The Nature and Significance of Hyperamylasemia Following Operation

RICHARD MORRISSEY, M.D., J. EDWARD BERK, M.D., LOUIS FRIDHANDLER, Ph.D., DANIEL PELOT, M.D.

From the Gastroenterology Division of the Department of Medicine, University of California, Irvine, California

Total serum amylase activity was found to be significantly elevated postoperatively in 11 (10%) of 110 patients undergoing various surgical procedures. Isoamylase analysis revealed that the rise was chiefly in the pancreatic-type isoamylase in seven of the 11 patients showing postoperative serum amylase elevations; in the other four patients, the elevation occurred principally in the salivary-type isoamylase. These data demonstrate that postoperative hyperamylasemia occurs surprisingly often and that serum amylase activity may rise even when the surgical procedure is extra-abdominal. Moreover, elevation of serum amylase activity after surgery is not necessarily an indication of pancreatitis and may reflect instead a rise in salivary-type isoamylase.

THE DIAGNOSIS of acute pancreatitis complicating the postoperative state[1,11,13,14,19,22] usually is founded on the presence of hyperamylasemia. Since amylase activity may be affected by a variety of factors and conditions, not all directly involving the pancreas, there is an element of uncertainty attaching to the diagnosis of acute postoperative pancreatitis when based on a rise in serum amylase.[19] Moreover, Harada *et al.*[11] have recently presented evidence indicating that the origin of the elevated serum amylase occurring after operations may not always be pancreatic. It would be of decided clinical value, therefore, to know the specific source of the serum amylase which may rise after an operation. This report concerns a study of the isoenzyme pattern of the serum amylase elevation occurring in patients undergoing various operative procedures. Not only was serum amylase activity found to increase often after surgical procedures, but the rise was not always in the pancreatic-type component.

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Reprint requests: J. Edward Berk, M.D., Department of Medicine, Orange County Medical Center, 101 City Drive South, Orange, California 92668.

Materials and Methods

A randomly selected group totalling 110 patients undergoing various surgical procedures was studied. Serum was obtained prior to operation and again approximately 3, 24 and 48 hours after operation. Due to circumstances beyond control, including duration of the operation, it was not possible to secure postoperative samples in some of the cases at the precise intervals stated. An additional blood sample was taken 7 days after operation in those patients showing serum amylase elevations during the first 48 hours following operation. Each serum sample was assayed for amylase activity using an automated saccharogenic method.[8] This method expresses amylase activity in terms of mg of glucose generated per 100 ml. The presently adopted upper limit of normal for serum amylase activity by this method, based on a limited analysis of normal subjects, is approximately 100 mg glucose/100 ml.[9]

The serum samples of those patients whose postoperative levels were greater than 50 mg glucose/100 ml above the corresponding preoperative value were further analyzed for isoamylase pattern using methods previously described.[9] These methods separate serum amylase that arises from the pancreas (P-type) from another component (S-type) that originates in the salivary glands and possibly in other tissues as well. Serum amylase was considered to be elevated when the total serum amylase in any postoperative sample exceeded

TABLE 1. *Summary of Serum Amylase Changes Following Various Operations*

Type of Operation		Serum Amylase Elevations	Isoamylase Mainly Responsible for Elevation	
			Pancreatic Type	Salivary Type
Abdominal	28	4 (14%)	3	1
Non-Abdominal	82	7 (9%)	4	3
TOTAL	110	11 (10%)	7	4

100 mg glucose/ml *and* the activity of either the P-type or S-type components exhibited a rise of at least 100% above the corresponding preoperative value.

Results

Of the 110 patients surveyed, 11 (10%) met the criteria for significant postoperative elevation of serum amylase activity (Tables 1 and 2). Table 2 lists the operations performed and shows the pre- and postoperative levels of the individual isoamylases in those patients showing a postoperative elevation. Representative cases illustrating the changes occurring postoperatively in the major isoamylase components are shown in Fig. 1.

Four (14%) of the 28 patients undergoing abdominal procedures met the criteria for a rise in serum amylase (Tables 1 and 2). In the two patients with the most marked elevations in this group (Cases 6 and 7), the amylase rise was mainly in the P variety. Of the other two patients in this group, the rise was in the P-type in one (Case 3) and the S-type in the other (Case 10).

