

Amylase creatinine clearance ratio after biliary surgery

L. A. DONALDSON, W. McINTOSH, AND S. N. JOFFE

From the Departments of Surgery and Biochemistry, Stobhill Hospital and the University Department of Surgery, Glasgow Royal Infirmary, Glasgow

SUMMARY The amylase creatinine clearance ratio (ACCR) is considered to be a more sensitive index of acute pancreatitis than the serum amylase level. Serial ACCR estimations were undertaken in 25 patients undergoing an elective cholecystectomy. Using accepted criteria, 28% of these patients developed, in the postoperative period, biochemical evidence of pancreatic gland damage, although the serum amylase level remained normal. This raised ACCR was particularly noted in patients who had undergone an exploration of the common bile duct. The ACCR would appear to be a more sensitive index of pancreatic gland disruption secondary to biliary surgery than the serum amylase level.

The development of acute pancreatitis after surgery is often asymptomatic (Keighley *et al.*, 1969). This delays diagnosis and may contribute to the high mortality in patients in whom it develops after routine biliary surgery (Imrie, 1974). Confirmation and even recognition of postoperative pancreatitis usually depends on a raised serum amylase level. Although serial serum amylase estimations have been recommended to establish an earlier diagnosis (Barbenheier *et al.*, 1968), the actual rise (Singh *et al.*, 1965; Barbenheier *et al.*, 1968; Keighley *et al.*, 1969; Miller *et al.*, 1973) not infrequently fails to reach the accepted level in most laboratories of 1200 IU/l using the Phadebas kit method (Imrie and Whyte, 1975).

Other criteria, therefore, must be considered for assessing postoperative pancreatitis. The amylase clearance, expressed as a percentage of the creatinine clearance, is a more reliable and sensitive method for diagnosing acute pancreatitis (Levitt *et al.*, 1969; Lesser and Warshaw, 1975) than the routine amylase estimation in blood and urine (Dreiling *et al.*, 1974).

This prospective study was undertaken to assess the value of the amylase creatinine clearance ratio (ACCR) in the early recognition of postoperative acute pancreatitis, and compare it with the serum amylase level.

Methods

Twenty-five patients undergoing an elective cholecystectomy were investigated. Simultaneous serum and urine samples were taken preoperatively, 24 hours after operation, and then daily until the serum amylase level was normal, and again between the seventh and ninth day after operation. In eight patients the common bile duct was explored, because 'filling defects' were present on operative cholangiography. The amylase level was estimated using a dyed starch polymer substrate (Phadebas Amylase Test); the normal range being between 80-300 IU/l at 37°C (Ceska *et al.*, 1969). The amylase clearance was calculated from a random volume of urine voided at the time of venesection and the amylase creatinine clearance ratio could then be determined from the equation:

$$\text{ACCR} = \frac{\text{Amylase clearance}}{\text{Creatinine clearance}} = \frac{\text{Urine amylase}}{\text{Serum amylase}} \times \frac{\text{Serum creatinine}}{\text{Urine creatinine}} \times 100.$$

The ACCR in normal healthy patients varies between 2.1 and 3.1% (Levitt *et al.*, 1969; Levine *et al.*, 1975; Warshaw and Fuller, 1975). A value greater than 4.0% is suggestive of acute pancreatitis (Dreiling *et al.*, 1974) and when in excess of 5.5%, in the presence of hyperamylasaemia, it indicates a significant

clinical attack of acute pancreatitis (Lesser and Warshaw, 1975).

Results

All 25 patients undergoing an elective cholecystectomy had an uneventful postoperative recovery and none developed any clinical features suggestive of acute pancreatitis. With the exception of one patient, the serum amylase level remained within normal limits. The mean ACCR before operation was 2.6% (SEM 0.3) which significantly increased to a mean of 4.9% (SEM 0.6) 24 hours after operation ($P < 0.005$) (Figure).

