Vitamin D deficiency after vagotomy

Metabolic bone disease is known to occur several years after gastrectomy.¹ A recent report based on plasma calcium and phosphate concentrations and alkaline phosphatase activity claimed that metabolic bone disease does not occur after truncal vagotomy and gastrojejunostomy.² Since the presence of normal plasma calcium, phosphate, and alkaline phosphatase values does not establish the absence of biochemical osteomalacia^{3,4} we decided to investigate the vitamin D (25(OH)D) and parathyroid hormone states of patients with truncal vagotomy and highly selective vagotomy.

Patients, methods, and results

Patients who had undergone surgery for a duodenal ulcer in the previous eight years were invited to attend the metabolic clinic. Twenty two patients responded and were divided into two groups—group 1, eight patients with truncal vagotomy and gastrojejunostomy or pyloroplasty (median age 61 years (range 41-84); median duration since operation 4 years (range 2-8 years)); group 2, 14 patients with highly selective vagotomy (median age 44 years (range 27-69); median duration since operation 5 years (range 1-8 years)). None of the patients had symptoms suggestive of dumping, intolerance to milk, or malabsorption. None of the patients was taking antacids, H₂ receptor blocking agents, anticonvulsants, calcium, or vitamin D replacement.

A fasting venous blood sample was collected from each patient. Blood was allowed to clot and then centrifuged immediately at 4°C; serum was stored at -20°C for estimation of parathyroid hormone and vitamin D concentrations. Plasma calcium, phosphate, albumin, and alkaline phosphatase values were measured using an SMAC Technicon autoanalyser (Basingstoke). Serum vitamin D was measured as described,⁴ while parathyroid hormone was measured by a radioimmunoassay directed at the mid-region of the hormone (Immuno-Nuclear Corporation, USA). Statistical analysis was carried out by the two tailed Mann-Whitney U test for non-parametric data. Results are expressed as medians and ranges.

Patient characteristics and values of plasma variables assessed in truncal vagotomy (group 1) and highly selective vagotomy (group 2) patients and controls. Values are medians (ranges in parentheses)

	Group 1	Group 2	Controls
No of subjects	8	14	24
Age (years)	61 (41-84)	44 (27-69)	36 (24-60)
Years since surgery	4 (2-8)	5 (1-8)	
Calcium (mmol/l)	2.40 (2.36-2.51)	2.45 (2.35-2.56)	2.40 (2.20-2.60)
Phosphate (mmol/l)	0.97 (0.86-1.41)	1.02 (0.67-1.46)	0.98 (0.70-1.25)
Alkaline phosphatase (IU/l)	99 (57-127)	70 (49-142)	85 (35-130)
Vitamin D (nmol/l)‡	5.6*† (5.0-18.1)	16.2* (5.0-43.8)	38.0 (12.7-59.5)
Parathyroid hormone (pmol/l)‡	52 (34-68)	53 (25-82)	54 (23-85)

*Compared with controls: $p < 0.001$.

†Compared with group 2: $p < 0.05$.

‡Lower limit for serum concentrations of vitamin D 15 nmol/l (6.0 ng/ml). Normal range for parathyroid hormone 20-85 pmol/l (2.0-8.5 pg/ml).

Conversion: SI to traditional units—Calcium: 1 mmol/l $\approx$ 4.0 mg/100 ml. Phosphate: 1 mmol/l $\approx$ 3.0 mg/100 ml. Vitamin D: 1 nmol/l $\approx$ 0.4 ng/ml. Parathyroid hormone: 1 pmol/l $\approx$ 0.1 pg/ml.

Plasma calcium and phosphate concentrations and alkaline phosphatase activity in both groups of operated patients were similar to those in controls. Serum vitamin D concentrations in both groups of patients were significantly lower than in controls (see table), those in patients with truncal vagotomy being lower than in patients with highly selective vagotomy. Six out of eight patients with truncal vagotomy had subnormal vitamin D concentrations, while six out of 14 patients with highly selective vagotomy had subnormal vitamin D concentrations. Parathyroid hormone concentrations in patients and controls were almost identical (see table). There was no relation between serum vitamin D and parathyroid hormone concentrations and time since operation.

