Physiology and potential use of insulin-like growth factor 1 in acute and chronic renal failure

Joel D. Kopple, Hu Ding and David Pei-Yuan Qing

Division of Nephrology and Hypertension and Department of Medicine, Harbor-UCLA Medical Center, Torrance, CA, and the UCLA Schools of Medicine and Public Health, Los Angeles, CA

Introduction

Insulin-like growth factor 1 (IGF-1) is a polypeptide (molecular weight ~7650 Daltons) that has been shown to increase renal blood flow (RBF) and glomerular filtration rate (GFR) [1–3], stimulate renal hypertrophy [4–6], enhance recovery of renal function in animals with experimental acute renal failure [7–13], and promote anabolism [7]. As a result of these properties, IGF-1 has elicited substantial interest as a possible therapeutic agent. This paper will briefly review the physiology of IGF-1 and summarize the evidence substantiating the potential uses for IGF-1 in patients with acute or chronic renal failure (CRF). There is less evidence to indicate a possible therapeutic role for IGF-2, another growth factor identified in plasma and tissues [14]. A discussion of IGF-2 is beyond the scope of this paper.

Physiology of IGF-1

IGF-1 is secreted by many cells. Hepatic secretion appears to be the primary source of serum IGF-1 [14]. In serum, IGF-1 is almost entirely bound to IGF binding proteins (IGFBPs) [15,16]. Six IGFBPs have been identified. The most abundant IGFBP in serum is IGFBP-3. Serum IGFBPs 1, 2, and 4 are less abundant, and IGFBPs 5 and 6 are virtually undetectable in serum [15,16]. The relative abundances of the IGFBPs in solid tissues are different from sera and also vary according to the tissue. Many factors affect serum IGF-1 and IGFBPs. Growth hormone is the most powerful stimulus for IGF-1 secretion [17]. Fasting, malnutrition, low intakes of protein or calories, severe sepsis and insulin suppress serum IGF-1 [18,19]. Growth hormone, insulin, IGF-1 and fasting reduce serum IGFBP-1 [20–23], and IGF-1 elevates serum IGFBP-2 [15,16,24]; serum IGFBP-3 is decreased by fasting and IGF-1 and is increased by growth hormone [15,16,24].

Only the free IGF-1 appears to be biologically active in serum, and the IGFBPs have been proposed as both reservoirs and regulators of IGF-1 bioactivity. The actions of IGFBPs are not well understood. Under some experimental conditions, IGFBPs may enhance the actions of IGF-1 on tissues. IGF-1 acts primarily through binding to the IGF-1 receptor which activates the tyrosine kinase system [25,26]. IGF-1 in pharmacological concentrations may also crosstalk with the insulin receptor, but the affinity of the insulin receptor for insulin is ~1000 times greater than for IGF-1 [27]. Similarly, the IGF-1 receptor has roughly 1000 times more affinity for IGF-1 than for insulin [27].

IGF-1 appears to mediate most but not all of the physiological effects of growth hormone [14]. IGF-1 has many insulin-like effects and promotes a number of anabolic processes including the following: (i) lowers blood glucose by enhancing uptake of glucose by skeletal and myocardial muscle and adipocytes, and suppresses hepatic glucose production by decreasing gluconeogenesis and glycogenolysis [14,28,29]; IGF-1 is only ~7% as potent as insulin as a hypoglycaemic agent; (ii) stimulates amino acid transport; (iii) enhances protein synthesis and suppresses protein degradation in many tissues [14,30,31]; (iv) stimulates renal synthesis of 1,25-dihydroxycholecalciferol [32] and renal tubular reabsorption of phosphate [33,34] and possibly sodium; (v) enhances replication and bone collagen synthesis by osteoblasts [35], and bone formation [36]; (vi) promotes cell hypertrophy and hyperplasia; (vii) increases RBF and GFR [1–3] and causes renal hypertrophy [15]; (viii) increases total body growth and enlargement of certain organs including bone, kidney, thymus and spleen [37,38]; (ix) reduces weight loss during starvation [39], and (x) enhances wound healing [40].

