

13536 COMPETITIVE PROBLEMS IN THE DRUG INDUSTRY

ence of sulfonylureas and the potentiation of alcohol by sulfonylureas with an occasional disulfiram-like reaction are well substantiated.

Phenformin increases anaerobic glycolysis and lactate production and may produce lactic acidosis; it increases blood pressure, heart rate, and need for digitalis; and it decreases gluconeogenesis and glucose absorption.

There has been a striking increase in death rate and a decrease in life expectancy in maturity-onset diabetes in America, Europe, Asia, Africa, and Australia during the last 20 years. These changes have paralleled the increasingly widespread neglect of diet therapy and the almost unbridled enthusiasm among many physicians and patients for the use of sulfonylureas and phenformin as treatments of choice.

If a drug is to be considered *safe*, it should not shorten life expectancy nor be associated with fatal side effects or with severe drug reactions. The increased number of cardiovascular deaths in the UGDP study, the not uncommon occurrences of irreversible hypoglycemic brain damage and death with sulfonylureas and fatal lactic acidosis with phenformin, and the previously noted decreased life expectancy of the maturity-onset diabetic population throughout the world are the dramatic consequences of unrestricted use of oral hypoglycemic drugs. Thus, one is forced to the conclusion that both sulfonylureas and phenformin are unsafe.

It has been known for a long time that primary and secondary drug treatment failures are common with the sulfonylureas and phenformin; these failures have usually necessitated insulin therapy. As early as 1957, it was noted that blood glucose levels were frequently as low on placebo as on tolbutamide therapy. In a 1974 report, blood sugar levels did not rise in 30 of 50 patients when single-blind placebo was substituted for chlorpropamide. In 20 patients, the level rose modestly on a placebo regimen; however, in only four of the 20 patients did chlorpropamide help attain fasting normoglycemia (blood glucose level, < 140 mg/100 ml).

If a drug is to be considered *effective*,

it should prevent or delay the appearance of complications or prolong life, as well as lower the blood glucose level in a dependable fashion. Since sulfonylureas and phenformin apparently shorten life expectancy, do not prevent or delay complications, and do not lower the blood glucose level in an optimal fashion in the majority of patients, neither sulfonylureas or phenformin can be considered effective therapy, despite the claims of several drug companies and some physicians to the contrary.

Safe and Effective Alternatives

Appropriate caloric restriction (including periods of fasting for up to one week) usually lowers the blood glucose level dramatically in the obese diabetic. With intensive instruction and follow-up, a diet adherence rate of 96% has been reported recently. Success rates in reducing the weight of obese diabetic patients at Grady Memorial Hospital and Emory University School of Medicine in Atlanta have varied in different groups of patients from 50% to 90%, with the most intensively instructed and monitored patients having the greatest degree of success (unpublished data). To modify successfully a patient's long-established habits of food intake, it is mandatory that the physician be competent in calculating ideal body weight and in writing the correct dietary prescription. The patient's adherence to diet is facilitated by use of an easily understood diet manual and intensive instruction over a long period of time by physician, nurse, and dietitian. Patients at Grady Hospital are now given about 25 hours of individual and group instruction over a one-year period. Diet therapy is universally *safe*, and when pursued aggressively it is *effective* in a large majority of maturity-onset diabetics.

In the diabetic above ideal body weight who is not acutely decompensated (plasma glucose level, 500 mg/dl or higher, or moderate to large acetoneuria), only a one-week fast and intensive follow-up caloric restriction is needed. In addition to appropriate diet and exercise therapy, optimal insulin therapy is needed in (1) the acutely decompensated diabetic (even

those above ideal body weight), (2) the hyperglycemic maturity-onset diabetic at or below ideal body weight, (3) the hyperglycemic pregnant diabetic, and (4) the hyperglycemic juvenile-onset diabetic. The prime therapeutic objective when insulin is used is to attain normoglycemia as frequently as possible, with hypoglycemia being as infrequent as possible. The slight discomfort of insulin injections is a minor price to pay for the generally acknowledged physiologic actions and life-sustaining properties of the hormone. In this therapy, optimally used, is safe, and it is almost universally effective in lowering the blood glucose level.

Responsibility for Indiscriminate Use

At the present time, about 1,500,000 Americans are being treated with oral hypoglycemic drugs. At the Nelson Committee hearings, different witnesses estimated that from less than 1% to 20% of the patients being treated with these agents were actually helped by such therapy. Depending on which opinion one accepts as valid, this means that from 1,200,000 to 1,485,000 Americans are being inappropriately treated and should have their oral agent therapy discontinued. The drugs are probably being used excessively because the physician wants to do something when he makes a diagnosis of diabetes, and the patient wants something done. The easiest thing to do is to write a prescription for a pill, because it takes only a little time and it necessitates no significant change in the patient's life-style. Thus, the physician writes a prescription for a medication that he has been led to believe is safe and effective, when it is almost certainly unsafe and is frequently ineffective.

The FDA has not required properly written package inserts for the sulfonylureas and phenformin because of a legal barrier erected by litigation instituted by the Committee on the Care of the Diabetic. For this reason, physicians and the drug-consuming public have not been honestly and fully informed of the dangers inherent in the continued widespread use of these drugs. This legal barrier