Eighty-two of the patients had non-abdominal surgical procedures and 7 (9%) showed a postoperative serum amylase rise by the criteria employed (Tables 1 and 2). The elevation was essentially of the S-type isoamylase in 3 (Cases 8, 9, 11) and of the P-type isoamylase in 4 (Cases 1, 2, 4, 5).

When the amylase levels rose significantly in the postoperative period, the peak usually appeared about 24 hours after operation (Fig. 2). Sixty-five of the 110 patients showed an initial drop in amylase activity at three hours after operation. Within 24 hours, the serum amylase either rose above normal, returned to preoperative levels, or maintained the level exhibited at three hours. Isoamylase analysis in two patients showing a diminution in serum amylase in the immediate postoperative period revealed that both the S- and P-components dropped, the more pronounced reduction occurring in the P variety.

Most operations that were followed by serum amylase elevations were done under general anesthesia. However, a cataract removal (Case 1), which was followed by a 320% rise of the P-type, was performed under local anesthesia. Meperidine and hydroxyzine HCL were given to this patient preoperatively.

Four patients exhibited preoperative total serum amylase levels greater than 130 mg glucose/ml (130–180) and thus had values above our presently accepted upper limit of 100 mg glucose/ml. Nine other patients had serum amylase levels above 110 mg glucose/ml both pre- and postoperatively. One of this group with levels of 255 and 225 mg glucose/ml, respectively, was subsequently found to have macroamylasemia using a rapid microcolumn chromatographic method.[10]

Discussion

Reports dealing with acute pancreatitis and hyperamylasemia in the postoperative period have dealt primarily with patients subjected to surgical procedures in the upper abdomen. Thus Perryman and Hoerr[18] reported on 85 patients undergoing upper abdominal surgical procedures. Twenty-seven (32%) had postoperative elevations of serum amylase. Included among

TABLE 2. *Comparative Serum Amylase Levels Before and 24 Hours After Operation in Patients Exhibiting Postoperative Rises*

Case	Surgical Procedure	Serum Amylase Values*					
		Preoperative			24 Hrs. Postoperative		
		P-type	S-type	Total	P-type	S-type	Total
1	Cataract Removal	32	25	57	103	25	128
2	Patellectomy	30	46	76	96	36	132
3	Vagotomy and Pyloroplasty	66	58	124	147	46	193
4	Facial Fracture Repair	34	30	64	81	37	118
5	Spinal Fusion	50	9	59	130	13	143
6	Aortic Aneurysm Repair	22	14	36	924	176	1100
7	Hepatectomy	40	32	72	732	68	800
8	Tendon Repair	26	60	86	30	596	626
9	Arthroplasty	37	74	111	42	180	222
10	Appendectomy	15	19	34	15	170	185
11	Open reduction & Internal Fixation of a Fractured Femur	22	25	47	47	883	930

* Expressed as mg glucose/100 ml.
Postoperative values underlined are those showing rises as defined in text.

the latter were two fatal cases of pancreatitis. However, only a few of the other patients with a postoperative serum amylase rise had clinical findings suggestive of pancreatitis. Mahaffey *et al.*[14] reported that nine (9%) of 100 patients were considered by them to have developed hyperamylasemia following abdominal surgery. Singh *et al.*[19] found that of 95 patients who underwent abdominal operations, 24 had an elevation in serum amylase. These observers also noted that patients with the highest serum amylase levels postoperatively did not develop clinical signs of pancreatitis, whereas patients developing fatal pancreatitis had only moderate serum enzyme elevations. Harada *et al.*[11] studied serum amylase behavior before and after surgical procedures in 114 patients. Of 75 patients undergoing abdominal procedures, 13 developed hyperamylasemia. Another group of 24 patients was separately classified as having procedures done under spinal anesthesia. Although the precise nature of these procedures was not given in detail, appendectomy was noted to have been among them. Five of the 24 patients in this category developed hyperamylasemia. Keighley and co-workers[12] noted postoperative hyperamylasemia in 13 of 107 patients undergoing upper abdominal operations, only three of whom were symptomatic. Bardenheier and associates[1] studied 840 patients who underwent cholecystectomy; 180 also had common bile duct exploration. Thirty-four (4%) of the 840 had clinically evident pancreatitis. In addition, of the 547 patients without clinical signs of pancreatitis in whom amylase determinations were made, 52 had hyperamylasemia (greater than 200 Somogyi units).