Comment

Our data show clearly that a large proportion of patients treated by vagotomy for duodenal ulceration develop biochemical evidence of vitamin D deficiency within eight years. Concentrations of vitamin D in the serum of our patients were comparable to those found in Asian immigrants in Britain who often have florid osteomalacia.⁴ Furthermore, patients who had a truncal vagotomy had significantly lower concentrations of vitamin D when compared with the group who had a highly selective vagotomy, suggesting that the extent of vitamin D

deficiency may be related to the degree of vagal inhibition. The absence of secondary hyperparathyroidism in our patients may reflect either a marginal deficit of vitamin D or a relatively short duration of this deficit. This contrasts with our observation of frequent secondary hyperparathyroidism in asymptomatic Asian vegetarian subjects.⁴

The mechanism of vitamin D deficiency after vagotomy is not clear. While vagotomy may alter intestinal motility, none of these patients had symptoms of dumping or malabsorption. A decrease in vitamin D intake due to an altered diet has been suggested in patients after vagotomy. Bile acid excretion may be increased after vagotomy; this may interrupt the enterohepatic circulation of vitamin D metabolites and may, over a prolonged period, lead to vitamin D deficiency. Exocrine pancreatic function also changes after vagotomy⁵; this too may contribute to vitamin D malabsorption.

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Cryoanalgesia to relieve pain in diastasis of the symphysis pubis during pregnancy

Diastasis of the symphysis pubis is not common, occurring in about one in 20 000 births,¹ but relief of the pain during the final trimester of pregnancy is a difficult problem. The diastasis resolves completely after delivery, and so this problem of analgesia is of limited duration.¹ The pain increases with increasing size of the uterus and as it is aggravated by movement some relief can be achieved by bed rest. In the last third of pregnancy this usually results in admission to hospital because it is almost impossible for most mothers to have complete bed rest at home. There remains the problem of analgesia when movement is necessary, such as during washing and when using the commode. Non-narcotic analgesics rarely provide adequate analgesia, and most doctors are reluctant to prescribe narcotics for three months because of possible side effects.

We describe two patients with diastasis of the symphysis pubis in whom considerable pain relief was achieved by cryoanalgesia² through the caudal hiatus during the last third of pregnancy.

Case reports

During their first pregnancy both patients developed diastasis of the symphysis pubis. In their second pregnancy they complained of pain in the region of their symphysis pubis during the second trimester; diastasis was confirmed radiologically.

Case 1—A 30 year old woman was admitted to hospital in the 20th week of her pregnancy because of pain. As the uterus increased in size the pain worsened, particularly on movement. By the 30th week she was confined to bed. The worst pain was in and around her vagina rather than over her symphysis pubis. A caudal injection of 5 ml 0.5% bupivacaine plain resulted in complete relief of pain and enabled her to walk comfortably for six hours. Cryoanalgesia by the standard technique³ resulted in adequate analgesia until delivery six weeks later.

Case 2—A 26 year old woman was referred at 20 weeks' gestation because of pain. The pain was described as similar to that in case 1. A caudal injection of 3 ml 0.5% bupivacaine plain resulted in bilateral numbness in the S4-5 dermatomes and almost complete relief of pain for eight hours. At 30 weeks she was admitted to the maternity hospital because of the pain. Cryoanalgesia through the caudal hiatus by the standard technique³ resulted in considerable pain relief and enabled her to stay at home until the 36th week.

Comment

Cryoanalgesia results in a reversible destruction of peripheral nerves, the major advantage over other methods being that painful neuralgia has not been reported after this technique.² The regrowth of the nerve in animal models after a cryolesion is anatomically normal when examined under a light microscope.⁴ All other techniques entailing destruction of nerves are followed by the formation of neuromas and by pain in a high proportion of patients.² Numbness in the area of distribution of the infraorbital nerve after cryoanalgesia lasted a mean of 49 days (range 21-339 days). After this time the nerve was functionally normal.⁵ Thus although cryoanalgesia results in destruction of the peripheral nerves, full function returns within a few weeks, and the technique would seem ideal for the pain of diastasis of the symphysis pubis, which resolves spontaneously after delivery.

