It may produce a temporary, apparently beneficial effect, but is it correct to attribute this to the drug? Is it not possible that these periods of improvement—short or prolonged—are, in fact, periods of remission?

The results of the present trial do not substantiate the excellent results which have been claimed in the past.

We wish to thank the patients for being so co-operative in an attempt at 'cure'; Dr J. G. Burger, Medical Superintendent of Groote Schuur Hospital, for permission to publish; and Protea Pharmaceuticals for providing the trial material.

REFERENCES

Prolonged Paresis Following the Administration of Gallamine Triethiodide (Flaxedil) to a Patient With Acute Pancreatitis *

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SUMMARY

A patient was submitted to laparotomy and found to be suffering from acute pancreatitis. Gallamine triethiodide (Flaxedil) was the main relaxant used. A prolonged paresis lasting 40 hours followed. This was resistant to reversal by atropine and neostigmine, and was precipitated by an associated renal insufficiency with an inability to excrete the gallamine. Prolonged postoperative mechanical ventilation was necessary. Additional aggravating factors were also present. The association of acute pancreatitis and acute renal failure is stressed.


CASE REPORT

A 52-year-old man was admitted to hospital complaining of upper abdominal pain, and vomiting. A history of heavy alcohol consumption over the previous 3 days was given. A tentative diagnosis of acute pancreatitis was made, and blood for serum amylase estimation was taken, but unfortunately the specimen haemolyzed. The patient’s general condition at the time of admission did not give rise to anxiety. The blood pressure was 130/90 mmHg, the pulse rate was 100/min and the haemoglobin concentration was 18.2 g/100 ml. He was mildly dehydrated and intravenous therapy, including ampicillin and prochlorperazine (Stemetil), was instituted.

The following day the patient’s condition deteriorated, vomiting increased and abdominal distension was a feature. A revised diagnosis of acute intestinal obstruction was made and laparotomy planned.

Anaesthetic Technique

On arrival in the theatre the blood pressure was 110/70 mmHg, and the pulse was 110/min. Atropine 0.6 mg and diazepam (Valium) 2.5 mg were given intravenously. The patient was pre-oxygenated, placed in the reversed Trendelenburg position to obviate possible regurgitation and vomiting, and intubated by use of the ‘crash induction’ technique. For this thiopentone 200 mg and suxamethonium 50 mg were administered. The patient resumed breathing after 3 minutes. Gallamine 120 mg was used as the main relaxant. Anaesthesia was conducted, using
mechanical ventilation (Manley respirator) set to deliver a minute volume of 9 litres/min with a 30% concentration of inspired oxygen. The average halothane concentration was 0.5%, and a further dose of gallamine 20 mg was required during the operation.

Laparotomy showed an acute pancreatitis with small calculi in the gall bladder. A cholecystectomy was performed, and an uneventful closure of the abdomen followed. The duration of the procedure was 90 minutes.

Attempts reversal of the gallamine effect with 0.6 mg of atropine and 2.5 mg of neostigmine resulted in the return of some muscular tone after 3 minutes, but spontaneous respiration could not be supported. Ten minutes later a further dose of 0.6 mg atropine and 2.5 mg neostigmine were again administered intravenously, but resulted in no improvement in the respiratory excursion. At this stage the patient was conscious, he was able to put out his tongue on command, but was unable to lift his head. Chest movement was poor and his hand grip was feeble. He was also restless and apprehensive and unable to speak coherently. The respiratory excursion was inadequate and ventilation was maintained by using a Bird Mark VIII ventilator. Metabolic acidosis was suspected and 75 mEq sodium bicarbonate was given empirically, without any apparent improvement.

Postoperative Course

Three hours postoperatively ventilation was still totally inadequate. In view of the fact that gallamine is excreted by the kidneys, the possibility of renal insufficiency was entertained, and a catheter inserted to determine the urinary output. The bladder contained 5 ml of urine. Over the next 5 hours, 2 litres of fluid were given, but only 10 ml of urine obtained. It was obvious that the patient had a gross oliguria and his respiratory insufficiency was due partially to an inability to excrete the gallamine.