In seven patients, the ACCR exceeded the 5.5% level (Lesser and Warshaw, 1975) and the mean was 8.7% (SEM 1.3). Five of these seven patients underwent an exploration of the common bile duct during the cholecystectomy. This was in comparison with only two of the 17 patients who had a cholecystectomy in whom the ACCR was raised ($P < 0.05$, Snedecor's F-test). By the ninth day after operation the ACCR had returned to normal in all patients. The mean serum amylase level significantly fell from a preoperative mean of 173 IU/l (SEM 9.6) to 140 IU/l (SEM 10.6) 24 hours after operation ($P < 0.01$, paired t test). At the time of discharge the

mean serum amylase level was 214 IU/l (SEM 10.0).

In one patient who underwent an exploration of the common bile duct, the ACCR remained persistently raised at 7%, but the serum amylase level was normal until the seventh postoperative day, when after a T-tube cholangiogram, it increased to 1300 IU/l. Throughout this period, the patient was asymptomatic and 48 hours later both estimations had returned to normal.

Discussion

The serum amylase is considered to be of value in the diagnosis of postoperative pancreatitis in view of the lack of positive clinical signs, particularly as many patients are asymptomatic in the presence of their hyperamylasaemia (Keighley *et al.*, 1969). Serial estimations of the serum amylase level have been recommended as a routine investigation in the postoperative management of patients who have undergone common bile duct exploration to aid the early diagnosis of postoperative pancreatitis (Barbenheier *et al.*, 1968). As indicated, the actual rise in serum amylase (Singh *et al.*, 1965; Barbenheier *et al.*, 1968; Keighley *et al.*, 1969; Miller *et al.*, 1973) not infrequently fails to reach the accepted level for acute pancreatitis—namely, four times the upper limit of normal (Imrie and Whyte, 1975). Therefore other criteria must be considered for assessing postoperative pancreatitis.

A raised plasma clearance of amylase > 4 ml/min collected over four hours, in conjunction with a raised serum amylase level and defined clinical signs is considered to be diagnostic of acute pancreatitis (Imrie and Whyte, 1975). However, the significance of pain and vomiting in the immediate postoperative period is not easily assessed and unless the patient is catheterised, timed collections of urine after operation are difficult. Since blood sampling can be easily arranged to coincide with spontaneous micturition, the ACCR would appear to be a more convenient index to measure, especially in the postoperative period.

The mean ACCR in published control series and our preoperative patients varied between 2.1% and 3.1% (Levitt *et al.*, 1969; Levine *et al.*, 1975; Warshaw and Fuller, 1975), and an ACCR greater than 5.5%, in the presence of a raised serum amylase level, has been considered to indicate a clinically significant attack of acute pancreatitis (Lesser and Warshaw, 1975). In addition, serial ACCR estimations give a more accurate assessment of the clinical course of the pancreatic inflammation than routine amylase estimations in blood or urine (Dreiling *et al.*, 1974), as these remain raised for a few days after the serum amylase level has returned to normal,

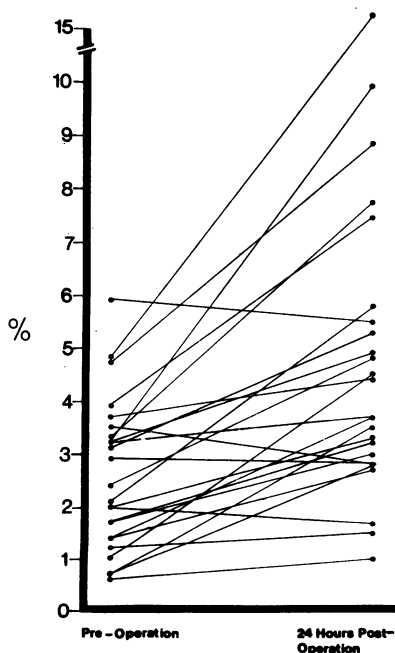


Figure The amylase creatinine clearance ratio (ACCR) before operation and 24 hours postoperatively in 25 patients undergoing biliary surgery.

(Levitt *et al.*, 1969). Furthermore, a rise in the ACCR in acute pancreatitis can occur in the presence of a normal serum amylase level (Levitt and Duane, 1975). These findings suggest that the ACCR might be a more sensitive index both in the diagnosis and in following the natural history of acute pancreatitis than the serum amylase level.