Resistance to IGF-1 in CRF

In the late 1970s and early 1980s it was shown that although the serum concentrations of IGF-1 (or somato-
tomedin C as it was then called) are usually normal or near normal, the bioactivity of this hormone is reduced in uremic sera [41]. Several mechanisms for resistance to IGF-1 have been identified. These include the following.

(i) Increased plasma concentrations of two classes of compounds: sufficiently small to be haemodialysed [41] or too large [42] for effective removal by haemodialysis.

(ii) Impaired phosphorylation of tyrosine kinase in the β-subunit of the IGF-1 receptor in skeletal muscle of rats with CRF [31].

(iii) Impaired phosphorylation of insulin receptor substrate 1 (IRS-1) by tyrosine kinase in the IGF-1 receptor in skeletal muscle [31].

(iv) Elevated basal cytosolic calcium \([Ca^{2+}]_i\), in cardiomyocytes of rats with CRF and a reduced increase in \([Ca^{2+}]_i\) in response to IGF-1 stimulation [43].

We examined the mechanisms of action and causes for resistance to IGF-1 in skeletal muscle in CRF. Rats with CRF and sham-operated, pair-fed control (SO) rats were studied [31]. The rats were given NaHCO₃ to prevent acidemia. After 21 days of pair-feeding, rats were killed, and the dose-response effects of IGF-1 on muscle protein synthesis and degradation were determined. As compared to SO rats, the CRF rats had enhanced protein degradation and suppressed protein synthesis in the epitrochlearis muscle (P < 0.01 vs SO rats). When the epitrochlearis muscle was incubated with recombinant human IGF-1 (rhIGF-1), both the rhIGF-1 induced reduction in protein degradation and increase in protein synthesis were suppressed in the CRF rats as compared to the SO animals (P < 0.01 vs SO rats), indicating resistance to rhIGF-1 in CRF rats. Serum and skeletal muscle IGF-1 and muscle IGF-1 mRNA were reduced in CRF rats as compared to pair-fed, SO rats. In CRF rats, skeletal muscle IGF receptor mRNA was increased. Ligand binding assays and displacement binding studies indicated that the CRF rats displayed an increase in the IGF-1 receptor number with a normal receptor binding affinity. Affinity labelling studies also indicated that the \(\alpha\)-subunit of the muscle IGF-1 receptor was not different in either the \(M_1\) or the binding affinity to IGF-1 or insulin in the CRF rats as compared to SO animals. However, in CRF rats, the rhIGF-1-induced autophosphorylation of the IGF-1 receptor β-subunit was markedly suppressed, and the in vitro tyrosine kinase activity of the partially purified IGF-1 receptor β-subunit towards exogenous IRS-1, a natural substrate for the IGF-1 receptor tyrosine kinase, was significantly reduced [31].

The tyrosine kinase activity of the β-subunit of the IGF-1 receptor phosphorylates IRS-1. Therefore, the reduced phosphorylation of exogenous IRS-1 in the CRF rats could be solely due to the impaired tyrosine kinase activity of the β-subunit. To examine this possibility, in another experiment [31], a greater quantity of the partially purified β-subunit of the IGF-1 receptor from the CRF rats was admixed with exogenous IRS-1 so that the amounts of radiolabelled phosphorylated tyrosine kinase from the skeletal muscle of the CRF and pair-fed, SO rats were similar. Under these conditions, the phosphorylation of exogenous IRS-1 was still impaired in skeletal muscle of the CRF rats. This finding suggests that this reduced phosphorylation of exogenous IRS-1 in the CRF rats may be a separate defect from the impaired phosphorylation of the tyrosine kinase in the β-subunit of the IGF-1 receptor in these animals.

