

Chronic Disease Surveillance

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The process of medical care has received little scientific attention. This lack of investigation of an enterprise that consumes almost 11 percent of the gross national product of the United States is truly astounding. The National Ambulatory Medical Care Survey has been a significant attempt to remedy this paucity of information. Begun somewhat more than ten years ago and employing a probability sample of physicians who record patient care data for one-week periods, its several surveys are a major source of information about what physicians do in their offices. Yet even these splendidly planned and conducted studies are lacking in the kinds of information required for intelligent appraisal of health resource utilization. Data are not patient-specific or longitudinal, and outcome studies are not possible. In addition, specificity of the 15 items recorded by participating physicians is limited. For example, type of x-ray examination or clinical laboratory procedure is not recorded.

Another approach to the study of the phenomena of office-based care has been taken by networks of primary care physicians. Patient data are recorded either continuously in a surveillance mode or intermittently for specially designed research projects. The Ambulatory Sentinel Practice Network (ASPN)¹ and the sentinel stations of The Netherlands² are examples of national networks, while the Dartmouth Primary Care Cooperative Information Project (COOP) is a group of regional cooperating physicians. The International

Primary Care Network (IPCN) composed of nine national networks provides a framework to compare physician behavior between countries.

Reporting in this issue of *The Journal of Family Practice* on opinions about visit frequency for essential hypertension, Doctors Lichtenstein, Sweetnam, and Elwood used a group of 50 randomly selected South Glamorgan general practitioners. Their analysis of the several variables that have an impact on visit frequency and decision to treat, such as level of pretreatment diastolic blood pressure, patient's age and sex, and the interaction between these variables provide new insights into how physicians make decisions. These aspects of physician behavior have profound implications for the costs of medical care. For example, one less annual physician visit by each of the estimated 18.3 million hypertensive adults receiving medical care for their hypertension³ would result in a saving of \$366 million, assuming a cost of \$20 per office visit. The subject, however, is far from simple because cost consequences are only part of an equation that is balanced by optimal care, and an evaluation of optimal care requires outcome data. For hypertension patients, outcome data are reasonably straightforward, including blood pressure levels and cardiac events such as congestive heart failure and stroke. For some diseases, however, such as type II diabetes mellitus (NIDDM), the relationship between blood glucose control and complications is more uncertain, and the effect of therapy including frequency of visits on blood glucose levels is not established.

The importance of scientific investigations often relates to the asking of appropriate questions, even if the particular study fails to provide the answers. Clearly, Dr. Lichtenstein and his colleagues have addressed an important issue and have suggested additional means

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to obtain answers. Prospective studies employing networks of primary care physicians collaborating in well-designed studies is one method with considerable potential for providing the required data. Regional, national, and international networks can make separate, yet complementary, contributions to the study of costs vs quality of care for chronic disease surveillance. With cost containment an ever-increasing factor constraining medical care, there are few primary care investigations more compelling at this time.

References

1. Green LA, Wood M, Becker L, et al: The ambulatory sentinel practice network: Purpose, methods, and policies. *J Fam Pract* 1984; 18:275-280
2. Continuous Morbidity Registration Sentinel Stations. The Netherlands. Foundation of the Netherlands Institute for General Practice from 1-1-85. Utrecht, The Netherlands Institute of Primary Health Care, 1984
3. Rowland M, Roberts J: Blood pressure levels and hypertension in persons ages 6-74 years. United States 1967-1980. In National Center for Health Statistics (Hyattsville, Md): Advance Data from Vital and Health Statistics, No. 84. DHHS publication No. (PHS) 82-1250. Government Printing Office, 1982

BRIEF SUMMARY
DIABINESE® (chlorpropamide)
 TABLETS, USP

CONTRAINDICATIONS

- DIABINESE is contraindicated in patients with:
1. Known hypersensitivity to this drug
 2. Diabetic ketoacidosis, with or without coma. This condition should be treated with insulin.

WARNINGS

SPECIAL WARNING ON INCREASED RISK OF CARDIOVASCULAR MORTALITY

The administration of oral hypoglycemic drugs has been reported to be associated with increased cardiovascular mortality as compared to treatment with diet alone or diet plus insulin. This warning is based on the study conducted by the University Group Diabetes Program (UGDP), a long-term prospective clinical trial designed to evaluate the effectiveness of glucose-lowering drugs in preventing or delaying vascular complications in patients with non-insulin-dependent diabetes. The study involved 823 patients who were randomly assigned to one of four treatment groups (*Diabetes*, 19 [supp. 2]:747-830, 1979). UGDP reported that patients treated for 5 to 8 years with diet plus a fixed dose of tolbutamide (1.5 grams per day) had a rate of cardiovascular mortality approximately 2 1/2 times that of patients treated with diet alone. A significant increase in total mortality was not observed, but the use of tolbutamide was discontinued based on the increase in cardiovascular mortality, thus limiting the opportunity for the study to show an increase in over-all mortality. Despite controversy regarding the interpretation of these results, the findings of the UGDP study provide an adequate basis for this warning. The patient should be informed of the potential risks and advantages of DIABINESE and of alternative modes of therapy.

Although only one drug in the sulfonylurea class (tolbutamide) was included in this study, it is prudent from a safety standpoint to consider that this warning may also apply to other oral hypoglycemic drugs in this class, in view of their close similarities in mode of action and chemical structure.