In only one patient did the serum amylase level rise after biliary surgery. However, in seven patients (28%) the ACCR exceeded the 5.5% level, which is suggestive of a clinically significant acute pancreatitis (Lesser and Warshaw, 1975). This included five of the eight patients who had undergone exploration of the common bile duct, a procedure that is considered to precipitate postoperative pancreatitis (Miller *et al.*, 1973). In spite of the 25 to 50% mortality associated with postoperative pancreatitis (Barbenheier *et al.*, 1968; Imrie, 1974) none of the seven patients with a postoperative ACCR which exceeded the 5.5% level developed any of the clinical features or complications of acute pancreatitis. This apparent anomaly can be explained by the fact that the 5.5% level suggested by Lesser and Warshaw (1975) was in the presence of hyperamylasaemia and that the serum amylase was normal in these patients. The combination of a raised ACCR with a normal serum amylase level is found in patients during the resolving phase of their acute pancreatitis, when the ACCR will remain raised for several days after the serum amylase has returned to normal (Levitt *et al.*, 1969). This can be interpreted as indicating a continuing process of pancreatic gland damage.

The transient rise in the ACCR after biliary surgery may reflect pancreatic disruption which had been produced by the operative manipulation of the pancreas and biliary tree, but which was not detectable using the more insensitive serum amylase level. We suggest that patients with a raised ACCR in the postoperative period have suffered some degree of pancreatic gland damage and they should

be carefully observed for development of the full clinical picture of acute pancreatitis.

References

- Barbenheier, J. A., Kaminski, D. L., and Willman, V. L. (1968). Pancreatitis after biliary tract surgery. *American Journal of Surgery*, **116**, 773-776.
- Ceska, M., Birath, K., and Brown, B. (1969). A new and rapid method for the clinical determination of α -amylase activities in human serum and urine. Optimal conditions. *Clinica Chimica Acta*, **26**, 437-444.
- Dreiling, D. A., Leichtling, J. J., and Janowitz, H. D. (1974). The amylase-creatinine clearance ratio. *American Journal of Gastroenterology*, **61**, 290-296.
- Imrie, C. W. (1974). Observations on acute pancreatitis. *British Journal of Surgery*, **61**, 539-544.
- Imrie, C. W., and Whyte, A. S. (1975). A prospective study of acute pancreatitis. *British Journal of Surgery*, **62**, 490-494.
- Keighley, M. R. B., Johnson, A. G., and Stevens, A. E. (1969). Raised serum amylase after upper abdominal operation. *British Journal of Surgery*, **56**, 424-427.
- Lesser, P. B., and Warshaw, A. L. (1975). Differentiation of pancreatitis from common bile duct obstruction with hyperamylasaemia. *Gastroenterology*, **68**, 636-641.
- Levine, R. I., Gauser, F. L., and Berk, J. E. (1975). Enhancement of the amylase-creatinine clearance ratio in disorders other than acute pancreatitis. *New England Journal of Medicine*, **292**, 329-332.
- Levitt, M. D., and Duane, W. C. (1975). *Surgery of the Liver, Pancreas and Biliary Tract*, pp. 233-241. Edited by J. S. Najarian and J. P. Delaney. Stratton. Intercontinental Medical Book Corp.: New York.
- Levitt, M. D., Rapoport, M., and Cooperband, S. R. (1969). The renal clearance of amylase in renal insufficiency, acute pancreatitis and macroamylasaemia. *Annals of Internal Medicine*, **71**, 919-925.
- Miller, S. F., Whitaker, J. R., and Snyder, R. D. (1973). Incidence of elevated serum amylase levels and pancreatitis after upper abdominal surgery. *American Journal of Surgery*, **125**, 535-537.
- Singh, L. M., Okukubo, F., James, P. M., Salmon, J., and Howard, J. M. (1965). Further studies on postoperative pancreatitis. *Archives of Surgery*, **90**, 43-49.
- Warshaw, A. L., and Fuller, A. F. (1975). Specificity of increased renal clearance of amylase in diagnosis of acute pancreatitis. *New England Journal of Medicine*, **292**, 325-328.