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ORIGINAL ARTICLE

Effectiveness of alendronate for bone disorder after gastrectomy for gastric cancer

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activated vitamin D3;
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Summary *Background:* Routine therapy of metabolic bone disorder (MBD) after gastrectomy for gastric cancer has not been established yet. We have reported that administering an active vitamin D3 agent to patients who had undergone gastrectomy for gastric cancer improved MBD. Recently, the usefulness of alendronate, an osteoclast inhibitor, has been reported for MBD. Here we report the effects of alendronate for MBD after gastrectomy for gastric cancer.
Methods: Dual energy X-ray absorptiometry was performed consequently in 14 patients, who had been gastrectomized for gastric cancer and survived more than 5 years without recurrence, to evaluate the MBD and compared before and after treatment. The 14 patients were divided into two groups: in group VD3, 1 μg/d of alfacalcidol, an active vitamin D3 agent, was administered; and in group ALN, 5 mg/d or 35 mg/wk of alendronate or both alfacalcidol and alendronate were administered. These drugs had been administered to the patients for > 2 years, and the patients were followed up.
Results: After 12 months, dual energy X-ray absorptiometry revealed that bone mineral density and T score were significantly increased in group ALN. Changes in serum bone-specific alkaline phosphatase after 24 months were −9.1 μg/L in the ALN group and 3.75 μg/L in the VD3 group, showing a significant difference ($p = 0.02$). No serious adverse events were observed in either group.

Conflicts of interest: There are no financial or other relations that could lead to a conflict of interest.

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Conclusion: These results showed the usefulness of alendronate and alendronate+activated vitamin D3 combination therapy, suggesting that these treatments might prevent postgastrectomic MBD.

1. Introduction

Metabolic bone disorder (MBD) has drawn attention as one of the consequences of malabsorption following gastrectomy.[1,2] Our previous study[3] on the pathophysiology of the MBD after gastrectomy for gastric cancer found that the incidence of MBD increased with time after operation irrespective of surgical procedures and that the decreased food intake after operation might be one of its main causes. A therapeutic method for MBD has not been established. We have reported that giving an active vitamin D3 agent to patients who had undergone gastrectomy improved MBD.[4] Recently, the usefulness of alendronate, an osteoclast inhibitor, has been revealed for bone disorders.[5–7] Therefore, in the present study, we assessed whether MBD following gastrectomy could be treated by administration of alendronate.

2. Methods

Fourteen consecutive patients with no evidence of recurrence, who underwent gastrectomy for gastric cancer at the Department of Surgery, Yokohama City University, Yokohama, Japan, were enrolled in this study. Patients were 11 men and three women with an average age of 66.5 $\pm$ 8.96 years. After obtaining informed consent, the 14 patients were divided into two groups based on their record numbers. In group VD3, 1 μg/d of alfacalcidol, an active vitamin D3 agent, was administered. In group ALN, 5 mg/d or 35 mg/wk of alendronate or both alfacalcidol and alendronate were administered. Groups VD3 and ALN consisted of eight patients and six patients, respectively. Two patients received alendronate alone and four patients received both alfacalcidol and alendronate in group ALN. Roux-en-Y total gastrectomy was performed for two patients in group VD3, and for four patients in group ALN. Billroth I distal gastrectomy was performed for six patients in group VD3, and for two patients in group ALN. Bone mineral density (BMD) and T score were measured by dual energy X-ray absorptiometry (DEXA). The measurement site was the lumbar vertebra (L2–L4). The T score is the standard deviation from the normal mean value of a reference population of young adult controls. The serum bone specific alkaline phosphatase (BAP), parathyroid hormone (PTH), calcium, phosphorus, calcitriol, and urinary deoxypyridinoline (DPD) were evaluated before surgery and 6 months, 12 months, 18 months, and 24 months after surgery. The treatment was continued in both groups for $>$ 2 years, and the patients were then followed up.

2.1. Definition

We defined MBD by the extent to which they reduce bone density. Osteopenia is defined as bone density that is more than one standard deviation below peak bone density (T score -1), and osteoporosis is defined as bone density that is $\geq$ 2.5 standard deviations below the mean peak bone density (T score -2.5).

2.2. Statistical analysis

Mann–Whitney *U* test, Wilcoxon signed-rank test, and Fisher's exact test were used for statistical analysis and $p < 0.05$ was considered statistically significant. All statistics analyses were performed with EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Australia). More precisely, it is a modified version of R commander designed to add statistical functions frequently used in biostatistics.[8]

3. Results

3.1. Before treatment

Patients were followed for a median of 7 (interquartile range, 4.75–11) years after gastrectomy in group VD3 and 5.5 (interquartile range, 4.25–6.75) years after gastrectomy in group ALN. The averages of the BMD were 0.91 $\pm$ 0.17 g/cm^2 in group VD3, and 0.86 $\pm$ 0.13 g/cm^2 in group ALN group, showing no statistically significant difference between the groups ($p = 0.595$). The averages of the T score were -1.16 ± 1.46 in group VD3, and -1.52 ± 1.05 in group ALN group, showing no statistically significant difference between the groups ($p = 0.625$). There were five patients with osteopenia ($-2.5 <$ T score ≤ -1) in group VD3, and three patients in group ALN. There was 1 patient of osteoporosis (T score ≤ -2.5) in each group (Table 1).

3.2. After treatment

3.2.1. BMD

In group VD3, there was no significant difference in BMD and T score before and after the 24-month treatment. In group ALN, the DEXA revealed that BMD was significantly increased by 0.057 $\pm$ 0.021 g/cm^2 at the 12-month treatment ($p = 0.031$). After the 24-month treatment, the DEXA revealed that BMD was increased by 0.077 $\pm$ 0.026 g/cm^2 in