Hyperamylasemia and pancreatitis have also been reported postoperatively in patients with extra-abdominal operations.[11,13,19,22] Illustrative is the report of Levine *et al.*[13] which describes 6 cases of necropsy-confirmed pancreatitis following transurethral resection of the prostate. Anesthesia in these cases varied from spinal to general. Singh *et al.*[19] found that 17 of 80 patients undergoing various extra-abdominal procedures developed hyperamylasemia postoperatively. Of the series of 114 patients observed by Harada *et al.*,[11] 15 underwent extra-abdominal procedures. In addition, some of the 24 patients they classified as having minor operations performed under spinal anesthesia probably had non-abdominal procedures. Of the 15 patients in whom the operative procedure clearly did not involve the abdomen, none developed hyperamylasemia. By contrast, five of the 24 patients who were operated on under spinal anesthesia developed hyperamylasemia.

Mahaffey *et al.*[14] found that none of 31 patients who underwent operative procedures not involving the abdomen developed hyperamylasemia by their criteria. White *et al.*[22] reported on 70 cases of postoperative

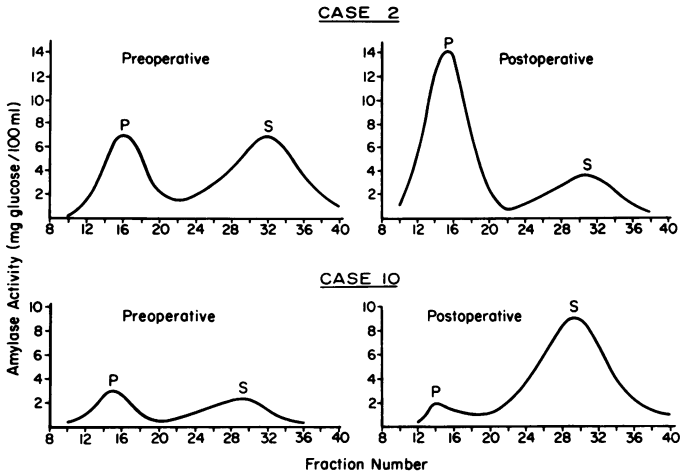

FIG. 1. Serum isoamylase patterns before and after operation. (Case 2) Elevation of P-type; (Case 10) Elevation of S-type.

pancreatitis following various operative procedures; in at least seven (10%) the procedures were clearly extra-abdominal procedures.

It has been generally assumed that elevation in serum amylase activity occurring postoperatively, even in the absence of signs and symptoms of pancreatitis, is the result of release of amylase from the pancreas. Harada, Kitamura, and Ikenaga,[11] however, have recently studied the isoamylase pattern in the sera of patients showing postoperative hyperamylasemia. Agar gel electrophoresis was used for this purpose. They found that of the 18 patients in their series who showed an increase in serum amylase activity after surgery, the rise in six was in pancreatic amylase. In the other 12 patients, the rise

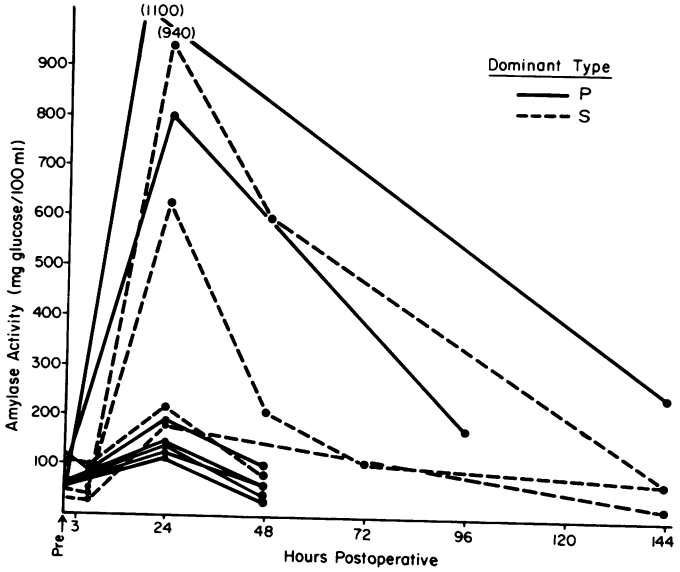

FIG. 2. Postoperative total serum amylase values in patients showing significant rise after operation. Also indicated is the isoamylase component principally affected.

was in an amylase component that displayed electrophoretic properties on agar gel identical to those of salivary amylase. Moreover, the most striking elevations were of this salivary-type amylase.

