

Determination of the functioning of autotransplanted parathyroid tissue in muscle

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Abstract Twenty dialysis and renal transplant patients with parathyroid hyperplasia underwent a total parathyroidectomy and an autotransplantation in forearm muscle. Twelve patients were available for investigation of the function of the transplanted parathyroid tissue. Differential studies of the two arms revealed functioning of the transplanted tissue in all cases. This was more readily demonstrated by determining the intact hormone in both arms.

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Traditionally the surgical treatment of parathyroid hyperplasia has been subtotal excision of the parathyroid glands (i.e. 3½ glands). More recently total parathyroidectomy and autotransplantation (TP-A) of some parathyroid tissue in muscle has been advocated.^{1,2} This latter strategy may be indicated in certain clinical situations. We have used TP-A in patients on dialysis and in renal transplant patients. The functioning of the transplanted tissue and calcium homeostasis were investigated in these patients.

Patients and methods

Over a period of 6 years, 20 dialysis and renal transplant patients underwent parathyroid transplantation in forearm muscle after total parathyroidectomy. The indication for parathyroidectomy in the majority of cases was tertiary hyperparathyroidism with severe metabolic bone disease. Five patients presented with rapidly progressing calciphylaxis. Three patients had grossly elevated serum calcium levels (1 was comatose and 1 was confused) and an emergency parathyroidectomy was performed in these patients. Other symptoms were severe pruritus in 2 patients and depression and constipation in another.

Parathyroid gland extirpation was performed via a standard thyroid exposure. Four hyperplastic glands were found in the neck of every patient. All glands were removed. Part of one gland was used for autotransplantation by cutting 10 small pieces of approximately 1,5 × 1,5 mm and placing each piece into a separate pocket in the belly of the brachioradialis muscle. Each pocket was marked with a non-absorbable suture.

The serum calcium levels declined in all patients postoperatively. Most patients needed high doses of intravenous calcium in the immediate postoperative period to maintain these levels.

The surviving patients were recently recalled and investigated for functioning of the transplanted parathyroid tissue. Parathyroid hormone (PTH) levels were determined in blood from antecubital veins in both arms using both a mid-molecule (RIA, Incstar Corporation) and an intact hormone (Allegro Immunoradiometric assay, Nichols Institute) kit.

Results

Of the 20 patients, 8 had died of renal failure and 12 were available for investigation. The minimum follow-up period was 6 months. Ten had functional renal transplants and 2 had returned to dialysis. All the patients showed a difference in PTH levels between the autografted arm and the normal arm. The ratio ranged from 1,68 to 17,69 using the intact hormone method (mean 6,26; SD 4,37) and from 1,13 to 2,37 (mean 1,68; SD 0,39) using the mid-molecule method (Fig. 1).

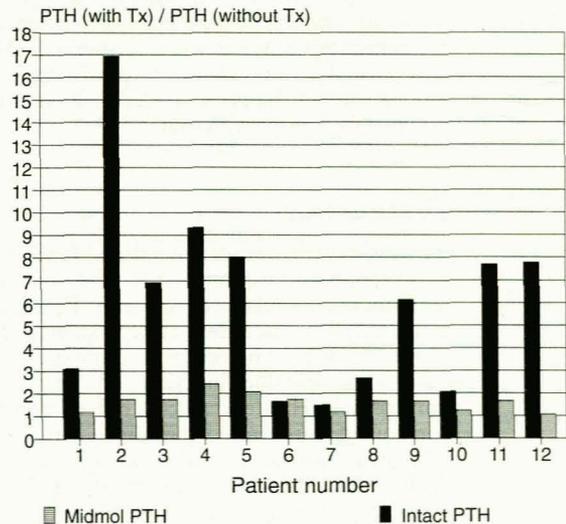


FIG. 1. PTH levels in blood drawn from antecubital veins in transplanted and non-transplanted arms for the intact hormone (dark bars) and mid-molecule (light bars) assays. The levels are higher using the intact hormone method.

Fig. 2 shows the mid-molecule PTH levels in both arms. Mean systemic value is 2,45 µg/l (SD 2,43; normal 0,44 - 0,9) and the mean value on the transplanted side is 3,96 µg/l (SD 4,02). The ratio was less than 1,5:1 in 4 patients.

Fig. 3 shows the intact PTH levels in each arm. Mean systemic value is 94,08 pg/ml (SD 86,13; normal 10 - 65 pg/ml) and the mean value on the transplanted side is 373,08 pg/ml (SD 320,27). In all patients, the ratio was more than 1,5:1.