Thus, in skeletal muscle of CRF rats, as compared to pair-fed, SO controls, there is (i) resistance to IGF-1, (ii) up-regulation of the IGF-1 receptor number, (iii) normal structure and binding affinity to ligands in the ligand-binding domain (the \(\alpha\)-subunit) of the IGF-1 receptor, (iv) impaired activation of the intrinsic receptor tyrosine kinase domain (the β-subunit) of the IGF-1 receptor, and (v) decreased phosphorylation of IRS-1 by this tyrosine kinase domain.

Studies of other investigators indicate that in rats with CRF, the basal cytosolic calcium ((\([Ca^{2+}]_i\)) is increased in a number of different tissues, including heart [44,45]. Moreover, the increment in cytosolic calcium in response to stimuli is impaired in these animals, and this is associated with a reduction in the effector response to various stimuli by these cells. Since IGF-1 also stimulates an increase in cytosolic calcium [46,47], we hypothesized that resistance to IGF-1 in CRF rats might also be caused by elevation of basal \([Ca^{2+}]_i\). We examined this question in cardiomyocytes from CRF rats in the following experiment [43]. Sprague-Dawley rats were randomly assigned to one of four groups: CRF, CRF with parathyroidectomy (PTX), CRF with felodipine (F, a calcium channel blocker) added daily to the drinking water, and sham-operated (SO) controls. Each group contained seven or eight rats. The CRF-PTX and CRF-F groups were examined because PTX and calcium channel blockers are known to decrease basal \([Ca^{2+}]_i\) in CRF rats [44]. Rats from each group were fed the same diet for 20–22 days, and three groups of rats were pair-fed to the CRF animals. The CRF-PTX rats were also given calcium in drinking water. Basal \([Ca^{2+}]_i\) in cardiomyocytes was significantly increased in the CRF rats (CRF rats vs each other group, P < 0.05) and was not different from SO control values in the CRF-PTX and CRF-F animals. When the cardiomyocytes were incubated for 120 min with 50, 100, 200 or 400 μg/ml of rhIGF-1, the increment in \([Ca^{2+}]_i\) above basal levels was markedly impaired only in the CRF rats as compared to the pair-fed, SO rats, whereas the increment in \([Ca^{2+}]_i\) in the CRF-PTX and CRF-F rats was not different from that of the SO rats. The maximum \([Ca^{2+}]_i\) after rhIGF-1 stimulation was similar in all four groups. Incorporation of \([\text{H}^3]\)-leucine into cardiomyocyte proteins without rhIGF-1 added and after incubation with the foregoing concentrations of rhIGF-1 was significantly decreased in the CRF, CRF-PTX and CRF-F rats as compared to the SO rats (P < 0.05). However, the \([\text{H}^3]\)-leucine incorporation into the cardiomyocyte proteins in the CRF-PTX and CRF-F rats was also significantly greater than in the CRF rats. These data suggest that in...
myocardial cells of CRF rats: (i) basal $[Ca^{2+}]$, is elevated, (ii) rhIGF-1 stimulation of protein synthesis is impaired; (iii) PTX or the calcium channel blocker felodipine reduces basal $[Ca^{2+}]$, to the levels in the SO rats and increases the rhIGF-1 induced rise in $[Ca^{2+}]$, to the control levels; (iv) PTX and the calcium channel blocker increase the rhIGF-1 induced stimulation of protein synthesis, although not to the levels of the pair-fed, SO rats; and (v) the impaired response to IGF-1 appears to be caused at least partly by the elevation in the basal $[Ca^{2+}]$.