PRECAUTIONS

General

Hypoglycemia: All sulfonylurea drugs are capable of producing severe hypoglycemia. Proper patient selection, dosage, and instructions are important to avoid hypoglycemic episodes. Renal or hepatic insufficiency may cause elevated blood levels of DIABINESE and the latter may also diminish gluconeogenic capacity, both of which increase the risk of serious hypoglycemic reactions. Elderly, debilitated or malnourished patients, and those with adrenal or pituitary insufficiency are particularly susceptible to the hypoglycemic action of glucose-lowering drugs. Hypoglycemia may be difficult to recognize in the elderly, and in people who are taking beta-adrenergic blocking drugs. Hypoglycemia is more likely to occur when caloric intake is deficient, after severe or prolonged exercise, when alcohol is ingested, or when more than one glucose-lowering drug is used. Because of the long half-life of chlorpropamide, patients who become hypoglycemic during therapy require careful supervision of the dose and frequent feedings for at least 3 to 5 days. Hospitalization and intravenous glucose may be necessary.

Loss of control of blood glucose: When a patient stabilized on any diabetic regimen is exposed to stress such as fever, trauma, infection, or surgery, a loss of control may occur. At such times, it may be necessary to discontinue DIABINESE and administer insulin.

The effectiveness of any oral hypoglycemic drug, including DIABINESE, in lowering blood glucose to a desired level decreases in many patients over a period of time, which may be due to progression of the severity of the diabetes or to diminished responsiveness to the drug. This phenomenon is known as secondary failure, to distinguish it from primary failure in which the drug is ineffective in an individual patient when first given.

ADVERSE REACTIONS

Hypoglycemia: See PRECAUTIONS section.

Gastrointestinal Reactions: Cholestatic jaundice may occur rarely. DIABINESE should be discontinued if this occurs. Gastrointestinal disturbances are the most common reactions; nausea has been reported in less than 5% of patients, and diarrhea, vomiting, anorexia, and hunger in less than 2%. Other gastrointestinal disturbances have occurred in less than 1% of patients including proctocolitis. They tend to be dose related and may disappear when dosage is reduced.

Dermatologic Reactions: Pruritus has been reported in less than 3% of patients. Other allergic skin reactions, e.g., urticaria and maculopapular eruptions have been reported in approximately 1% or less of patients. These may be transient and may disappear despite continued use of DIABINESE; if skin reactions persist the drug should be discontinued.

Porphyria cutanea tarda and photosensitivity reactions have been reported with sulfonylureas. Skin eruptions rarely progressing to erythema multiforme and exfoliative dermatitis have also been reported.

Hematologic Reactions: Leukopenia, agranulocytosis, thrombocytopenia, hemolytic anemia, aplastic anemia, pancytopenia and eosinophilia have been reported with sulfonylureas.

Metabolic Reactions: Hepatic porphyria and disulfiram-like reactions have been reported with DIABINESE.

Endocrine Reactions: On rare occasions, chlorpropamide has caused a reaction identical to the syndrome of inappropriate antidiuretic hormone (ADH) secretion. The features of this syndrome result from excessive water retention and include hyponatremia, low serum osmolality, and high urine osmolality.

DOSAGE AND ADMINISTRATION

There is no fixed dosage regimen for the management of diabetes mellitus with DIABINESE or any other hypoglycemic agent. In addition to the usual monitoring of urinary glucose, the patient's blood glucose must also be monitored periodically to determine the minimum effective dose for the patient; to detect primary failure, and to detect secondary failure. Glycosylated hemoglobin levels may also be of value in monitoring the patient's response to therapy.

The total daily dosage is generally taken at a single time each morning with breakfast. Occasionally cases of gastrointestinal intolerance may be relieved by dividing the daily dosage. A LOADING OR PRIMING DOSE IS NOT NECESSARY AND SHOULD NOT BE USED.

Initial Therapy: 1. The mild to moderately severe, middle-aged, stable, non-insulin-dependent diabetic patient should be started on 250 mg daily. Older patients should be started on smaller amounts of DIABINESE, in the range of 100 to 125 mg daily.

2. No transition period is necessary when transferring patients from other oral hypoglycemic agents to DIABINESE. The other agent may be discontinued abruptly and chlorpropamide started at once. In prescribing chlorpropamide, due consideration must be given to its greater potency.

Many mild to moderately severe, middle-aged, stable non-insulin-dependent diabetic patients receiving insulin can be placed directly on the oral drug and their insulin abruptly discontinued. For patients requiring more than 40 units of insulin daily, therapy with DIABINESE may be initiated with a 50 per cent reduction in insulin for the first few days, with subsequent further reductions dependent upon the response.

Five to seven days after the initial therapy, the blood level of chlorpropamide reaches a plateau. Dosage may subsequently be adjusted upward or downward by increments of not more than 50 to 125 mg at intervals of three to five days to obtain optimal control. More frequent adjustments are usually undesirable.

Maintenance Therapy: Most moderately severe, middle-aged, stable non-insulin-dependent diabetic patients are controlled by approximately 250 mg daily. Many investigators have found that some milder diabetics do well on daily doses of 100 mg or less. Many of the more severe diabetics may require 500 mg daily for adequate control. PATIENTS WHO DO NOT RESPOND COMPLETELY TO 500 MG DAILY WILL USUALLY NOT RESPOND TO HIGHER DOSES. MAINTENANCE DOSES ABOVE 750 MG DAILY SHOULD BE AVOIDED.

HOW SUPPLIED

Blue, D-shaped, scored tablets in strengths of 100 mg, tablet code 393; (100's, NDC# 0663-3930-66, 500's, NDC# 0663-3930-73, and 100 unit dose of 10 x 10, NDC# 0663-3930-41) and 250 mg, tablet code 394; (100's, NDC# 0663-3940-66, 250's, NDC# 0663-3940-71, 1000's, NDC# 0663-3940-82; 100 unit dose of 10 x 10, NDC# 0663-3940-41, and 30's D-Pak, NDC# 0663-3940-30)

RECOMMENDED STORAGE: Store below 86°F (30°C)

CAUTION: Federal law prohibits dispensing without prescription.

