# A CASE OF TOXICITY TO EXCESS 'CARBOCAINE' WITH PROBABLE

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There can be no doubt that the use of local anaesthesia, where possible, is safer for the patient than the use of general anaesthesia. This is especially so in the practice of midwifery, where, as is well known, the use of general anaesthesia is attended by greater dangers and complications than in other conditions not associated with pregnancy or labour.[9,14,6] Pregnant women, particularly when in labour, are much more prone to vomit under general anaesthesia than are other patients. Inhalation of vomitus, especially the acid juices of the stomach which produce Mendelson's syndrome, is a very real and grave complication.[5] According to Eastman[4] 10% of all maternal deaths in the USA are attributable to anaesthesia, the greatest single cause of anaesthetic death being inhalation of vomitus.[13] In addition, general anaesthesia may have a depressant effect on the respiratory centre of the foetus, and further, it has an adverse effect on uterine action with an increase in the incidence of postpartum haemorrhage and manual removal of the placenta.

Hence it is not surprising that in the field of operative obstetrics, local anaesthesia has ousted general anaesthesia to a great extent. The repair of perineal tears and episiotomies, breech deliveries, low-forceps deliveries, mid-forceps deliveries (with or without manipulation of the foetal head) and even, in certain circumstances, Caesarean sections are, today, being performed with greater frequency under local anaesthesia.

Nevertheless, the use of local anaesthesia is not entirely without danger to the patient. Very occasionally one sees a severe generalized reaction to the local anaesthetic agent being used, and such a reaction can be fatal if proper and adequate treatment is not instituted immediately.

This article reports a case of severe reaction to the local anaesthetic agent used (in this instance carbocaine) and describes the interesting sequela of probable reactivation of previously quiescent rheumatic disease.

## CASE REPORT

The patient, Mrs. V.D.H., was a primigravida aged 20 years. She had suffered from acute rheumatic fever at the age of

10 and again at the age of 16 years. This had left her with a mitral stenosis and aortic incompetence of mild degree.

*Antenatal History*

She attended the antenatal clinic at the Queen Victoria Hospital, Johannesburg, from 22 September 1959, when she was 11 weeks' pregnant. Her menstrual cycles had always been regular (C.13 3-4/21-22). Her last menstrual period was on 8 July 1959 and the expected date of delivery was 14 April 1960. She was referred to the Cardiac Clinic for assessment and the diagnosis of mitral stenosis and mild aortic incompetence was confirmed. She was regarded as a cardiac Type 1 case and was given a good prognosis for this pregnancy.

At 12 weeks' gestation she was admitted with mild hyperemesis gravidarum. This was soon controlled and she was discharged after a few days' treatment. Thereafter she attended the antenatal clinic regularly, paying 16 visits throughout her pregnancy. Her blood pressure varied between 110 and 130 mm.Hg systolic and 40 and 60 mm.Hg diastolic. At no stage was albuminuria present. Slight oedema was found on 2 occasions and her weight had increased from 124 pounds at 11 weeks to 148 pounds at 37 weeks. Her cardiac status remained unimpaired.

*Labour*

She was admitted to hospital at 37 weeks' gestation for reassessment of the cardiac state and for rest before labour. She commenced labour spontaneously at 6.45 a.m. on 11 April 1960, when she was pregnant for 39 weeks and 4 days according to her dates. The first stage of labour lasted 8 hours 25 minutes and progressed normally. At the beginning of the second stage the vertex was found to be 1 inch below the ischial spines with the sagittal suture in the direct anteroposterior diameter. After 10 minutes in the second stage, with good contractions and bearing-down efforts, there was no appreciable advance of the head. Since the patient had a cardiac lesion and since some slight meconium-staining of the liquor was noted, it was decided to apply low forceps under a pudendal block. Forty ml. of 2% carbocaine (without adrenaline) were used in performing the pudendal block. Anderson's forceps were applied, an episiotomy was done and an easy low-forceps extraction was performed. The infant was a male, weighing 8 lb. 9 oz., and was alive and well. The second stage had lasted 25 minutes and the third stage lasted 5 minutes, the placenta delivering spontaneously with a total blood loss of 250 ml.