**Pharmacokinetics and anabolic effects of IGF-1 in patients with CRF**

In order to treat patients receiving maintenance haemodialysis (MHD) or individuals undergoing chronic peritoneal dialysis with rhIGF-1, it was first necessary to establish whether the pharmacokinetics of rhIGF-1 are altered in these individuals. We examined this question in three groups of adults: MHD patients, continuous ambulatory peritoneal dialysis (CAPD) patients and normal individuals [48]. Each subject was given a subcutaneous injection of rhIGF-1 on two separate days. One injection provided 50 μg rhIGF-1/kg body weight and the other injection 100 μg rhIGF-1/kg. Blood was drawn serially after each rhIGF-1 injection. Individuals were fasted from the night before the study until after the 4-h blood drawing after the injection. After the subcutaneous dose of 50 μg/kg of rhIGF-1, the pharmacokinetics of serum IGF-1 in the MHD and CAPD patients were not different from normal. With a subcutaneous dose of 100 μg/kg, peak serum IGF-1 concentrations were significantly greater in the MHD (1015 ± 86 SEM μg/l) and CAPD (1049 ± 156 μg/l) patients in comparison to the normal adults (637 ± 85 μg/l) [48]. Also, the half-life and volume of distribution of IGF-1 were significantly decreased in both the MHD and CAPD patients. The $T_{max}$ area under the curve and serum clearance of IGF-1 were not different in the three groups. The foregoing alterations in serum IGF-1 concentrations were transient. By 12–14 h after the injection, serum IGF-1 levels were not different among the MHD patients, CAPD patients and normal individuals. These findings are similar to the results of other studies of rhIGF-1 kinetics in patients with advanced CRF [49] and indicate that the dosage of rhIGF-1 does not need to be modified in patients with CRF because of altered pharmacokinetics.

In *in vivo* studies of patients with CRF support the thesis that they display resistance to the actions of IGF-1. In the pharmacokinetic study described above, blood was obtained before the injection of rhIGF-1 and serially for 4 h afterwards for measurement of other compounds [50]. After the rhIGF-1 injection, there was a reduction in plasma insulin, C-peptide, cortisol, most amino acids, and glucose in the normal individuals. In all three groups of subjects, the magnitude of the decrease tended to be greater with the larger dose of rhIGF-1. The decrease in plasma insulin, C-peptide, and concentrations of many of the amino acids was less, and the reduction in plasma glucose was similar in the MHD and CAPD patients as compared to the normal individuals. With the 50 μg rhIGF-1/kg dose, plasma insulin and C-peptide fell more rapidly and often to a greater magnitude in the normal subjects as compared to the MHD and CAPD patients. For some of these compounds, there was no significant decrease in plasma levels with the 50 μg rhIGF-1/kg dose in the MHD or CAPD patients during the 4 h of observation.

With the 100 μg rhIGF-1/kg dose, plasma insulin, C-peptide and amino acids decreased almost as frequently in the MHD and CAPD patients as in the normal individuals, but the magnitude of the reduction was often significantly less in the two chronic dialysis groups [50]. This impaired response occurred in both the MHD and CAPD patients even though with the 100 μg rhIGF-1/kg dose, their plasma IGF-1 concentrations were significantly greater than in the normals during most of the first 4 h after the rhIGF-1 injection (see above). These observations provide the first *in vivo* evidence for resistance to the metabolic actions of rhIGF-1 in patients with advanced CRF.

Notwithstanding this evidence for resistance to IGF-1, the MHD and CAPD patients did respond to rhIGF-1, particularly at the 100 μg/kg dose. We therefore examined whether rhIGF-1 could induce an anabolic response in maintenance dialysis patients who had protein-energy malnutrition [51]. Patients undergoing MHD or chronic peritoneal dialysis frequently are malnourished. Although there are many causes for protein-energy malnutrition in maintenance dialysis patients, inadequate intake of nutrients is probably one of the most common and decisive contributors to this condition. Prescription of greater food intakes usually does not correct this problem. Thus, we asked whether in malnourished patients ingesting their typical diets, rhIGF-1 injections would improve nitrogen balance.

