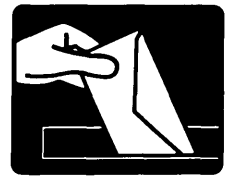
Letters to the Editor and Comments on Practice



Readers will note a change in the title of this section. The intent of this change is to provide a forum for clinical commentary on patient care. As has been the policy with Letters to the Editor, in order to encourage free exchange of ideas, this section will not be peer reviewed. The opinions presented here do not necessarily reflect the opinions of the Editors or the American Diabetes Association.

Hyponatremia and Sulfonylureas

I believe a brief comment is in order concerning the article by Kadowaki et al.[1]

First, in the original report by Fichman et al.,[2] which called attention to the entity of diuretic-induced hyponatremia, 4 of their 25 patients were taking chlorpropamide as well as hydrochlorothiazide. They pointed out that "apparently the synergistic effect of both hydrochlorothiazide and chlorpropamide were required to produce hyponatremia" in at least one of their patients.

Second, while there certainly is support for the view that chlorpropamide results in the "inappropriate" release of antidiuretic hormone, there is also evidence to support a direct effect at the renal tubular level to enhance the activity of low concentrations of vasopressin.[3]

Third, Moses et al.[4] investigated the effect of three sulfonylureas on water excretion as compared with chlorpropamide and found that acetohexamide, tolazamide, and glyburide enhanced water excretion in diabetic patients. As they pointed out, this must mean that the sulfonylurea part of the molecule is not the critical moiety in regard to water metabolism. They further commented that since there are effective oral hypoglycemic agents (to which glibenclamide can now be added) that are not antidiuretic, the use of these agents should be seriously considered in patients who have a tendency toward water retention.

While Kadowaki et al. found that tolbutamide had a lower incidence of causing hyponatremia than did chlorpropamide, there is a small literature supporting an antidiuretic role for this agent as well.[5,6]

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REFERENCES

[1] Kadowaki, T., Hagura, R., Kajinuma, H., Kuzuya, N., and Yoshida, S.: Chlorpropamide-induced hyponatremia: incidence and risk factors. Diabetes Care 1983; 6:468–71.

[2] Fichman, M. P., Vorherr, H., Kleeman, C. R., and Telfer, N.: Diuretic-induced hyponatremia. Ann. Intern. Med. 1971; 75:853–63.

[3] Ingelfinger, J. R., and Hays, R. M.: Evidence that chlorpropamide and vasopressin share a common site of action. J. Clin. Endocrinol. Metab. 1969; 29:738–40.

[4] Moses, A. M., Howanitz, J., and Miller, M.: Diuretic action of three sulfonylurea drugs. Ann. Intern. Med. 1973; 78:541–44.

[5] Luethi, A., and Studer, H.: Antidiuretic action of chlorpropamide and tolbutamide. Minn. Med. 1969; 52:33–36.

[6] Hagen, G. A., and Frawley, T. F.: Hyponatremia due to sulfonylurea compounds. J. Clin. Endocrinol. Metab. 1970; 31:570–75.

Hyponatremia and Sulfonylureas: A Reply

Our thanks to Dr. Matz for his interest in our article[1] recently published in DIABETES CARE.

A variety of conditions have been assumed to enhance the likelihood of chlorpropamide-induced hyponatremia. To our knowledge, however, no systematic and confirmative study of this issue, based on a long-term follow-up of a sizable population taking chlorpropamide, has been made thus far.

It should be noted that the hyponatremic patients in the report of Fichman et al.[2] were all hypokalemic, which they suggested to be the primary factor responsible for the hyponatremia; however, hypokalemia was not observed at all in our cases of hyponatremia.

As Dr. Matz pointed out, the mechanisms of the chlorpropamide-induced SIADH-like syndrome are generally accepted as twofold: a potentiation of the action of vasopressin and an "inappropriate" release of the hormone.[3] One of the authors of our article (S. Yoshida) has previously provided

supportive evidence for the presence of the former mechanism.[4]

We are well aware of the reported antidiuretic action of tolbutamide.[5] In the article, however, we stressed the fact that a much higher incidence of hyponatremia (serum sodium ≤ 129 meq/L) existed in chlorpropamide-treated patients (6.3%) than in tolbutamide- or glibenclamide-treated patients (0.9% and 0.0%, respectively).

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REFERENCES

[1] Kadowaki, T., Hagura, R., Kajinuma, H., Kuzuya, N., and Yoshida, S.: Chlorpropamide-induced hyponatremia: incidence and risk factor. Diabetes Care 1983; 6:468–71.

[2] Fichman, M. P., Vorherr, H., Kleeman, C. R., and Telfer, N.: Diuretic-induced hyponatremia. Ann. Intern. Med. 1971; 75:853–63.