The postoperative course was stormy and the patient required diazepam (Valium) 10 mg t.d.s. for sedation. This was combined with ampicillin 500 mg q.i.d. and Trasylol 25 000 KIU. He was maintained on a Bird ventilator set at 9 litres/min on an air-oxygen mixture. All attempts at ‘weaning’ him proved unsuccessful. Efforts were made to stimulate the excretion of urine. During the first 24 hours he was given 80 mg of furosemide (Lasix). His fluid intake was 3 500 ml and this was made up of 2 000 ml 5% dextrose in water, 1 000 ml dextrose in saline, and 500 ml plasmalyte B. In addition, he was given 1.5 g potassium chloride for replacement. His urinary output during this period was only 800 ml. The electrolyte picture is shown in Table I.

Twenty-four hours later the patient showed slight improvement and could be disconnected from the ventilator for short periods. During the following 24 hours he was given 3 300 ml of fluid comprising 1 000 ml of 5% dextrose in water, 1 000 ml plasmalyte B, and 1 300 ml GSH maintenance fluid. In addition he was given 75 mEq sodium bicarbonate. The patient passed 1 650 ml of urine. Towards the end of this period the ventilator was disconnected and the endotracheal tube left in situ.

From the case history it can be seen that the patient had an almost complete renal shutdown, as only 15 ml of urine was excreted in the first 8 hours after the start of the operation. This was followed by a period of improvement during the next 36 hours, although the blood urea rose from 29 mg/100 ml to 124 mg/100 ml. The electrolyte levels remained within normal limits postoperatively, and it can be surmised that the oliguria was due to acute renal insufficiency. The haemoglobin level of 18.2 g/100 ml on admission suggests that the patient was dehydrated. This was probably an aetiological factor for the acute renal insufficiency. The paresis wore off 36-40 hours after the start of the operation.

Beisel et al.1 in 1959 emphasized the occurrence of acute renal failure complicating acute pancreatitis. Until then basic texts and review articles on pancreatitis made no mention of acute renal failure as a complication of acute pancreatitis, and a survey of the literature revealed very few reports of this association. More recent writers have noted this combination.2,3 Meyer4 states that he has seen several cases of acute pancreatitis accompanied by renal insufficiency or acute renal failure, and that the mortality rate is high.

The aetiology of the renal failure in cases of acute pancreatitis, is probably due to a combination of factors among which are oligoemia, haemolysis, and a direct toxic effect on the kidney. Oligoemia appears to be the main cause of the renal failure. It is brought about by dehydration due to poor fluid intake, and vomiting. There is also a sequestration of fluid into the peritoneal and retroperitoneal spaces. Kinins are released from the dama-

### TABLE. I SEE TEXT

<table>
<thead>
<tr>
<th>Blood urea (mg/100 ml)</th>
<th>Potassium (mEq/L)</th>
<th>Sodium (mEq/L)</th>
<th>Chloride (mEq/L)</th>
<th>Serum CO₂ (mEq/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate postoperative</td>
<td>29</td>
<td>4,2</td>
<td>134</td>
<td>103</td>
</tr>
<tr>
<td>24 hours later</td>
<td>115</td>
<td>4,3</td>
<td>142</td>
<td>100</td>
</tr>
<tr>
<td>48 hours later</td>
<td>124</td>
<td>4,1</td>
<td>143</td>
<td>107</td>
</tr>
<tr>
<td>72 hours later</td>
<td>115</td>
<td>5,0</td>
<td>138</td>
<td>114</td>
</tr>
</tbody>
</table>

At this stage he was able to maintain an adequate tidal volume.

Forty-eight hours later the patient extubated himself and could maintain spontaneous respiration with an adequate tidal volume. Intravenous therapy was maintained with 1 000 ml dextrose in saline, 1 000 ml plasmalyte B, and 2 150 ml GSH maintenance fluid. An additional 50 mEq sodium bicarbonate was given. He was given 4 150 ml of fluid and passed 2 600 ml of urine.