Six CAPD patients with protein or calorie malnutrition were admitted to the Clinical Research Center at Harbor-UCLA Medical Center for 35 days [51]. Patients were fed a constant diet providing 26 ± 2 kcal/kg/day and 1.03 ± 0.09 g protein/kg/day and received a constant CAPD regimen throughout the study. After the first three 5-day baseline periods, patients were given subcutaneous injections of rhIGF-1, 50 or 100 μg/kg every 12 h, for the next four 5-day periods. Serum urea nitrogen (SUN) decreased from 68 ± 12.5 to 54 ± 8 mg/dl during the baseline periods ($P < 0.07$) and was significantly lower, 40 ± 6 mg/dl, at the end of the treatment periods ($P = 0.05$). After equilibration, nitrogen balance, adjusted for estimated changes in body urea nitrogen and unmeasured losses, became significantly more positive during rhIGF-1 treatment (baseline vs treatment, $P < 0.001$). Nitrogen balance during baseline was not different from zero and was strongly positive during rhIGF-1 treatment ($P < 0.001$). The major cause for improved nitrogen balance was reduced dialysate nitrogen. These data
Insulin-like growth factor 1 and renal failure

Indicate that rhIGF-1 may increase protein balance in stable, malnourished CAPD patients who are ingesting marginally adequate or submarginal diets. Further studies will be necessary to assess whether long-term treatment of CAPD patients with protein-energy malnutrition will improve body composition, clinical status, rehabilitation or mortality rates.

Effects of IGF-1 on renal function in patients with CRF

IGF-1 increases renal blood flow and glomerular filtration rate in the normal kidney of rats and humans [1–3,52] and engenders renal hypertrophy in the rat kidney [4–6,15]. O’Shea and associates, Miller and coworkers administered rhIGF-1 to patients with advanced CRF to assess whether their renal function can be increased and thereby decrease uraemic symptoms and postpone the need for maintenance dialysis therapy or renal transplantation [53,54]. In one study, four CRF patients with a GFR of 22–55 ml/min/1.73 m² given rhIGF-1, 100 μg/kg twice-daily for 4 days, showed an increase in inulin and para-aminohippurate (PAH) clearances and kidney volume [53]. In a second study, patients with more advanced CRF (baseline inulin clearances less than 21 ml/min/1.73 m²) were given rhIGF-1, 100 μg/kg, twice-daily for 4 days (four patients) or for 13–27 days (five patients) [54]. In the short term four day studies, inulin and PAH clearances were increased with rhIGF-1 treatment, but kidney volume did not change. In the longer term studies, there was no sustained increase in inulin clearance, and PAH clearance also rose transiently. Moreover, a number of patients developed symptoms associated with rhIGF-1 injections, most commonly jaw pain or nasal congestion, which caused rhIGF-1 treatment to be discontinued prematurely in four of the five patients. In addition, serum IGFBP-3, the major binding protein for IGF-1 in serum, declined during rhIGF-1 treatment. These investigators questioned whether the refractoriness to rhIGF-1 in these patients might be caused by the reduction in serum IGFBP-3 [54].

Therefore, this research team carried out another study in five patients with advanced CRF who were treated intermittently with low doses of rhIGF-1 (50 μg/kg/day) subcutaneously for up to 7 months [55]. rhIGF-1 was given daily for cycles of 4 days followed by three consecutive days without hormone injections. Serum IGF-1 and IGFBP-2 increased during the IGF-1 treatment, and serum IGFBP-3 did not change. Inulin clearances increased by 42–81% during the first 24 days of treatment, and PAH clearances also increased. In one patient treated for 7 months, the inulin clearance remained elevated. Side effects associated with the rhIGF-1 therapy were mild.

