposes; the intravenous route may be utilized when prompt correction of markedly low levels of blood pressure is imperative. The probable role of naturally secreted epinephrine in maintenance of normal hemodynamics prompted the use of this drug (in 1:250,000 concentration) by intravenous injection to combat shock during spinal anesthesia (10). The consistently superior value of ephedrine, in comparison to that of other drugs recently introduced, has been attested by repeated investigations. It remains the vasopressor agent of choice.

The search for the ideal spinal anesthetic agent has been unremitting. The confusion brought about by the advent of numerous drugs in the early days has been resolved in part by adherence to a few standard preparations and methods of their administration. Within the past ten years, the major proportion of subarachnoid blocks has been established with procaine, pontocaine, or nupercaine when a single injection has been employed (11, 12, 13, 14). The method of utilization of both procaine and pontocaine was considerably clarified in the early 1930's. Recommendations that drugs be dispensed in solutions of uniform strength, and that they be employed in suitable proportions have contributed greatly to the safety and efficiency of spinal anesthesia (15). The need for anesthesia of longer duration than that produced by procaine prompted further investigation of the mechanisms of hypobaric and hyperbaric solutions. Mixtures of procaine, pontocaine or nupercaine with glucose, dilute (1:1500) or concentrated (1:200) solutions of nupercaine, and mixtures of nupercaine with procaine have been designed to suit varying needs (16, 17, 18, 19, 20, 21, 22). The usefulness of spinal anesthesia with nupercaine for intrathoracic procedures has been explored (13, 23). Its use for obstetrical purposes was recently suggested (24). The disturbing frequency of complications attending the administration of longer acting drugs has stimulated interest in dilute solutions of these agents. The preliminary reports concerning dilute mixtures of pontocaine are promising (25).

Small doses may be employed in this manner for short surgical procedures within limited areas (e.g., anorectal region).

There has been a rekindling of interest in the production of spinal anesthesia of longer duration by combining vasoconstricting drugs with small amounts of standard anesthetic agents. Former trials with such combinations produced untoward results too frequently to warrant their routine use. Continued experimental work by a few proponents, however, served to maintain some interest in the problem. Epinephrine and ephedrine have been employed for this purpose with greater frequency. Interest in the mechanism of their action following intrathecal injection led to experimentation with combinations of these agents with procaine or pontocaine-glucose (26, 27, 28, 29). Prolongation of the period of anesthesia has been observed when small doses of anesthetic agents have been injected. The systemic effects of epinephrine and ephedrine introduced in this manner have been infrequent, according to report. Undue increases in blood pressure have been observed, however. This possibility remains as a serious source of concern which merits further evaluation. Much investigation is needed to determine whether the intrathecal administration of vasoconstricting agents has any deleterious effect on the spinal cord or its outflow.

Continued experience with simple solutions of the less toxic agents has not altered the considered opinion that procaine and pontocaine, either singly or preferably in combination, produce spinal anesthesia adequate for the vast majority of surgical procedures in which anesthesia of this form is employed. They are consistently safer than the longer acting agents or combinations involving substances of nonanesthetic character.

The greatest changes in the practice of spinal anesthesia are reflected in those technics involving the intermittent injection of anesthetic agents beneath the dura (30, 31, 32, 33, 34, 35, 36, 37, 38). The need for prolonged anesthesia for many modern surgical procedures had been only partially satisfied by the introduction of long acting agents. The applicability of nupercaine was limited in terms of frequency of deleterious effects; extensive experience and extreme caution were necessary to provide a high degree of efficiency with maximal safety. The adoption of the continuous or fractional methods of injection provided means for obtaining anesthesia of the desired duration with less toxic agents. With Lemmon's method it became possible to establish a level of anesthesia with a small original dose. Maintenance for the desired duration was made possible by the addition, at regular intervals, of similar or smaller doses. Untoward reactions or signs of intolerance were minimized by the ability to withdraw spinal fluid. Concentrations of procaine varying from 0.1 per cent to 5.0 per cent have been investigated to ascertain their range of efficiency; solutions of 2 per cent or 3 per cent concentration are now most frequently em-

ployed. Other agents and combinations have been adapted to the fractional technic, the most notable of which are pontocaine and glucose. They are, however, not necessarily the most commendable.