*Severe Reaction and Treatment*

Approximately 15 minutes after the pudendal block was given and just after the third stage had been completed, the patient was seen to become very excitable, restless, emotional and almost maniacal. This excitable phase lasted about 30 seconds. She then commenced to twitch, developing typical Jacksonian movements in her left arm. These progressed to generalized epileptiform convulsions. Morphine, gr. ¼, was given intravenously soon after the fit had ended and paraldehyde, 8 ml., was injected intramuscularly. The convulsions recommenced almost immediately after these injections and in a relatively short time the patient had about 10 convulsive seizures in rapid succession. The outstanding feature was the high level of excitability, in that the slightest stimulus precipitated another fit. A general anaesthetic was administered and the fits were controlled.

The patient was found to be cold and clammy and quite pulseless, manifesting the signs of severe shock. One ampoule of 'levophed special' was given intravenously and an intravenous drip containing 100 mg. of 'solucortef' was begun. On this regime her general condition improved, though the blood pressure fluctuated between 90/50 and 120/60 mm.Hg for the next 1½ hours, after which it remained at about 120/60 mm.Hg. The heart rate when the anaesthetic was begun was 140 per minute, but this gradually dropped to about 116 per minute and remained at this rate for the next 4 hours. For a short time, while she was under the anaesthetic, there was evidence of mild pulmonary oedema in the form of bilateral crepitations and moist bronchiolar sounds, but these signs disappeared and did not recur. A catheter specimen of urine taken just after the start of the anaesthetic had revealed a faint trace of albumin on the cold test but no albumin on the hot test. Albuminuria, however, was definitely present in the next specimen of urine, obtained 3 hours after the fits had occurred. All specimens of urine obtained thereafter were normal, and albuminuria was not found again. This one instance of albuminuria was probably due to the series of fits that occurred.

On several occasions an attempt was made to discontinue the general anaesthetic, but, as soon as the level of anaesthesia dropped, twitching of the limbs was seen, indicating that convulsions would probably recur if the anaesthetic was stopped. There were no obvious localizing signs in the central nervous system and the ECG showed only a tachycardia and some signs of left auricular enlargement. The uterus remained well contracted. 'Somnifaine', 1 ml., was given intramuscularly about an hour after the original convulsion and this was repeated again an hour later.

*Progress and Diagnosis*

The anaesthetic was finally stopped 2¼ hours after it had been started. There was no twitching of muscles and the patient's condition appeared satisfactory, though she was still unconscious. She was nursed in an oxygen tent and close watch was kept on her blood pressure, pulse rate and respirations. The patient regained consciousness 3¼ hours after the anaesthetic was stopped and 5½ hours after the series of convulsions. She appeared quite normal and was orientated as to time, place and person. Her blood pressure was 120/60 mm.Hg, the lung fields were clear, her pulse rate was 108 per minute and there were no abnormal signs in the central nervous system. Her good general condition was maintained thereafter.

When the first convulsive episode occurred, the immediate diagnosis that was considered was that of postpartum eclampsia. However, on further consideration this seemed unlikely, since at no stage in pregnancy or labour had the patient shown any signs of pre-eclampsia. When the state of severe shock developed, a sensitivity reaction to a rather large dose of the local anaesthetic agent was considered and was found to be the most feasible explanation for the convulsions and the collapse. A possible amniotic embolization or, as the patient had a cardiac lesion, a cerebral embolism, or even a cerebral haemorrhage, was entertained in the differential diagnosis but, as the case developed, these appeared more and more unlikely. The diagnosis, therefore, that appeared most likely to be correct, was that of sensitivity to the local anaesthetic agent, and the subsequent clinical picture appeared to confirm this diagnosis.