A potential concern with the long term use of rhIGF-1 to treat CRF patients is the possibility that the IGF-1 might induce glomerulosclerosis. Rats with increased growth hormone levels and mice transgenic for growth hormone develop glomerulosclerosis [56,57]. However, mice transgenic for IGF-1 who have serum IGF-1 levels similar to that present in the mice transgenic for growth hormone appear less likely to develop glomerulosclerosis [56,57]. Children with CRF who are given regular growth hormone injections do not appear to have a more rapid loss of renal function [58]. Also, adult patients with chronic acromegaly have increased glomerular filtration rates and renal hypertrophy but do not develop progressive renal failure [59,60]. Further monitoring of patients treated chronically with IGF-1 will be necessary to determine whether this hormone will maintain a sustained increase in the glomerular filtration rate without promoting glomerulosclerosis or progressive renal damage.

Role of IGF-1 in acute renal failure

Early during the investigation of the potential therapeutic actions of IGF-1, it was hypothesized that IGF-1 might accelerate the rate of recovery from acute renal failure. Interest in this possibility was stimulated by the following observations: (i) IGF-1 stimulates hypertrophy or mitosis of a number of renal cell types [4–6,15]; (ii) IGF-1 receptors are present in the glomerulus and proximal tubules [15]; (iii) IGF-1 is synthesized in the glomerulus and collecting ducts of certain animals [15]; (iv) In normal rats and humans, rhIGF-1 acutely increases renal blood flow and glomerular filtration rate [1–3,52]; these actions are probably mediated by nitric oxide [61].

Several studies [7–13] have now examined whether rhIGF-1 will enhance recovery from experimental acute renal failure (ARF). The results indicate that in rats, rhIGF-1 will accelerate recovery from ARF caused by ischaemia [7–11] or mercuric chloride toxicity [12,13] but possibly not when ARF is caused by radiocontrast media [62]. rhIGF-1 was observed to accelerate the recovery of renal function even when the rhIGF-1 injections were not commenced until as long as 5 or 24 h [7,13] after the onset of ARF. rhIGF-1 also reduces net protein breakdown in rats with ischaemic ARF; this effect is associated with a suppression of protein degradation and enhanced protein synthesis in skeletal muscle [7].

There appear to be at least two mechanisms by which rhIGF-1 increases renal function in rats with ARF. First, rhIGF-1 stimulates replication of new cells in the proximal renal tubules and elsewhere in the kidney [7,8,12]. However, rhIGF-1 probably also acutely increases renal blood flow and glomerular filtration rate in ARF [7,8] by haemodynamic effects. These haemodynamic effects of rhIGF-1 may be mediated by nitric oxide [9,61,63].

Evidence for a haemodynamic effect on the recovery of renal function is inferential and based upon the following observations. As indicated above, rhIGF-1 increases renal blood flow and the glomerular filtration rate in the normal kidney [1–3,52] and the chronically and severely damaged kidney [53–55]. Rats with ischaemic ARF that receive rhIGF-1 injections may
increase urine nitric oxide excretion [9,63], a compound that appears to be a mediator of the stimulating effects of rhIGF-1 on haemodynamics of the normal kidney [61]. Moreover, the rapid improvement in serum creatinine concentrations in rats with ARF that received injections of rhIGF-1, as compared to those rats that received vehicle injections, would appear to have occurred too quickly to be accounted for by healing of injured cells or by new cell formation.

Based on these observations, a multicentre, randomized, placebo-controlled, double-blind trial was conducted to examine whether IGF-1 will enhance recovery of ARF in patients [64]. Subjects with ARF of no more than 6 days’ duration were randomized to receive rhIGF-1, 100 μg/kg, or placebo subcutaneously twice-daily for 14 days. The causes of ARF in these patients were surgery, trauma, hypotension, sepsis, or drugs. An interim analysis was conducted after 72 patients had been studied. During the baseline phase at the onset of study there were no differences in age, sex, height, weight, causes of ARF, APACHE II scores, creatinine clearances or 24 h urine sodium, potassium, or volume between the patients given the rhIGF-1 (N = 35 patients) or placebo (N = 37 patients). During the 14 days of treatment, there were no differences between the groups in the final values or the change in values for glomerular filtration rate, 24 h urine creatinine clearance, serum creatinine or urea, or 24 h urine output of sodium, potassium, or volume. There were no differences between the two groups with regard to the frequency or total hours per patient of haemodialysis treatments or the mortality rates.