The fractional or continuous form of spinal anesthesia quickly gained wide acceptance. The ability to establish high levels of analgesia with dilute solutions has led to its use in some quarters for operations above the level of the diaphragm. Instances of high spinal block, inadvertent and intentional, are known. It is indeed questionable whether production of high analgesia by this means is considered safer than that obtained from a single injection. In general, the indications for continuous spinal anesthesia are those recognized for the single injection methods. Analgesia may be established with smaller doses for aged and debilitated patients who might otherwise be denied the benefits of spinal anesthesia. This technic is best applied to surgical procedures below the level of the diaphragm. The ease with which "balanced anesthesia" may be established is an outstanding feature.

Several innovations have already extended the field of usefulness of continuous spinal anesthesia. Introduction of a ureteral catheter through a suitable needle dispenses with the need for special mattresses and permits greater freedom of movement of the patient (37). The catheter must be handled with some caution to avoid breakage. Prior to withdrawal of the catheter, the patient should be turned on his side and flexed to permit widening of the intervertebral spaces. The use of a catheter is particularly suited to the employment of continuous spinal anesthesia for obstetrical purposes. The pains of labor may be abolished effectively by dilute solutions of procaine (0.25 per cent). A more concentrated solution (1 per cent) is necessary for delivery and repair of an episiotomy. The principle involved is one of selective block of sympathetic and small pain-carrying fibers ("differential spinal anesthesia") (39). A method utilizing a continuous flow of dilute solutions into the subdural space has also been explored (40). The drip mechanism used for an ordinary intravenous infusion is readily adapted to this purpose. It is possible that this technic (a variation of "differential spinal anesthesia") may find some application in the treatment of peripheral vascular disorders of the lower extremities. Recently, the mechanism of segmental spinal anesthesia was outlined in preliminary report. Dilute solutions of the anesthetic agent (pontocaine) are placed at optimal levels in the dural canal by means of a catheter. The anesthesia produced is segmental in distribution and is considered suitable for operations within the upper part of the abdomen.

The introduction of new general anesthetic agents and related adjuvants into clinical practice has usually caused some decrease in the frequency of employment of spinal anesthesia. The advent of cyclopropane and pentothal made safer general anesthesia possible for many procedures. The greater utilization of improved endotracheal technics

removed a number of hazards from the administration of inhalational agents (41). Curare provided means for obtaining a degree of relaxation afforded heretofore only by deep general anesthesia or subarachnoid block. Combinations of cyclopropane and curare, or pentothal, nitrous oxide and oxygen and curare are now frequently used in cases in which spinal anesthesia might also be applicable (42, 43, 44, 45, 46, 47, 48, 49). Experiences in World War II afforded unrivaled opportunity for evaluation of the use of spinal anesthesia in the presence of severe trauma. It became apparent that this method was not suitable for operative procedures undertaken in forward positions where the incidence of shock was high (50, 51, 52). Its use in station and general hospitals was not unlike that encountered in the peace-time civilian hospital. It is possible that future indications for spinal anesthesia may undergo revision; however, improvement in agents and technics for their administration will contribute to continued acceptance of this form of anesthesia.

It seems fair to say that development of continuous spinal technics has made possible a revolution in our thinking in regard to agents and methods for spinal anesthesia. If the need for anesthesia is to be of short duration we can employ relatively nontoxic agents such as procaine or pontocaine or both in single dose. If the need for anesthesia is to be of long duration, the continuous technic employing the same relatively nontoxic drugs is warranted. The day has gone by when we need to employ heroic doses of the more toxic agents in single doses to provide anesthesia of sufficient duration. The need for hyperbaric solutions is also past, when dilute solutions of nontoxic agents given by the continuous method provide sufficiently high anesthesia for those procedures for which spinal anesthesia is indicated. Freedom from anxiety, nausea and vomiting may be assured if one is prepared to administer pentothal in dilute solution (0.2 per cent concentration) by means of an intravenous drip.

