Professor M. P. Vessey and Sir Richard Doll gave helpful advice and encouragement.

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Treatment of Paget's Disease of Bone with once a week Injections of Salmon Calcitonin

Human, porcine, and salmon calcitonins are effective in treating Paget's disease in doses of 1-8 M.R.C. units/kg body weight daily or three times weekly.^{1 2} We have used 50 M.R.C. units of salmon calcitonin (S.C.T.) three times weekly as the minimal practical dose for long-term treatment of symptomatic generalized disease,² but the similarity of clinical and biochemical results on 100 units/day prompted us to explore the effectiveness of smaller doses given less often in patients with limited symptomatic disease.

Patients, Methods, and Results

Nine patients were treated with S.C.T. 50 units/week by self-injection for 10-16 months. Three patients had generalized and six limited lesions of Paget's disease (see table). All had pain in afflicted areas and none had neurological complications. Before S.C.T. treatment each patient had physical, neurological, slit lamp, audiometric, and complete skeletal examinations and an electrocardiogram. Fasting blood for serum calcium, phosphorus, magnesium, alkaline phosphatase, and creatinine and a 24-hour urine collection for calcium, phosphorus, total hydroxyproline, and creatinine were obtained each week for three weeks before treatment and were repeated at six to eight-week intervals.² Our patients had partial restrictions on foods containing hydroxyproline. All biochemical determinations were performed in duplicate; the reproducibility of the hydroxyproline determination was 5%. Plasma was tested for binding antibodies to S.C.T.²

Before treatment serum alkaline phosphatase was raised in eight patients (mean 76 K.A. units). Mean minimal and final values during treatment were 39 and 51 K.A. units respectively. The decrease in serum alkaline phosphatase averaged 28%. Urinary hydroxyproline was initially raised in all patients (mean 1.30 mmol/24 h (170 mg/24 h)). Urinary hydroxyproline decreased in six patients during S.C.T. treatment (mean decrease after eight months' treatment 28%, and after 16 months 18%). Three patients (cases 3, 5, and 7) showed no significant trend in hydroxyproline values during treatment. Binding antibody studies after 7-16 months gave uniformly negative results. The hypocalcaemic effect of 50 units of S.C.T. was tested in five patients at the end of treatment. Serum calcium decreased by 0.25-0.65 mmol/l (1.0-2.6 mg/100 ml) during one to eight hours in all five patients.

Clinical and Biochemical Characteristics of Nine Patients with Paget's disease

Case No.	Age and Sex	Clinical Features						Biochemical Features	
		Duration of Disease (Years)	Extent of Disease*	Bone Pain	Deformity and/or Increased Head Size	Impaired Hearing	Increased Temperature over Afflicted Area	Serum Alkaline† Phosphatase (K.A. Units)	Urinary Total Hydroxyproline‡ (mmol/24 h)
1	68 F.	15	Sk., S., L., P.	+	+	-	+	186	2.82
2	64 M.	6	S., L., P.	+	-	-	-	69	1.65
3	66 F.	20	S., L., P.	+	-	-	-	38	0.97
4	78 M.	25	S., P.	+	-	+	-	61	0.98
5	54 F.	6	S., P.	+	-	-	-	25	0.76
6	49 F.	5	L.	+	+	-	+	41	0.85
7	70 F.	10	Sk.	+	+	+	-	166	2.46
8	62 M.	2	P.	+	-	-	-	20	0.65
9	55 M.	5	L.	+	-	-	-	7	0.52

*Sk. = Skull. S. = Spine. L. = Long bones. P. = Pelvis.
†Normal <14 K.A. Units
‡Conversion: SI to Traditional Units—1 mmol/24 h ≈ 131 mg/24 h. Normal <0.34 mmol/24 h on hydroxyproline-free diet.

S.C.T. was well tolerated except in four patients who experienced mild nausea after injections, which did not necessitate withdrawal of S.C.T. On treatment pain disappeared or decreased appreciably in cases 1, 3, 4, 6, 7, and 8; decreased slightly in case 9; and was unchanged in cases 2 and 5. Improvement often started within four weeks, but maximum benefit was not achieved until after three to four months of treatment. In the two patients (cases 1 and 6) with increased skin temperature, tested by palpation of afflicted legs, the temperature decreased significantly during treatment.

Discussion

Serum alkaline phosphatase and urinary hydroxyproline levels and bone pain, deformities, and neurological complications indicate the activity of Paget's disease. S.C.T. 50 units/week decreased the biochemical values in most patients, and this was not a placebo effect.³ Seven cases of pain relief was beyond the expected 30% spontaneous improvement rate reported with placebos.⁴ After a mean of 19 months' treatment with S.C.T. 50-100 units three times weekly mean serum alkaline phosphatase and urinary hydroxyproline decreased by 48% and 52% respectively.² Corresponding mean changes for our patients treated with 50 units/week were, as expected, smaller—28% and 18%. Three patients' failure to decrease total hydroxyproline may have been a further example of dissociation in the responses of individual values which is not due to antibody formation.² S.C.T.'s continued biological effectiveness was attested to by its ability to induce significant hypocalcaemia. Over half our patients improved on this low dose without incurring S.C.T. antibody formation, which supports the suggestion that hormones in small doses given infrequently may influence bone metabolism. Possibly, weekly injections of S.C.T. might maintain therapeutic benefits achieved by more vigorous treatments such as daily S.C.T., mithramycin,⁵ or diphosphonates.⁴

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