As a result of these negative findings, the study was terminated. These results suggest that treatment with rhIGF-1 will not accelerate the recovery of renal function in patients with ARF. However, it is possible that the severity of the systemic illnesses in many of the patients, the heterogeneity of causes of ARF in the study patients, or the fact that rhIGF-1 treatment was not started until as long as 6 days had elapsed after the onset of the ARF may have contributed to the negative results of this study.

In summary, this brief review indicates that IGF-1 has a multitude of biological actions, many of which promote anabolic processes or growth. A number of studies in animals and patients with acute or chronic renal failure suggest that some of the actions of IGF-1 may be translatable into beneficial treatments. Further studies will be necessary to confirm whether rhIGF-1 can become a useful therapeutic agent, either as a medicine to be used by itself or possibly when used in combination with other medicines including growth factors.

References

8. Miller SB, Martin DR, Kasane J, Hammerman MR. Insulin-like growth factor-1 increases renal plasma flow and glomerular filtration rate in patients with ARF. However, it is possible that the severity of the systemic illnesses in many of the patients, the heterogeneity of causes of ARF in the study patients, or the fact that rhIGF-1 treatment was not started until as long as 6 days had elapsed after the onset of the ARF may have contributed to the negative results of this study.

In summary, this brief review indicates that IGF-1 has a multitude of biological actions, many of which promote anabolic processes or growth. A number of studies in animals and patients with acute or chronic renal failure suggest that some of the actions of IGF-1 may be translatable into beneficial treatments. Further studies will be necessary to confirm whether rhIGF-1 can become a useful therapeutic agent, either as a medicine to be used by itself or possibly when used in combination with other medicines including growth factors.

References

8. Miller SB, Martin DR, Kasane J, Hammerman MR. Insulin-like growth factor-1 increases renal plasma flow and glomerular filtration rate in patients with ARF. However, it is possible that the severity of the systemic illnesses in many of the patients, the heterogeneity of causes of ARF in the study patients, or the fact that rhIGF-1 treatment was not started until as long as 6 days had elapsed after the onset of the ARF may have contributed to the negative results of this study.

In summary, this brief review indicates that IGF-1 has a multitude of biological actions, many of which promote anabolic processes or growth. A number of studies in animals and patients with acute or chronic renal failure suggest that some of the actions of IGF-1 may be translatable into beneficial treatments. Further studies will be necessary to confirm whether rhIGF-1 can become a useful therapeutic agent, either as a medicine to be used by itself or possibly when used in combination with other medicines including growth factors.

References

8. Miller SB, Martin DR, Kasane J, Hammerman MR. Insulin-like growth factor-1 increases renal plasma flow and glomerular filtration rate in patients with ARF. However, it is possible that the severity of the systemic illnesses in many of the patients, the heterogeneity of causes of ARF in the study patients, or the fact that rhIGF-1 treatment was not started until as long as 6 days had elapsed after the onset of the ARF may have contributed to the negative results of this study.

In summary, this brief review indicates that IGF-1 has a multitude of biological actions, many of which promote anabolic processes or growth. A number of studies in animals and patients with acute or chronic renal failure suggest that some of the actions of IGF-1 may be translatable into beneficial treatments. Further studies will be necessary to confirm whether rhIGF-1 can become a useful therapeutic agent, either as a medicine to be used by itself or possibly when used in combination with other medicines including growth factors.


49. Stabler PA, Feigelson JD, Kopple JD, Hershman JM, Striker GE, Russell DJ. Rate of decline of eGFR during hemodialysis: Studies in acromegaly and growth hormone deficiency. J Clin Endocrinol Metab 1984; 59: 226–236


55. Qing DP, Vadgama J, Ding H, Wu Y, Kopple JD. Elevated...