REGIONAL ANESTHESIA FOR OBSTETRICS

Conduction or infiltration anesthesia for the management of outlet deliveries has been endorsed by only a few proponents and has never enjoyed more than a local popularity. The difficulties and uncertainties inherent in execution of these technics and the limited distribution of anesthesia provided by them confined their use largely to uncomplicated cases (53, 54, 55, 56). Caudal-transsacral block met with moderate approval (57, 58, 59, 60). Its application was limited in similar fashion. The block could be reestablished when necessary but was time-consuming. It provided a sharply circumscribed area of analgesia. The level of analgesia, however, could be raised by means of larger doses for the management of cesarean section (58). Paravertebral block of appropriate segments of the thoracic sympathetic chain (T₁₁,

T₁₂) demonstrated that the pain of uterine contraction could be abolished in this manner (61, 62, 63). This procedure provided analgesia limited in both duration and extent and had to be repeated when necessary during the first stage of labor. Many of these methods were supplemented by general anesthesia at the time of delivery. Infiltration anesthesia has been used in some quarters for cesarean section (64). It has apparently provided excellent results in skilled hands. Light general anesthesia, employing either pentothal or cyclopropane, is usually necessary at the moment of extraction of the infant from the uterus.

Spinal anesthesia was used rather infrequently for obstetrical purposes until recently. There has been some renewal of interest, as shown by descriptions of techniques employing procaine (65, 66) and nupercaine (24). In the hands of trained anesthetists using small doses, spinal anesthesia may be established for cesarean section (67, 68, 69, 70). No significant effect on the fetus can be demonstrated and the incidence of difficult resuscitation is appreciably decreased. Continuous spinal anesthesia is well suited to this procedure (71). It permits avoidance of some of the possible hazards of the method of single injection. The use of the indwelling catheter and the administration of dilute solutions of an anesthetic agent for the relief of pain are warranted.

By far the greatest amount of time and thought given to any one technic in the past few years have been devoted to the perfection and evaluation of continuous caudal analgesia (72, 73, 74, 75, 76, 77, 78). A large measure of success of the method has depended upon the replacement of the malleable needle by the ureteral catheter (79, 80). Much of the initial work was performed using solutions of metycaine. It has now been demonstrated that solutions of procaine (in 1 per cent concentration) will provide satisfactory analgesia for all practical purposes. The possibility of rapid development of a refractory phase with the use of this agent has not been a significant source of concern. Recently, the advantages of pontocaine (with epinephrine) were reported (81, 82). The inherent toxicity of this agent is offset by the use of dilute solutions and by the duration of analgesia provided by each injection. Extensive experience with continuous caudal analgesia for obstetrics has more clearly defined the indications and contraindications for its use. The method is indicated in management of labor for the parturient patient suffering from cardiac disease.

Many of the over-all complications originally reported are now avoided by judicious selection of patients. It is likely that the more frequent use of balanced anesthesia may contribute an increased measure of safety and efficiency to the procedure. Smaller amounts of local anesthetic agents are required since light general anesthesia can be employed as a supplement during the terminal stages of labor. Rational use of supplemental agents (e.g., cyclopropane) in this manner

spares chagrin over the occasional partial failure. In addition, it reduces the possible incidence of toxic reactions. The time required for management of the procedure constitutes a major objection to its widespread use at the present time. Wider application of the method would force the reorganization of departments of anesthesia and obstetrics. The appointment of full-time, qualified personnel to execute and supervise the necessary details would be essential.

