THE USE OF PETHILORFAN FOR GENERAL HYPALGESIA

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How often is it that a medical practitioner without the help of an anaesthetist is called upon to perform on a patient a painful procedure that is usually carried out under some form of general anaesthesia, which 'higher authority' frowns upon his administering himself? A country doctor might promptly answer, 'Only too often'. Or, if an anaesthetist is available, the patient may have food or drink in his stomach or for some other reason general anaesthesia may not be advisable. These points are made to emphasize the need for a form of general analgesia or hypalgesia that is easy to induce and adequate for the performance of certain painful manipulative manoeuvres, treatment, or repair work.

At the present time we have such an agent in the form of the proprietary preparation 'pethilorfan'. This is the trade-name for a combination of pethidine (ethyl-1-methyl-4-phenyl-piperidine-4-carboxylate hydrochloride) and levallorphan tartrate (lorfan) ((-)-3-hydroxy-N-allylmorphinan hydrogen tartrate). Each ml. of pethilorfan solution contains 50 mg. of pethidine and 0·625 mg. of levallorfan tartrate, i.e. a ratio of 80:1. Pethidine has an analgesic property similar to that of morphine and 15 mg. of morphine is equivalent to 100 - 150 mg. of pethidine. In larger doses lorfan can counteract the analgesic effect of pethidine but lorfan itself has little or no analgesic quality and has no effect upon heart rate or blood pressure. Its important property is its ability to prevent or reduce the respiratory depression caused by pethidine. The combination of the two drugs in the ratio of 80:1 leaves the analgesic property of pethidine uninhibited and removes its depressing influence upon respiration.

A contraindication to the intravenous administration of pethidine, often referred to in order to dissuade one from using it intravenously, is the risk of bringing about a severe degree of hypotension, which is alleged to be due to respiratory depression that produces a marked hypoxia, or anoxia, of the medullary centres—a hazardous state. However, King *et al.*[1] have shown that in therapeutic doses pethidine has little effect upon the cardiovascular system in recumbent patients; and, while 5% of ambulant

patients experience syncope with a fall in blood pressure and a slowing of the heart rate, this can quickly be relieved by having the patient lie down and put his feet up. Sometimes *rapid* intravenous administration will have this sequel in a recumbent patient; 4 out of 24 healthy volunteers suffered a marked fall in blood pressure within 10 - 20 minutes after 100 - 150 mg. of pethidine was injected intravenously while they were lying horizontally with heads tilted up to 60°. If any reservations about the intravenous use of pethidine remain despite the findings of King *et al.*, the introduction of pethilorfan should remove them.

The pharmacological properties of the two drugs combined in pethilorfan have brought this preparation into medicine for producing a general state of hypoaesthesia or hypalgesia. In 1960 Pearson[2] reported how very useful he had found this solution of the two drugs in certain surgical orthopaedic procedures that he had previously carried out under general anaesthesia, with its attendant disadvantages. He used pethilorfan to reduce or eliminate painful sensibility in 39 patients with fractures and dislocations, and in children it proved most effective even when the patient was subjected to considerable force. His list of conditions so managed included Colles' fractures in adults, fractures of radius and ulna in children, and fractures of tibia and fibula, of the shaft of the femur, and of the first phalanx of the finger. Dislocations reduced were those of the shoulder, jaws, elbow, metacarpophalangeal of the thumb, and 'locked knee'. To these I can add a Potts-Dupuytren fracture-dislocation of the ankle, posterior dislocation of the hipjoint, multiple fractures of radius and ulna in an adult, fracture of the nasal bone, compound dislocation of an interphalangeal joint, and partial amputation of digits.

In the next year Smith *et al.*[3] reported a year's experience with pethilorfan in the manipulation of joints that had for long been immobilized in plaster-of-paris for fractures in or near them, in 38 patients. Their aim was to secure not only hypalgesia but also an adequate amount of muscular relaxation in order to manipulate the stiff joints that had not responded to the more usual methods of rehabilitation and physiotherapeutic procedures; and in this they included cases of chronic backstrain. They carried out their treatment about 10 minutes after injecting the pethilorfan, for it usually took this time for a desirable state of drowsiness, euphoria and relaxation to develop. They found that relaxation of muscle and inhibition of spasm during manipulation were uniformly good and enabled a satisfactory manipulation to be carried out.

The pethilorfan is given intravenously in doses from 50 mg. in children to as much as 250 mg. in adults, according to age and size. It is injected slowly for 30 seconds to 2 minutes, during which time the patient is told that he will become drowsy but will not lose consciousness, that he will feel no pain or very little, and that he might be asked to cooperate at some stage in the procedure and would, for example, be quite capable of holding a limb in the required position for the application of a plaster cast. The power of suggestion coupled with pethilorfan injection is sometimes remarkably effectual. The patient is cooperative in a limited way, euphoric, and amnesic (which permits a treatment to be repeated if necessary without unwillingness on the part of the patient); serious or alarming side-effects are absent, as well as post-anaesthetic nausea or vomiting; and sleep usually follows treatment. There are thus positive advantages that go with this method of producing a state of general hypalgesia of a degree sufficient to enable the surgeon to perform various procedures.

In the field of obstetrics, intravenous pethilorfan has also found a place. Delivery of the baby can be happily facilitated by the production of muscular relaxation and mild euphoria before the performance of a pudendal block. The general practitioner will find that he can revolutionize his management of cases in this way. The amnesic influence is most marked; the mother can be made to cooperate throughout delivery, after which she will fall asleep in the third stage to awaken later with little or no recollection of the event.

In this regard it is as well to draw attention to a rewarding advance made in obstetrics by the addition of chlorpromazine to the pethilorfan combination. A mixture of 150 mg. of pethilorfan and 50 mg. of chlorpromazine, given intravenously in 15 - 20 ml. of saline about 10 - 15 minutes before operative delivery is begun, is considered safe from the point of view of the child.[4] The mother is allowed to settle down and is then placed in the lithotomy position, when it is helpful to infiltrate the line of the episiotomy with 10 ml. of 1% lignocaine. Amnesia is produced for such an operative delivery with forceps or vacuum extractor, and the mother remains pleasantly drowsy for 2 or 3 hours afterwards, although she can be engaged in conversation. No alarming changes in blood pressure have been recorded, and nausea and vomiting have been remarkable by their absence. Even more difficult manipulations might be possible under hypoaesthesia produced in this manner.

It is feasible to administer intravenous pethilorfan in domestic midwifery in conjunction with local infiltrative anaesthesia or pudendal block for forceps delivery, which usually requires general anaesthesia. Even a preliminary manual or forceps rotation can be performed under pudendal block supplemented by slow intravenous injection of pethilorfan.[5] Crawford[4] states that pethilorfan and chloropromazine in combination appear to offer the possibility of a considerable advance in anaesthesia for obstetrics, and especially for the practitioner on his own, in domiciliary practice or in country districts. It may prove to be the answer to many problems in anaesthesia for obstetrics.

Conclusion

For the general practitioner a safe method of inducing hypalgesia or hypoaesthesia in a patient to a degree that helps him to perform certain painful procedures almost painlessly, will add much to his independence by increasing his competence, and in this connection perhaps Gardner[6] will not object if I slightly tamper with a thought he recently published to say this: 'Should the general practitioner add the new technology to his armamentarium, professionals from other fields need not take his place.

SUMMARY

A safe and easy method of inducing a state of general hypalgesia is described and published work is quoted to illustrate its definite advantages in different fields.

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