[3] Davis, F. B., and Davis, P. J.: Water metabolism in diabetes mellitus. Am. J. Med. 1981; 70:210–14.

[4] Murase, T., and Yoshida, S.: Mechanism of chlorpropamide action in patients with diabetes insipidus. J. Clin. Endocrinol. Metab. 1973; 36:174–77.

[5] Luethi, A., and Studer, H.: Antidiuretic action of chlorpropamide and tolbutamide. Minn. Med. 1969; 52:33–36.

The Potential Usefulness of Postprandial Urine C-Peptide Measurement in Classifying Diabetic Patients

Measurement of 24-h urine C-peptide excretion has proven to be a useful means of distinguishing patients with insulin-dependent (IDDM) and non-insulin-dependent (NIDDM) diabetes mellitus.[1,2] However, data evaluating the utility of shorter, more easily obtained urine collections for C-peptide have not been reported. We therefore wish to present our experience in using 4-h, postprandial urinary C-peptide to confirm the classification of typical IDDM and NIDDM patients.

Ten healthy subjects (mean age, 39; range, 22–69 yr), 12 subjects with IDDM (mean age, 26; range, 19–35 yr), and nine subjects with NIDDM (mean age, 63; range, 44–82 yr) were evaluated. All IDDM subjects were taking daily or twice-daily insulin injections. Their mean duration of diabetes was 10 yr (range, 1–27 yr). Nine of the IDDM subjects had experienced at least one episode of ketoacidosis or were ketotic at the time of diagnosis of diabetes. The remaining three IDDM subjects developed diabetes before the age of 20, had taken insulin continuously since the time of diagnosis of diabetes, and demonstrated labile plasma glucose concentrations. The nine NIDDM subjects all had fasting plasma glucose concentrations greater than 140 mg/dl on more than one occasion. Their mean duration of diabetes was 7 yr (range, 2 mo to 17 yr). None of the NIDDM subjects was taking insulin or oral hypoglycemic agents. All subjects had normal renal function as determined by a normal serum creatinine and the absence of proteinuria.

Research subjects were asked to fast overnight and report to the General Clinical Research at 8:00 a.m. At approximately 8:30 a.m., a 700-kcal mixed meal composed of 48% carbohydrate, 20% protein, and 32% fat was served. Subjects voided before eating and all urine output during the following 240-min period was collected. Plasma glucose and serum insulin concentrations were determined after the meal and are the subject of a separate report.[3] On study mornings, IDDM subjects administered their usual dose of insulin 30 min before the test meal. Urine C-peptide was determined by radioimmunoassay as previously described.[4]

Mean postprandial urinary C-peptide excretion was 7.8 ± 2.9 (±SD) nmol/4 h in healthy subjects, 0.4 ± 0.4 nmol/4 h in IDDM subjects, and 11.1 ± 2.8 nmol/4 h in NIDDM subjects (Figure 1). C-peptide excretion was significantly less in IDDM subjects than in either healthy or NIDDM subjects. Urinary creatinine excretion was greater than 1.7 mg/kg

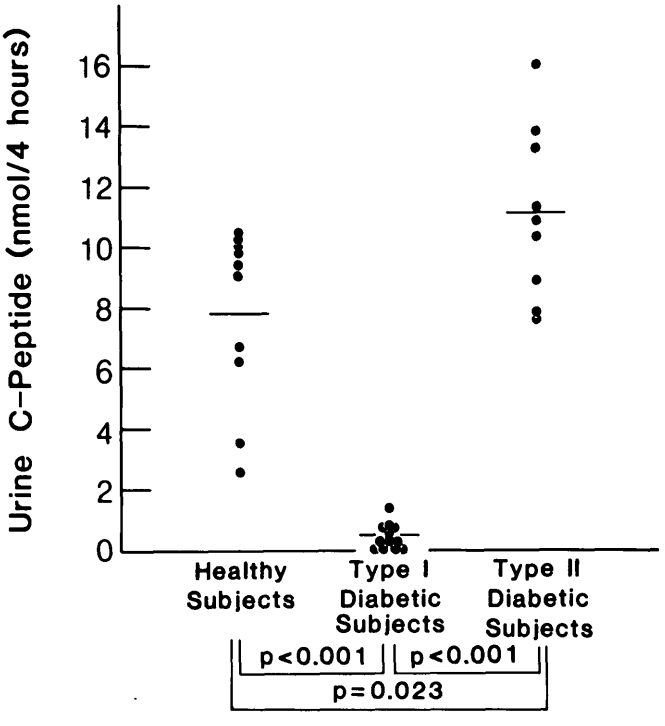

FIG. 1. Urinary C-peptide excretion during a 4-h postprandial period in healthy, IDDM (type I), and NIDDM (type II) subjects. Lines indicate the group means.