REGIONAL ANESTHESIA FOR SURGICAL PURPOSES

Head and Neck

Improvement in the use of inhalational and intravenous methods of anesthesia has removed much of the need for local anesthesia of the head and neck. The insertion of an endotracheal catheter provides a patent airway during surgical procedures on and about the head (83, 84). Adequate oxygenation and maintenance of normal intracranial pressures are assured during operations within the calvarium. The patient is spared the burden of an extensive procedure performed either under local anesthesia alone or under general anesthesia without benefit of proved patency of the airway. For the same reasons, local anesthesia for the fenestration operation will undoubtedly be replaced by more rational inhalational methods utilizing the endotracheal route. Major operations involving the eyes, ears, nose and paranasal sinuses, mouth and throat may be undertaken once the principle of adequate and uninterrupted respiratory exchange is established (85, 86). Proper attachment of the endotracheal catheter to the anesthetic apparatus permits the anesthetist practically complete control of the patient's respiration while the anesthetist must remain at a distance from the field of operation.

The need for blocks of major divisions of the fifth cranial nerve for extensive operations on the nose, paranasal sinuses and lower jaw has been superseded by the improvements noted. The more frequent use of general anesthesia in the hospital practice of dentistry has reduced considerably the exhibition of local anesthesia for this purpose (87). In most quarters, major surgical procedures on the neck—when the air-passages are not involved—are conducted under general anesthesia with the aid of an endotracheal catheter.

Numerous indications, however, for local and regional anesthesia for operations involving the head and neck are worthy of consideration. Many small lesions involving the scalp, face and neck may be removed or remedied with the aid of local anesthesia. Lacerations of the scalp and depressed fractures in the presence of probable intracranial damage are also best managed in this manner. Many operations on the eye can be completed following the establishment of regional and topical anesthesia. Local and topical anesthesia are preferable in many cases for the simpler procedures involving the nose and contiguous

structures: intranasal antrotomy, submucous resection, rhinoplasty, and so forth (88, 89). Infiltration around and beneath the tonsils is a method of choice for tonsillectomy in the adult (90).

Lesions or other conditions threatening the airway call for considerable exercise of judgment (91, 92, 93). General anesthesia must be conducted with extreme caution. Following trauma, secretions, blood, detritus and foreign material must be removed from the throat prior to induction of general anesthesia. The insertion of an endotracheal tube is mandatory. Insertion can be accomplished safely following establishment of anesthesia of the larynx by means of topical application but it is hazardous during pentothal anesthesia. In most instances, regional anesthesia provides adequate coverage of the field of operation while the natural protective mechanism of the larynx is preserved. Fractures of the lower jaw may be treated following bilateral block of the third (mandibular) division of the trigeminal nerve. Lesions involving the larynx and contiguous structures demand the anesthetist's utmost caution. Combined deep and superficial cervical blocks are adequate for most major procedures in this region, (94, 95). The superior laryngeal nerves may be blocked with relative safety after tracheotomy has been performed within a small field block.

The hazard of discharge of the contents of an esophageal diverticulum during induction of general anesthesia is sufficient reason for the use of regional methods. Combined deep and superficial cervical block provides ample anesthesia for the first stage of the repair. Preservation of ability to swallow is an advantage to the surgeon in demonstration of the diverticulum, but ballooning of a large sac may interfere with exposure. The second stage may be accomplished with the patient under general anesthesia after insertion of an endotracheal tube.

THE EXTREMITIES

Regional anesthesia of the brachial plexus is growing more popular for surgical procedures involving the upper extremity (96). Block of the plexus must be supplemented by an intracutaneous and subcutaneous line of infiltration about the arm for operations above the elbow. The patient's ability to use the muscles of the arm and hand is retained; this is of assistance to the surgeon in finding the ends of the severed tendons following trauma or during the performance of kineplasty. Treatment of fractures of the arm is facilitated for the elderly or debilitated patient and for those who have recently ingested food or fluids. The robust, rugged patient undergoing surgical procedures involving the arm can be managed efficiently by means of brachial plexus block; light general anesthesia (e.g., a dilute solution of pentothal) will add to his over-all comfort. This form of anesthesia is indicated for extensive injuries of the forearm or hand when general anesthesia is not elected. It is preferable to blocks of indi-