It is generally accepted that the nerves that supply the area around a joint also supply the joint. Our results suggest that the pain in our patients originated from the pelvic floor, not from the symphysis pubis. After cryoanalgesia both patients stated that they could feel the movement of the symphysis pubis but that it was not painful.

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Cryoglobulinaemia in haemophilia

Most cryoglobulins are immunoglobulins and can be classified into three types: type I, composed of monoclonal immunoglobulins; type II, containing a monoclonal component possessing antibody activity to polyclonal IgG; and type III, mixed polyclonal immunoglobulin.¹ We report on a patient with type III cryoglobulinaemia who presented with vasculitis after treatment with factor VIII concentrate.

Case report

The patient was a 40 year old man with haemophilia A (factor VIII concentration <10 U/l). He had been given blood transfusions for recurrent epistaxis at age 8, for haematuria at age 16, and for haematemesis after ingestion of aspirin at age 18. He had first been treated with cryoprecipitate in 1968 and from 1969 to 1978 received roughly 8000 units factor VIII a year (figure). During this time a home treatment programme was established. Four weeks after his first treatment with intermediate purity factor VIII concentrate in June 1978 he developed non-A, non-B hepatitis.

Vasculitic lesions on both lower legs first developed in autumn 1978, and in January 1979 he developed a bilateral red blotchy rash, ankle swelling, and calf tenderness. During the next two years he treated recurrent episodes of vasculitis with increasing doses of both National Health Service and commercial factor VIII concentrate. In 1981 skin biopsy showed non-specific vasculitis. The haemoglobin concentration was 15 g/dl, white cell count $9.4 \times 10^9/l$, platelet count $290 \times 10^9/l$, and erythrocyte sedimentation rate 40 mm in

first hour. The titre of rheumatoid factor (sheep cell agglutination test) was positive at 1/5120; although the C3 concentration was normal at 0.9 g/l (normal range 0.6-1.35 g/l), C4 was low at <0.1 g/l (normal range 0.5-1.2 g/l). He continued to have intermittent rashes on the lower legs accompanied by tender calf muscles and ankle oedema. His use of factor VIII concentrate gradually increased (figure) because he thought that his painful muscles were associated with bleeding and his symptoms improved after treatment. In May 1982 he started steroid treatment, initially 30 mg/day and then 10 mg/day for the next two years. In November 1982 he developed painful small joints of the hands. At this time his renal function and creatinine clearance were normal, but the IgM concentration was increased (3.2 g/l, normal range 0.6-2.8 g/l).

In October 1983 he developed haemorrhagic herpes zoster in the T4 division, which was treated with acyclovir. Cryoglobulins (1100 mg/l, normal <40 mg/l) were found in his serum. When it was suggested that this might be related to factor VIII concentrate he began to curtail his use of it and slowly reduced the steroid dose, which he stopped in May 1984.

Treatment with factor VIII in relation to vasculitis.

For 11 months from January 1984 he used only 500 units of factor VIII for one elbow bleed. In December 1984 the serum cryoglobulin concentration had fallen to 290 mg/l, both the antigenic and functional C4 concentrations were normal (0.83 g/l and 1.0 g/l, respectively), and there was complete remission of the vasculitis and small joint pain. Antibody to human T cell lymphotropic virus was positive.

Comment

Patients with cryoglobulinaemia often exhibit vasculitis, purpura, arthralgia, and nephritis.² This patient exhibited vasculitis, cryoglobulinaemia, and hypocomplementaemia. The onset, exacerbation, and remission of the vasculitis corresponded to the patient's use of factor VIII concentrate, suggesting an immune mediated process in which the primary antigenic stimulus resulted from administration of the concentrate. Circulating immune complexes have been detected in a high proportion of patients with haemophilia,³ and in one study a significant correlation existed between the presence of immune complexes and chronic synovitis and haematuria.⁴ Clinical improvement correlated with a return of C4 concentrations to normal. Complement may play a part in maintaining immune complexes in solution,⁵ and this mechanism was probably overwhelmed by massive antigenic stimulation. Older patients with haemophilia often have a smaller requirement for replacement treatment, and thus this patient was able to reduce drastically his use of factor VIII concentrate.

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