Quantitation of the Renal Effect of Calcitonin in the Hypercalcaemia of Malignancy

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Summary. The renal effect of calcitonin (independent of changes due to variations in sodium excretion) was quantitated in malignancy associated hypercalcaemia. There was considerable inter- and intra-patient variability in response but this was unaffected by tumour type. Humoral hypercalcaemia tended to be resistant to control. In responsive patients the renal effects of calcitonin unlike those described in bone did not diminish with time.

Key words: calcitonin, malignancy, hypercalcaemia; renal effects, sodium excretion

Severe hypercalcaemia due to increased bone destruction and impaired calcium excretion [1, 2] is a serious but not necessarily terminal feature of malignancy. Management has largely centred on rehydration to improve renal function [3] and pharmacological means of reducing bone destruction [4–9].

Calcitonin is particularly useful in these circumstances because it both inhibits bone destruction [10] and increases calcium excretion [11]. Moreover the serum calcium begins to fall within hours of the start of treatment and in this respect calcitonin is superior to other agents currently available for the control of hypercalcaemia. However, this early effect is largely a renal, rather than a skeletal, phenomenon [12] and it is therefore of practical importance to identify factors which might modify this response.

This may be difficult to achieve in clinical practice because concurrent rehydration with saline, which is almost invariably under these circumstances, will also increase calcium excretion [3], albeit by a different mechanism from that of calcitonin. However, during moderate salt loading in malignancy associated hypercalcaemia there is a predictable relationship between the setting of renal calcium reabsorption and the prevailing rate of sodium reabsorption and the prevailing rate of sodium excretion [13]. This can be used to quantitate the calciiuretic effect of calcitonin independently of changes due to sodium flow.

In the present paper we describe the basis for this assessment and consider some of the factors which might modify the efficacy of calcitonin in the treatment of severe malignancy associated hypercalcaemia.

Methods

Eighteen patients with malignancy associated hypercalcaemia (> 3 mmol/l) persisting despite rehydration were studied before and during treatment with salmon calcitonin (SCT). Studies of the renal handling of calcium were made on fasting urine and blood samples and on timed urine collections (1500–1700 h) with a midpoint blood sample. Sodium excretion (E_{Na}) was expressed in mmol/l glomerular filtrate and the notional setting of renal tubular calcium reabsorption (TmCa/GFR) calculated from a nomogram [14].

In order to assess the specific effects of SCT on the renal handling of calcium it is necessary to eliminate the influence of urinary sodium flow [3, 13]. This can be calculated as shown in Fig. 1 which uses Case 9 as an example:

AB is the relationship between TmCa/GFR and E_{Na} in a group of 37 patients (which includes those in the present study) with malignancy associated hypercalcaemia at the completion of rehydration [13]. The shaded area shows the 95% confidence limits of the line AB which can be calculated from: \log_{10} TmCa/GFR = 0.374 - 0.127 \log_{10} E_{Na}.

The solid symbol (●) shows the relationship between these variables for Case 9 at the end of rehydration and the open symbols (O) the measured values during SCT therapy.
CD can be calculated from the above regression equation: it runs parallel to AB and provides an estimate of the post rehydration setting of TmCa/GFR for Case 9 at any given value of ENa. In this way the (calculated) setting of TmCa/GFR before the introduction of calcitonin can be compared with the measured values during treatment at the same level of ENa. Thus the vertical distance between the line CD and any of the open symbols indicates the renal effect of SCT independent of changes due to sodium excretion.

Results

The mean (±SEM) pre-SCT serum calcium for the 18 patients was 3.48 ± 0.08 mmol/l. Individual responses to SCT are shown in Figs. 1–3: All patients had skeletal metastases except those in Fig. 3 (B).

Five patients (Cases 1–3, 7, 9) showed a marked reduction in the setting of TmCa/GFR in response to SCT.