vidual nerves at the elbow or wrist and to multiple metacarpal blocks for the fingers. The metacarpal blocks may be employed for lesser degrees of trauma of the fingers and palm. Several methods for establishing brachial plexus block have been reported (97, 98, 99). The supraclavicular approach popularized by Labat, however, remains the standard; it has provided eminently satisfactory anesthesia in skilled hands (100). Injection of the anesthetic solution at the point where paresthesia is produced insures the greatest degree of success; the infiltration of several points in the region of the plexus contributes little to the procedure. The block is adequate for most operations on the shoulder. The establishment of a line of intracutaneous and subcutaneous infiltration about the shoulder in horseshoe fashion following completion of the brachial block permits incision in the area overlying the point of the shoulder; light general anesthesia may be necessary when procedures involve structures proximal and medial to the glenoid fossa. Extensive operations on the shoulder are more frequently managed by endotracheal administration of inhalational agents. Within the past one or two years, continuous anesthesia of the brachial plexus (101) has been provided by means of an indwelling needle or catheter. Great caution must be observed in inserting and securing the needle or catheter; undue movement of either instrument could injure the plexus or neighboring structures (e.g., subclavian vessels, or dome of pleura).

Regional procedures for the lower extremity have largely been replaced by spinal or general anesthesia. Many operations of minor character may be performed using cyclopropane or a combination of pentothal and nitrous oxide-oxygen. Operations of major severity are best managed under spinal or inhalation anesthesia. Continuous spinal anesthesia is particularly suitable for the nailing of hips in elderly or debilitated individuals. The indications for sacral or sciatic block for operations on the lower extremity are practically nonexistent. Continuous caudal analgesia has been suggested for anesthesia of the lower extremity (102). Major degrees of shock following fracture of the leg may be allayed by the prompt establishment of this form of anesthesia at the time of admission. The procedure may be continued in the operating room to permit further treatment of the fracture. Blocks of individual nerves in the lower leg frequently provide inadequate anesthesia. The metatarsal block may be established for minor procedures involving the toes. Regional anesthesia for the lower leg and foot is not advisable in the presence of advanced vascular disease.

The infiltration of copious amounts of an anesthetic solution into the fascial planes of the lower extremity was introduced by Russian surgeons during the last decade (103). Strategic deposition of the solution provides adequate anesthesia distal to the cross-section of infiltration. This technic may be limited to early treatment of severe trauma

or may be applied when other methods of anesthesia are not available (104).

THORAX AND ABDOMEN

The application of regional anesthetic methods to the thoracic area is limited (105, 100). Many extrathoracic procedures of minor character may be performed with the aid of pentothal and nitrous oxide-oxygen. Lesions of the breast or chest wall in the aged or seriously ill patient warrant the use of regional anesthesia. Intercostal block or field block or both may be employed. Intercostal block will provide adequate anesthesia for drainage of empyemata thoracis and for simple thoracotomies. This procedure is a valuable adjuvant to general anesthesia for major intrathoracic operations. Simple infiltration of the region of operation may be employed in the management of thoracoplasties. Unduly large doses of premedicating drugs, however, must be administered both prior to and during the procedure to assure an adequate degree of comfort for the patient. Various regional methods have been advocated as alternatives: intercostal block, paravertebral block, brachial block plus paravertebral block and epidural block. It is questionable whether adequate anesthesia can be produced consistently by these methods alone. A regional procedure supplemented by general anesthesia is preferable. Major intrathoracic procedures require standard inhalational methods.

Local anesthesia for operations within the abdomen has been supplanted to a great extent by spinal anesthesia and by combinations of general anesthetic agents with curare. Field block of the abdomen or intercostal block was formerly employed to produce the desired degree of muscular relaxation; a light plane of general anesthesia was established to provide comfort for the patient and satisfactory working conditions for the surgeon (106, 107, 108, 109). Cyclopropane or pentothal is favored as the supplementary agent. The combination of infiltration of the abdominal wall and splanchnic block has been less popular in this country than in Europe and is now rarely selected (110, 111). In recent years, however, an occasional revival of interest in splanchnic analgesia has become manifest (112, 113, 114, 115). These methods may still be considered seriously for the aged or debilitated patient when surgical intervention is advisable. When general and spinal anesthesia are contraindicated, the skillful use of field block and splanchnic block will facilitate surgical procedures within the upper abdomen; selected blocks of the lower abdominal wall may be established for operations below the level of the umbilicus. Regional procedures involving the inguinal region may be employed. Early surgical intervention in the presence of an incarcerated hernia in an elderly patient can be managed successfully following the completion of a suitable block (100). The hernial sac must be scrupulously avoided to prevent transfixing its

contents with the needle. Modifications of the block for hernia are satisfactory for ligation of femoral and saphenous veins.