*Rheumatic Fever Exacerbation*

On the sixth postpartum day the patient was found to have a painful and swollen right knee joint and some effusion was also found in the left knee joint. There was no throat infection but the lochia was seen to be somewhat offensive. The swollen joints were thought to be due to a possible exacerbation of rheumatic fever resulting from the violent movements of the convulsive state, and 'disprin', grs. 10 *t.d.s.*, was prescribed. The following day she complained of pain in both ankle joints and these were found to be swollen as well. No other joints appeared involved. A pyrexia of 101° F. and a tachycardia of 110 per minute were recorded. She was given a broad-spectrum antibiotic and the disprin was continued. The pyrexia and tachycardia persisted for 3 days and then returned to normal levels.

The question whether the pyrexia and tachycardia were due to a rheumatic fever exacerbation or to a mild uterine sepsis was discussed, but in view of the swollen and painful knee and ankle joints, the senior physician considered it wiser to regard the episode as being due to a rheumatic exacerbation. Laboratory tests were of no help since the results obtained might normally have been found in the puerperium. We considered whether the swollen joints could have resulted purely from the violent movements of the convulsions *per se*, but since these joints were perfectly normal for the first 5 days of the puerperium this seemed unlikely.

The cardiac state remained unaffected. The pain and swelling

of the joints regressed gradually, the ankle joints returning to normal first. By the 22nd puerperal day there was no longer any pain in the knee joints but there was still slight excess fluid present. When this patient was seen at the postnatal clinic, 6 weeks after her delivery, she was fit and well and her knee joints had returned to normal.

## DISCUSSION

The use of local anaesthesia is an eminently safe and satisfactory procedure, but in a very small proportion of cases a severe reaction to the local anaesthetic agent is seen. This possibility is well recognized and documented. Martin[12] discussed a case of reaction to procaine, while Dutton,[3] Barnes,[1] Lock and Greiss,[11] Bennett,[2] and Goldman[7] reported reactions following the injection of xylocaine ('lignocaine'). Reports on the use of carbocaine are still scanty and, to our knowledge, no account appears in the literature of a convulsive reaction occurring after the use of carbocaine.

Adverse reactions to most types of local anaesthetics appear to have a basically common cause and pattern. The causes may be divided into two groups: (*a*) toxic, and (*b*) idiosyncrasy.

### *Toxic Reactions to Local Anaesthetics*

The toxic group comprises by far the largest number of patients who react to the local anaesthetic agent. Here the symptoms and signs are caused by too high a concentration of the local anaesthetic in the blood stream. Normally, the local anaesthetic agent is broken down in the blood stream and in the liver, and whenever the amount of local anaesthetic agent is in excess of that which the patient's body can deal with at any one time, toxic reactions will occur. The exact blood concentrations that bring about toxic reactions will vary from patient to patient, but drug manufacturers do impose a limit on the amount of local anaesthetic agent that should be used, this amount being well within the range in which the body can break down the agent sufficiently quickly to prevent reactions.

Special care must be exercised, therefore, to avoid conditions where too high a concentration of the local anaesthetic agent in the blood stream might be brought about. The first and most obvious of these is, of course, not to use more than the recommended amount of local anaesthetic. In the case of procaine and xylocaine the generally accepted maximum dose is 1 g., i.e. 50 ml. of a 2% solution, 100 ml. of a 1% solution or 200 ml. of a 0·5% solution. In a personal communication, A. B. Bofors (Sweden), the manufacturers of carbocaine, have informed us that the maximum permissible dose of carbocaine is 0·2 g. when used without a vasoconstrictor, or 0·5 g. when used with a vasoconstrictor such as adrenaline. The makers, however, point out that doses twice or even 3 times their recommended maximum dose have often been used without toxic effects. In the case reported above, 40 ml. of a 2% solution of carbocaine were used without the addition of adrenaline. Thus 0·8 g. of the local anaesthetic agent was used – which is 4 times the recommended dose without a vasoconstrictor, and this must obviously have been the cause of the toxic reaction seen.

