EXPERIMENTAL STUDIES ON DISTURBANCES IN CALCIUM-PHOSPHATE TURNOVER AND OSTEOPATHY FOLLOWING TOTAL GASTRECTOMY WITH SPECIAL REGARD TO THE ROLE OF VITAMIN D AND THE MAINTENANCE OF THE DUODENAL PASSAGE

SUMMARY

The consequences of total gastrectomy in humans and experimental animals include disturbances of phosphorus and calcium metabolism and osteopenia. The pathogenesis of these disturbances has not been clarified completely and therefore there is no basis for developing effective methods of prevention and treatment.

Since gastrectomized humans and animals show decreased $25(OH)D_3$ levels in serum, vitamin D deficiency is considered to be one of the causes of gastrectomy-related osteopenia. A number of researchers suggest that vitamin D should be used in the prevention and treatment of gastrectomy-related osteopenia. So far, neither the role of vitamin D deficiency in gastrectomy-related osteopenia nor the efficacy or necessity of vitamin D supplementation after gastrectomy have been evaluated. Some authors have proposed that lack of the duodenal passage, as a result of a Roux gastrectomy, may play a certain role in the development of gastrectomy-related osteopenia.

The currently used technique of esophagojejunal anastomosis performed in rats is associated with severe inflammatory and hyperplastic lesions within the esophageal wall. These lesions may significantly affect the general state of the experimental animal, thus obscuring results, especially when one tries to link differences in the parameters studied with the anatomic conditions caused by Roux and Longmire total gastrectomies.

The aim of this study was, first, to develop an experimental model that would eliminate or at least minimize these lesions and, second, to evaluate, using this model, the effects of normal, increased, or decreased dietary levels of vitamin D on calcium and phosphorus metabolism and on the development of osteopenia in rats after a Longmire or Roux gastrectomy. This also enabled evaluation of the significance of the duodenal passage for the development of gastrectomy-related osteopenia.

A Longmire or Roux total gastrectomy was performed in Sprague-Dawley rats. The control group included rats in which the small intestine was transected distally to the Treitz ligament and re-anastomosed.

In the first phase of the study, the invagination technique of esophagojejunal

anastomosis was adapted to the anatomic and physiologic conditions of the rat. Then the late outcome of this technique was compared with that of end-to-end anastomosis.

Fifteen weeks after gastrectomy all animals showed papillary and acanthotic epithelial hyperplasia and hyperkeratosis within the esophageal mucosa as well as inflammatory infiltrates in the mucosal, submucosal, muscular, and serosal layers of the esophagus. The extent of these pathologic changes was evaluated semiquantitatively.

The intensity of changes was significantly lower in animals treated with the invagination technique of esophagojejunal anastomosis. Moreover, animals subjected to a Roux gastrectomy with simple end-to-end anastomosis showed lower weight gain, more severe anemia, more marked inflammatory and hyperplastic changes in the esophageal wall, and more severe osteopenia, as compared with those after a Longmire gastrectomy. The above mentioned differences were to the great extend diminished when the invagination technique was applied. Thus, it can be concluded that stenosis of esophago-jejunal anastomosis with subsequent dilatation of the esophagus and concomitant inflammation and epithelial hyperplasia in its wall enhance osteopenia.

In the second phase of the study, rats were operated on using the invagination technique of esophagojejunal anastomosis. Both control and gastrectomized rats, the latter subjected to a Longmire or Roux gastrectomy, were divided into three subgroups fed on a diet containing 100, 1200 or 4800 IU of vitamin D_3 per kg of chow. The gastrectomized animals showed moderately reduced levels of calcium, phosphorus and magnesium - which were significant only when rats were fed on a diet suplemented with high doses of vitamin D, decreased gastrin and $25(OH)D_3$ levels, increased $1,25(OH)_2D_3$ levels and increased AP and AP-BI activities. The levels of PTH and calcitonin were normal. In contrast to control animals, in gastrectomized animals an increase in dietary vitamin D levels, which was reflected by increased $25(OH)D_3$ levels in blood, was paralleled by an increase in $1,25(OH)_2D_3$ levels in blood. Thus, gastrectomy disturbs the feedback between these vitamin D metabolites. These changes were accompanied by a reduction in bone mass, bone density, and by a decrease in calcium and phosphorus content per unit volume of bone. In gastrectomized animals fed on a low-vitamin D diet, calcium and phosphorus content per unit of dry bone mass did not differ from the control values. Such differences appeared only in gastrectomized animals fed on a diet supplemented with vitamin D.

Thus, it can be concluded that gastrectomy leads to loss of all components of bone and that it impairs, though to a lesser extent, mineralization of bone. Moreover, since a vitamin D-supplemented diet did not prevent osteopenia in gastrectomized rats (though it reduced its

extent), vitamin D deficiency is not the key cause of osteopenia in gastrectomized rats. The calcium, magnesium and phosphorus content of bone was correlated with dietary vitamin D levels. These parameters were similar in rats on a diet supplemented with low (100 IU/kg) or high (4800 IU/kg) levels of vitamin D, whereas they were significantly lower in rats on a diet supplemented with standard levels (1200 IU/kg) of vitamin D.

The effects of Longmire and Roux gastrectomies on most of the parameters studied did not differ significantly. Thus, the elimination of the duodenal passage does not significantly enhance disturbances of calcium and phosphorus metabolism and the extent of osteopenia in gastrectomized rats. It may cuntribute however, to the development of anaemia.