In some quarters, peridural block has been used rather widely for operations within the abdominal and inguinal regions (116, 117, 118). It is contended that satisfactory operative conditions can be produced with greater safety than with spinal anesthesia. The fractional method of peridural anesthesia has also been introduced (119). Peridural block established by way of the caudal canal (continuous caudal anesthesia) is a more facile and practical technic. It bids fair to replace the practice of single or multiple epidural injections along the vertebral column for diagnostic or operative procedures below the level of the diaphragm (102).

STRUCTURES INNERVATED BY THE SACRAL NERVES

A major proportion of regional anesthetic technics for the area supplied by the sacral nerves has been replaced by intravenous, inhalation and spinal anesthesia. The popularity of pentothal in the management of many procedures involving the lower urinary tract and genitalia is evident. Spinal anesthesia is extensively employed for both suprapubic and transurethral resections of the prostate, and for major operations involving the urinary bladder. Sacral block provides satisfactory anesthesia of the area traversed in perineal prostatectomy and in transurethral procedures (120, 121). It is warranted when spinal and general anesthesia are contraindicated. "Saddle-seat" anesthesia can be produced by either the sacral or spinal route. Anorectal operations performed in the prone position are facilitated by regional methods (122). The hazards of inhalation anesthesia employed in this position without benefit of an endotracheal tube render the use of regional anesthesia advisable.

VERTEBRAL COLUMN

A posterior paravertebral block of the cervical nerves may be established for explorations of the cervical spine (95). The use of the prone position makes the efficient application of inhalation anesthesia difficult. Ruptured intervertebral disks, lesions of the cervical nerves and tumors of the cervical cord can be managed satisfactorily with the aid of paravertebral block. This procedure provides excellent anesthesia for laminectomies in the thoracic and lumbar regions (123). The necessity for a depth of general anesthesia sufficient to permit the introduction and maintenance of an endotracheal catheter is surmounted. Preservation of the conscious state permits the patient to help in the identification of pain-carrying pathways; the relief of pain afforded by tractotomy can be evaluated immediately. Spinal anesthesia may be established for many explorations of the lumbar spine. It is contraindicated on legal grounds, however, when lesions of the cord or cauda equina are suspected.

The extensive areas involved in thoracolumbar sympathectomies necessitate the administration of general anesthesia. Regional methods (e.g., paravertebral block or intercostal block) may be employed as adjuvants to allow the maintenance of a lighter plane of anesthesia.

STANDARD LOCAL ANESTHETIC AGENTS

Procaine is without peer among the agents commonly employed for local anesthesia by infiltration or injection. As cocaine was once the standard in terms of toxicity and potency, reference is now made to procaine. Since the original synthesis of procaine, there has been an intensive search for more suitable agents. The natural relatives of cocaine (e.g., tropacocaine) and synthetic products utilizing its formula (e.g., eucaine "A" and "B") were found to be too irritant and too toxic. Higher homologues of procaine (e.g., butyn, tutocaine, larocaine, etc.) were active when applied topically but were unsuitable for use by infiltration or injection. Specific substitutions in the basic chemical structure of procaine created drugs closely paralleling it in efficiency, toxicity and potency (e.g., monocaine (124), intracaine (125, 126)). The addition of a piperidine ring to the basic benzoic acid structure produced metycaine, a potent nonirritant agent resembling procaine in terms of toxicity. The search for agents providing local anesthesia of greater duration led to the synthesis of pontocaine (tetracaine) and nupercaine. The essential para-aminobenzoic acid ester linkage is preserved in pontocaine. The chemical components of nupercaine, however, are wholly unlike those of the family from which procaine is derived. Pontocaine is ten times more potent than procaine; its toxicity is proportionately greater. Nupercaine, twenty times more potent than procaine, is one of the most toxic local anesthetic agents extant. The use of dilute solutions compensates in part for the greater toxicity and potency of these drugs.