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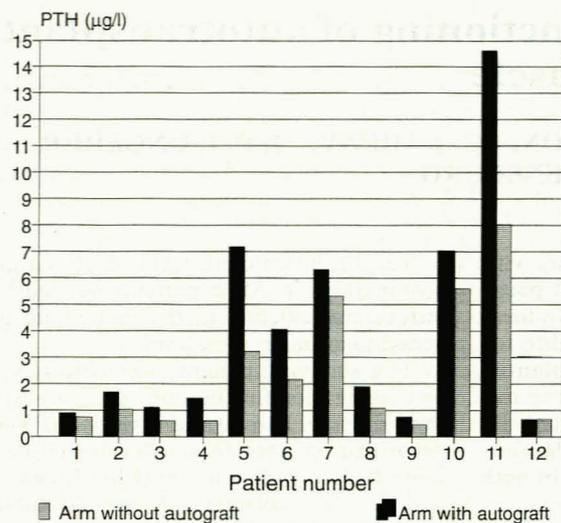


FIG. 2. Mid-molecule PTH levels in blood drawn from antecubital veins in transplanted (dark bars) and non-transplanted arms (light bars). Patients 1,7,10 and 12 have a ratio of less than 1,5:1.

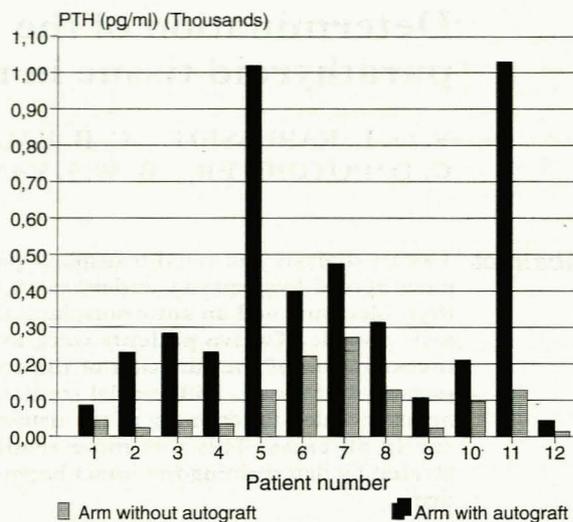


FIG. 3. Intact PTH levels in blood drawn from antecubital veins in transplanted (dark bars) and non-transplanted arms (light bars). All patients have a ratio of more than 1,5:1.

All the patients improved symptomatically after parathyroidectomy. The 2 patients with grossly elevated PTH levels do not have normal renal function and 1 has returned to dialysis.

All patients except 1 have intact PTH levels on the transplanted side. These are normal or above normal (10 - 6,5 pg/ml). The mean systemic PTH (non-transplanted arm) on intact hormone assay is less than normal in 1 patient, i.e. < 10 pg/ml (Fig. 3). This patient is normocalcaemic. Two patients are on oral calcium supplementation and 1 is hypercalcaemic. The rest maintain normal serum calcium levels. Mean serum calcium is 2,34 mmol/l: range 2,11 - 2,75. None of the patients is clinically hypoparathyroid.

Discussion

TP-A is a controversial procedure.³ It seems rather drastic to remove an essential endocrine organ and rely on a tenuous nonvascularised autograft. Proponents of 3^{1/2}-gland excision voice fears of permanent hypocalcaemia.⁴ However, there is no doubt that autografted parathyroid tissue in muscle does function and can maintain calcium homeostasis. Halsted,⁵ among others, demonstrated the survival of autografted parathyroid tissue in animals. This was subsequently also demonstrated in humans. Wells *et al.*¹ showed, by determining PTH in efferent veins from the graft site, that tissue was functioning. Subsequently many clinical studies have been published with convincing evidence of the effectiveness of the procedure.

Is there then an indication for TP-A? It is indicated in parathyroid hyperplasia and would seem to be a logical option in situations where the stimulus to hyperplasia is ongoing. TP-A has therefore been advocated for primary hyperplasia and especially familial forms of

the condition.¹ For the same reason it has been performed in patients with end-stage renal disease.⁶ The rationale is that it is easier and safer to treat recurrent disease by excising tissue in the arm than in the previously operated neck. TP-A has also been advocated in conjunction with total thyroidectomy for malignancy. This is to avoid the possibility of leaving devascularised parathyroid glands in the neck.⁷

Determination of intact hormone is superior to other methods for demonstrating the functioning of transplanted parathyroid tissue. Four of our patients had ratios between the transplanted and non-transplanted arms of < 1,5:1 on mid-molecule assay, whereas all had greater ratios using the intact hormone method. This is because the half-life of intact hormone is very short and the other fragments accumulate in renal failure.⁸

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