Our data confirm that postoperative hyperamylasemia in some cases may be due to an increase in salivary-type amylase. This finding may provide one explanation for those cases in which marked postoperative hyperamylasemia occurs without clinical evidence of pancreatitis. Our data also indicate that, excluding the two cases with abdominal operations during which the pancreas could have been affected (Cases 6, 7), the most striking rises in serum amylase activity were due to increases in the S-type isoamylase (Fig. 2 and Table 2).

Whether the S-type isoamylase originates solely from the salivary glands is not yet settled. Present evidence indicates that the salivary glands are clearly one source, and probably the principal source, of this isoamylase.[9] Amylase concentration in other organs with S-type isoamylase (liver and fallopian tubes), does not appear from our observations to be sufficient to make an appreciable contribution to the serum level.[9]

It is of interest that in every case in which the S-type isoamylase rose, there was an initial drop at 3 hours after surgery. Of note, too, was the observation that many of the patients studied demonstrated a slight drop in serum amylase levels at three hours with a return toward preoperative levels at 24 hours in most. This may reflect parasympatholytic effects of atropine administered preoperatively. The same mechanism might also explain the fall in serum amylase postoperatively in those patients whose levels were elevated preoperatively. It is conceivable as well that S-type hyperamylasemia may represent a rebound secretion by the salivary glands after the effects of atropine are dissipated.

Aside from the two cases in which surgical trauma to the pancreas could have occurred, and in which there was a pronounced rise in P-type isoamylase, it was not possible to establish any relationship between the type of postoperative isoamylase elevation and the nature of the surgical procedure. There was also no correlation with age, sex, pre- or postoperative medication, type of anesthesia, or receipt of blood.

Elevations of serum amylase occurring after upper abdominal operations have usually been explained by direct injury to the pancreas or pancreatic duct or to vascular impairment. Injury of the sphincter of Oddi by instrumentation has also been advanced as a pathogenetic factor. The consequence of such injury may be interruption of the flow of pancreatic secretion or reflux of duodenal contents.[22]

The pathogenesis of hyperamylasemia and pancreatitis following nonabdominal operations is much less readily explained. Morgan and his associates[16] found that the level of trypsin inhibitor in the pancreatic secretion of postoperative patients is decreased. They postulated that this may be a metabolic response to trauma and could occur following procedures removed from the area of the pancreas. The use of narcotics before, during, and after surgery may also be influential, since the serum amylase may rise following the administration of morphine and other analgesics.[3–5,17,21] There are still other factors involved with surgical procedures in general that could affect serum amylase activity. It is conceivable, for example, that a rise in S-type isoamylase may result from salivary gland injury when general anesthesia is administered and an endotracheal tube is inserted. Additionally, hyperamylasemia may represent a non-specific response mediated by stress-provoked mechanisms. Thus, Challis *et al.*[7] produced hyperamylasemia in dogs by the administration of adrenocorticotrophic hormone (ACTH). They suggested that the hyperamylasemia occurring in various pathological conditions may result from the spontaneous release of ACTH and activation of the adrenal cortex.

Isoproterenol and other catecholamines stimulate amylase secretion in the rat parotid glands,[6] probably through the mediation of cyclic AMP.[2] Adenyl cyclase in both the pancreas and parotid gland is stimulated by isoproterenol, but there is much less of this enzyme activity in pancreatic preparations. Parotid cyclic AMP levels are greatly increased after *in vivo* administration of isoproterenol in the mouse, whereas little change is observed in the pancreas.[15] Cellular or membrane functions may be altered and pancreatic macromolecular transport may be increased or decreased by certain chemical compounds. Illustrative of such actions are the observations of Singh *et al.*[20] using *in vitro* models. These investigators showed that streptomycin and lidocaine enhanced secretion of amylase, that atropine had no effect on basal secretion, and that tetracycline hydrochloride, amphotericin B, and valinomycin decreased secretion.

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