

Low somatomedin-C (Sm-C) concentrations measured by direct radioimmunoassay in patients with chronic renal failure

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Summary. Ten patients suffering from chronic renal failure and undergoing regular hemodialysis were tested immediately before and immediately after a 3-hour dialysis. Serum levels of immunoreactive Sm-C, estimated on unextracted non acidified serum at non equilibrium, were significantly lower than in normal controls and no consistent modifications were observed after dialysis.

In chronic renal insufficiency, growth is impaired despite good nutrition and normal levels of growth hormone (Phillips and Kopple, 1981). Circulating somatomedin (Sm) activity was found to be low and showed an increase after hemodialysis (Phillips and Kopple, 1981). This increase could reflect the removal of circulating Sm inhibitor(s) by the dialysis rather than increased Sm generation (Phillips and Kopple, 1981). However, radioreceptor- and radioimmuno-assays of native serum indicated elevated Sm levels in uremia (ref. in Goldberg *et al.*, 1982). Using an acid-ethanol extraction method, Goldberg *et al.* (1982) found reduced concentrations of IGF-I (= Sm-C). They also demonstrated increased protein binding of Sm in uremia and suggested that the discrepancies reported concerning Sm levels in this condition could be due to an artifactual rise of apparent immunoreactive Sm (IR Sm) concentrations when using a radioimmunoassay without extraction.

Material and methods. All patients were suffering from chronic renal insufficiency and undergoing regular 3-hour hemodialysis. Ten patients (6 men, 4 women) aged 21-67 y. were tested immediately before and immediately after dialysis. IR Sm-C was measured by two different techniques : — a direct assay (according to Furlanetto *et al.*, 1977) on unextracted non acidified serum at non equilibrium. The cross reactivity with IGF II is 2.4 % ; — an indirect assay (according to Daughaday *et al.*, 1980) on acid ethanol extracted serum at equilibrium. The cross-reactivity with IGF II is 2.9 %.

Results and discussion. Serum creatinine levels ranged from 7.2 to 17.0 mg/dl with a mean value of 11.8 mg/dl. Estimated by direct RIA, individual levels of Sm-C ranged from 0.29 to 1.17 U/ml, averaging 0.57 ± 0.11 U/ml (mean \pm SEM) which represents a 30 % decrease ($P < 0.02$) as compared to 56 normal controls (0.82 ± 0.05 U/ml). In uremic patients, there was an inverse relationship of borderline significance ($r = - 0.61$, $P = 0.06$) between individual values of Sm-C and of urea. With the indirect assay, individual values ranged from 0.10 to 2.30 U/ml, averaging 1.07 ± 0.24 U/ml, not significantly different from the values recorded in 38 controls (1.20 ± 0.06 U/ml). After a 3-hour

dialysis, there were no consistent changes in Sm-C values measured either by direct (0.64 ± 0.15 U/ml) or indirect (1.00 ± 0.21 U/ml) assay. There was no relation between individual basal levels of urea or creatinine and effect of dialysis on Sm-C concentrations.

Thus, in uremic patients, we found a significant decrease of Sm-C levels using our technique without acidification on unextracted serum at non equilibrium conditions and a slight but non significant decrease using the indirect assay. Since IGF II, which is markedly increased in chronic renal insufficiency (Goldberg *et al.*, 1982), cross-reacts with Sm-C in the various assays (2.4 % in our direct assay and 2.9 % in the indirect assay), we can assume that the Sm-C levels measured in our uremic patients are artifactually overestimated by 10 to 25 %. For instance, in the study of Takano *et al.* (1979), the cross-reaction of IGF II in Sm-A (~ Sm-C) determinations was 10 %, implying an artifactual rise of 50-130 % in Sm-A levels. Differences in cross-reactivity of IGF II could explain, at least partly, the discrepancies between elevated values of Sm-A previously reported (Takano *et al.*, 1979) and low or normal levels of Sm-C/IGF I found by Goldberg *et al.* (1982) and in the present study.

In *conclusion*, the present data suggest that in chronic renal insufficiency, Sm-C concentrations may be validly measured either on native serum by the method of Furlanetto *et al.* (1977) or on acid-ethanol extracted samples. The markedly decreased somatomedin bioactivity found in this condition (Phillips *et al.*, 1984) probably results from both low Sm-C/IGF I circulating levels (since biological activity of Sm-C/IGF I is more important than that of IGF II ; ref. in Goldberg *et al.*, 1982) and the presence of elevated concentrations of somatomedin inhibitor(s) (Phillips *et al.*, 1984).

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