Seventy-two hours later the patient was improving rapidly. He was able to sit up, his colour was good, and his respiratory excursion adequate. Towards the end of the third postoperative day, he unexpectedly collapsed and died. Permission for autopsy was not obtained.

DISCUSSION
...ged pancreas which give rise to peripheral circulatory collapse and intravascular pooling and sludging. The consequence of the oligoemia is a decreased plasma volume with diminished renal flow, a decreased glomerular filtration and a reduction of renal function. There is anoxia of renal tissue, with pooling, sludging, and disseminated intravascular coagulation. There is also a redistribution of blood from the cortex to the medulla and the release of renin which causes a further vasoconstriction.

The second factor, namely haemolysis, is thought to be due to the release of enzymes and also to play a part in producing the renal failure. The normally perfused kidney is usually able to deal with pigment, but in the presence of oligoemia and tissue anoxia, the pigment may precipitate out into the renal tubules.

In addition to these two factors there may also be a direct toxic effect on the kidney due to the release of proteolytic enzymes from the injured pancreas.

In 1949 Munshin and his colleagues showed that gallamine is excreted in the urine, 30 - 100% being recovered within 2 hours. Chagas found up to 80% in the urine of dogs within 3 - 5 hours. Since then a number of reports have appeared in the literature suggesting that a prolonged paresis may follow the use of gallamine in cases with poor renal function. Churchill-Davidson described the case of a patient given gallamine for a bilateral nephrectomy. He noted that, although reversal was achieved with an anticholinesterase drug, the signs of recurarization were clearly visible many hours after operation.

When gallamine is given to an oliguric patient there is usually a tendency for reversal with neostigmine. This is followed later by a recurarization as the neostigmine is broken down. The sequence of events here would suggest that what happened was not just a failure to excrete gallamine, but that additional aggravating factors were present. Firstly, there is the question of dehydration and muscle relaxants. The patient's haemoglobin level on admission was 18.2 g/100 ml, which suggests dehydration and reduction in the extracellular fluid volume. Since gallamine is distributed in the extracellular space there could be an increased concentration of the drug, and a so-called 'normal' dose could become an overdose. The other aspect is that with dehydration there is a diminution of renal function and a slower excretion of drugs. Secondly, there is the question of a pre-existing metabolic acidosis which is known to prolong the action of non-depolarizing muscle relaxants. Unfortunately, there is no record of the pre-operative assessment of the patient's electrolytes and acid-base status. Clinically, however, metabolic acidosis would appear to be highly likely, especially in view of the dehydration and the poor renal function. The early postoperative figures could be consistent with acidosis and an intracellular depletion of potassium, which could have led to prolonged block. Thirdly, it is known that in acute pancreatitis prolonged blocks can occur with muscle relaxants, as the result of the liberation of lipase, which splits fats into fatty acids and binds the serum calcium which is necessary for the release of acetylcholine at the neuromuscular junction. Fourthly, it has been reported by Chasapakis and Dimas that Trasylol therapy may potentiate the effects of muscle relaxants. In this instance, however, the dose of Trasylol given was small. Lastly, the possibility of myasthenia, or a myasthenic syndrome, should be considered. These patients are sensitive to non-depolarizing muscle relaxants. The conditions are not common and they would seem to be unlikely possibilities in this particular case.

CONCLUSION

In cases of acute upper abdominal pain the possibility of acute pancreatitis with an associated renal insufficiency should be considered. Drugs that are excreted through the kidneys should be avoided, where possible, under these conditions. There is also an increased sensitivity to non-depolarizing muscle relaxants under these circumstances, and the doses used should be less than normal.

I wish to thank Dr J. Meyer, Principal Physician at Edenvale Hospital, for his help and advice; and Dr H. B. Podlas, for permission to publish.

REFERENCES