Renal Effects of Amino Acid Infusions in Patients with Panhypopituitarism

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SUMMARY  Strong evidence indicates that a high protein diet accelerates end-stage renal disease by increasing glomerular capillary pressure subsequent to renal vasodilatation. The mechanisms underlying this vasodilatation remain undefined, but they have been suspected to be mediated by a pituitary factor. To test this possibility, we measured changes in renal plasma flow and glomerular filtration rate induced by an intravenous infusion of a solution of amino acids in two patients with panhypopituitarism. These patients exhibited changes in renal hemodynamics comparable to those recorded in nine healthy volunteers. The results do not support involvement of the pituitary gland in the acute renal response to amino acids. (Hypertension 11: 557-559, 1988)

KEY WORDS  • pituitary disease  •  protein intake  •  renal hemodynamics  •  amino acid-induced vasodilatation

A high protein diet significantly increases both renal plasma flow and glomerular filtration rate. This phenomenon is of clinical importance because glomerular hyperperfusion subsequent to afferent arteriolar vasodilatation has been postulated to accelerate end-stage renal disease, whereas a low protein diet slows the progression of chronic renal failure. The mechanisms underlying the renal vasodilatation induced by a high protein intake are unknown, although a slow, progressive vasodilatation has also been induced by intravenous infusion of an amino acid combination used for parenteral nutrition. Short-term protein load or amino acid infusions have been suggested to be reliable indicators of renal functional reserve. Because of these delayed renal responses, the renal effects of amino acids are not thought to be exerted directly. The preventive influence that hypophysectomy has on the effect of a high protein intake on renal hemodynamics in rats has led to consideration of the hypothesis that the renal vasodilatation is mediated by a humoral mechanism(s) of pituitary origin.

This study evaluated the effect of amino acid infusions in two men who had panhypopituitarism secondary to surgical ablation of hypophyseal adenomas.

Patients and Methods

One patient (Patient 1), a 39-year-old man, was evaluated for headaches and severe visual disturbances. Investigation disclosed a pituitary mass with suprasellar extension; however, pituitary function was normal. The other patient (Patient 2), a 40-year-old man, was initially evaluated for hypogonadism, and subsequently hyperprolactinemia (399 ng/ml) with a low serum testosterone value (40 ng/dl) was diagnosed. In both patients, surgical removal of the pituitary adenoma was successfully completed, and substitutional therapy (hydrocortisone, 30 mg/day, and thyroxine, 100 µg/day) was initiated 3 months postoperatively.

The efficacy of the surgical procedure was checked before the amino acid infusion with standard endocrine tests in the absence of substitutional therapy for 2 weeks. The tests, performed 8 and 12 months postoperatively, revealed the following data. The serum levels of growth hormone failed to increase (values remained <0.6 ng/ml) after insulin-induced hypoglycemia. The serum levels of testosterone remained elevated (330 ng/dl), and thyroxine levels were normal (100 µg/day). The tests were repeated after the amino acid infusion, and the results were normal. The results of the substitutional therapy were normal, and the patients were free of symptoms.

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diurnal variation in serum cortisol levels was absent. Serum prolactin levels were less than 5 ng/dl and did not increase during a standard thyroid-releasing hormone test (200 μg intravenously). The levels of thyroid-stimulating hormone were also very low in both patients, 0.89 and 2.3 μU/ml, without a response to the thyroid-releasing hormone test. A standard luteinizing hormone–releasing hormone test (100 μg intravenously) did not induce variations in the serum levels of follicle-stimulating hormone or luteinizing hormone. The basal levels of serum testosterone were 45.5 and 20 ng/dl. This study confirmed a marked state of panhypopituitarism in both patients.

In both patients, the changes in renal plasma flow (p-aminohippurate clearance) and glomerular filtration rate (inulin clearance) were measured in 30-minute periods every 2 hours during a 6-hour intravenous infusion of a 10% amino acid solution, according to a previously published experimental design. The data were compared with those obtained from a group of nine normotensive volunteers.

Results

The percent changes observed in the nine normal volunteers and the two patients with panhypopituitarism are depicted in Figure 1. In normal volunteers, a maximal increase in glomerular filtration rate (from 106 ± 6 to 165 ± 12 ml/min; 56%) and in renal plasma flow (from 517 ± 29 to 754 ± 60 ml/min; 45%) was recorded at 6 hours of amino acid infusion, although no noticeable increments were recorded until after 2 hours of infusion. Comparable increments were noted in the two patients with panhypopituitarism: In Patient 1, glomerular filtration rate increased from 106 to 143 ml/min/m² (35%) and renal plasma flow increased from 406 to 656 ml/min (62%); in Patient 2, the increments were, respectively, from 118 to 188 ml/min/m² (60%) and from 796 to 1325 ml/min (66%). However, these increments took place earlier in the infusion period than those in normal volunteers (see Figure 1).

Discussion

These results do not support the idea that the renal effects of amino acid infusions are mediated by the pituitary gland, as was suggested from preliminary studies in the rat. In the assessment of any demonstrable pituitary function in these patients, particular emphasis was placed on estimating the existing levels of growth hormone because a previous study suggested that growth hormone itself or a growth hormone–dependent factor could mediate the increase in glomerular filtration rate after a large protein load in adults. However, this may not have been the case in our study because the undetectable levels of growth hormone could not be stimulated during the insulin-induced hypoglycemia. Our study does not rule out the possibility of a pituitary-independent hormonal mediation, a concept that was recently supported in a report showing that the responses to amino acid infusion in humans can be prevented by somatostatin. Our study shows not only that humans with complete hypophysectomy are capable of increasing the glomerular filtration rate and renal plasma flow in response to amino acid infusion, but also that these responses occur at an earlier time than that evoked in normal subjects. In a previous study, we showed that renal responses to amino acid could be facilitated by a decrease in the formation of angiotensin II or by an increase in the synthesis of renal prostaglandin. However, these possibilities could not be ascertained in this study.

References

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