Too high a blood concentration of the local anaesthetic might also be produced by inadvertently injecting the anaesthetic agent into a vein during infiltration of the tissues. Hence it is essential to keep the needle moving or to draw back on the plunger of the syringe if a large amount of anaesthetic agent is to be injected in one area. This is particularly important when injecting into a very vascular area, such as the perineum, during pregnancy and labour, when the blood supply is very rich. This increased vascularity in itself would cause the anaesthetic agent to be absorbed into the blood stream much faster than normal. Finally, the use of such spreading agents as 'hyalase' (hyaluronidase) should not be used, since, with the potent spreading effect of hyalase, greater and faster absorption of the local anaesthetic takes place.

### *Idiosyncrasy to Local Anaesthetics*

Idiosyncrasy to the local anaesthetic being used is rare, and Hawksworth[8] is even doubtful whether it ever occurs. However, since there are many reports of reactions to local anaesthetics where doses well within the recommended limits have been used, such a condition of idiosyncrasy or drug sensitivity to the local anaesthetic agent must be accepted. This state is one peculiar to the individual patient, and such a patient should be warned specifically against the possible use of that agent in the future.

### *Signs and Symptoms of Toxicity*

Toxic reactions to local anaesthesia may be commoner than is generally thought, the milder reactions often being attributed to the patient's nervousness or excessive anxiety.

The toxic effect on the central nervous system is usually twofold. There is a stimulatory effect as shown by restlessness, loquacity, psychic disturbances,[7] vomiting, twitching of muscles, tremors, and finally generalized convulsions. A depressive effect on the vasomotor and respiratory centres in the medulla is seen, as shown by a sudden and marked drop in the blood pressure and respiration. Sudden inability of the patient to speak should be regarded as a grave symptom, since it heralds unconsciousness.[10] A typical generalized anaesthetic state then ensues which may be followed by death if vigorous and adequate treatment is not given immediately.

### *Treatment*

The aim of treatment is to control the stimulatory effects on the central nervous system and to counteract the depressive effects on the vasomotor and respiratory centres. The short-acting barbiturates are generally accepted as being specific for the control of convulsions and these are give intravenously in hypnotic doses. Sodium thiopentone would appear to be the drug of choice for this purpose.

Cardiovascular collapse should be treated by intravenous stimulants such as 'methidrine' in doses of 10 mg., by setting up an intravenous drip containing 'levophed' if necessary, or by giving 'levophed special', which can be given intravenously without dilution. The efficacy of this treatment will, of course, be judged by the blood pressure.

Depression of the respiratory centre will cause marked slowing or even cessation of respiration. It then becomes necessary to maintain respiration by artificial means. This is best achieved by passing an intra-tracheal tube if the patient is unconscious or, at least, an airway, and ensuring

an adequate oxygen supply by the use of the reservoir bag of an anaesthetic gas machine. This maintainence of respiration is possibly the most important part of the treatment.

## CONCLUSIONS

The following suggestions are made with a view to reducing or avoiding toxic reactions to local anaesthetic agents:

1. The maximum dose of these drugs must be respected. The smallest amount in the lowest effective concentration should always be used.

2. An aspiration test for blood must always be made. When large amounts of local anaesthetic are being injected over a large area, the needle should be kept moving.

3. The addition of a vasoconstrictor drug, such as adrenaline 1:1,000, to give a final concentration of 1:200,000 in the local anaesthetic solution injected, is recommended. Conversely, the use of spreading agents such as hyalase, should be avoided.

## SUMMARY

A case of a toxic reaction to excess carbocaine is described. The patient had had rheumatic fever and an exacerbation of this disease occurred after the severe central-nervous-system stimulation of the reaction.

The differences between toxic reactions and idiosyncrasy to local anaesthetics are discussed and treatment is described in some detail.

Suggestions for reducing or avoiding toxic reactions to local anaesthetic agents are made.

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