Repeated comparative studies have demonstrated the relative safety of procaine. The degree of irritation of tissues is small. When the drug is properly administered, its toxicity is low. In the event of a severe reaction progressing to convulsions, the seizures may be controlled by the intravenous injection of a soluble barbiturate; oxygen can then be administered under intermittent positive pressure during the period of respiratory depression. Death from severe poisoning by procaine is caused by primary respiratory failure. Conversely, primary cardiac failure is the mode of death from fatal reaction to nupercaine. "In general, we find, therefore, that nonirritant and efficient local anesthetics are invariably esters of benzoic acid or aminobenzoic acid or a substituted aminobenzoic acid" (127).

For local anesthesia by infiltration or injection, the concentration of procaine in solution is varied according to the type of block employed. A concentration of 0.5 per cent is sufficient for simple infiltration or

field block. Adequate anesthesia of smaller nerves, such as those comprising the sacral plexus, may be obtained with procaine in 1 per cent concentration. When a block of larger nerves is desired (e.g., the brachial plexus), a concentration of 2 per cent is indicated.

Surface anesthesia by topical application of procaine can be accomplished only by means of concentrated solutions (20 to 30 per cent). It has been noted that the higher homologues of procaine are potent surface anesthetics. The most potent—butyn (butacaine)—is highly toxic. None of this group is employed frequently at the present time. Nupercaine in dilute solution (0.5 per cent) is an efficient topical anesthetic. Its toxicity, however, precludes its use in immoderate amounts. Metycaine (in 1 to 2 per cent concentration) may be applied in the event of intolerance to pontocaine (in 0.5 to 1.0 per cent concentration).

A vasoconstricting agent must be added to solutions of procaine to prevent rapid absorption of the anesthetic medium. Epinephrine was used first for this purpose and is still extensively employed. It has been shown that the optimal concentration is 1:200,000. Greater concentrations predispose to an increased frequency of untoward reactions and add nothing to the degree of vasoconstriction produced (128). A search for substitutes for epinephrine led to the introduction of cobefrin (nordefrin) (129, 130), an isomer of epinephrine. The value of this agent has been adequately demonstrated. Its pressor activity is reported to be approximately one-fifth that of epinephrine. Untoward reactions to its use are infrequent and much less severe than those provoked by epinephrine. It is employed in a dilution of 1:80,000 with procaine in 0.5 per cent concentration, 1:40,000 with procaine in 1.0 per cent concentration, and 1:20,000 with procaine in 2.0 per cent concentration.

SUMMARY

Methods most frequently in the public and professional eye have been discussed. It is no less important to discuss agents for regional anesthesia that deserve a continuing place in our armamentarium. Procaine is still the agent of choice. As a vasoconstrictor capable of producing a local reaction without untoward systemic effects, cobefrin has proven its sterling worth. The secret of success is in employment of dilute solutions of procaine (0.5 per cent) with cobefrin (1:80,000) for infiltrative procedures. For field blocks the distribution of solution must be complete and evenly placed in all layers. For blocking of small nerve trunks, procaine in 1 per cent concentration with cobefrin (1:40,000) is adequate. For larger trunks, procaine in 2 per cent concentration with cobefrin (1:20,000) is adequate. The maximal safe dose is considered to be 1.0 Gm. of procaine.

Additional emphasis upon desirable regional methods by inclusion in a summary would constitute repetition. It is recognized that concepts have been altered by introduction of competing methods. It is,

however, quite evident that regional methods still have an important place in the practice of anesthesiology. If residents are taught to employ them, they, as clinicians, frequently will find them to be methods of first choice.

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