Day After the Night Before

Influence of evening alcohol on risk of hypoglycemia in patients with type 1 diabetes

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There is no evidence to suggest that individuals with type 1 diabetes adopt a different approach to their use of alcohol than the rest of the population. Nevertheless, in patients treated with insulin, alcohol has been implicated in up to one-fifth of hospital attendances with hypoglycemia (1). Recently, in a laboratory-based study, Turner et al. (2) reported that ingestion of alcohol with an evening meal increased the risk of hypoglycemia the next morning in patients with type 1 diabetes. However, this study was small, patients were admitted to a research unit, their “usual” insulin doses were reduced at meal times, and the overnight insulin was administered intravenously in a controlled environment. To date there has been no study examining the effect of alcohol in free-living patients with type 1 diabetes over a 24-h period.

**RESEARCH DESIGN AND METHODS** — We studied 16 free-living patients with type 1 diabetes aged 39 ± 7 years, with a duration of diabetes of 15 ± 11 years, who consumed alcohol on a regular basis (<28 units/week). All gave written informed consent for the study after approval from the local research ethics committee. All had normal awareness of hypoglycemia and stable glycemic control (HbA1c 8.1 ± 1.0%). The patients wore the continuous glucose monitoring system (CGMS) (Medtronic Minimed, Minneapolis) for 36 h on two occasions separated by 2 weeks. On both occasions they continued with their usual insulin and four-times-daily home blood glucose monitoring. The patients were provided with either placebo (orange juice alone) or vodka (0.85 g/kg) and orange juice to produce peak alcohol levels of 80–100 mg/100 ml ingested over 60 min with identical standardized evening meals (carbohydrate content 120–150 g). Both patients and investigators were blinded to the composition of the supplemental drink. An independent party not involved with the study randomized the patients. The same dose of insulin was given (calculated per carbohydrate content of the meal) with the meal and before bed. On the 2nd day, the patients abstained from alcohol and the CGMS was removed 24 h after the standardized meal. Over the 2 CGMS days, events such as meals, insulin doses, exercise, sleep, and hypoglycemic events were recorded. The study was repeated 2 weeks later with the other drink supplied. The definition of interstitial hypoglycemia (3) was based on the glycemic thresholds at which there was activation of the counterregulatory hormone cascade and onset of neuroglycopenia.

**RESULTS** — CGMS data were available from all 16 subjects. There were two patient-sensor failures during the study (error >28%). The specific arm of the study (i.e., alcohol or placebo) where the sensor had been invalid was subsequently repeated. After the alcoholic drink, patients reported more than twice as many hypoglycemic episodes per day than after the placebo drink [self-reported hypoglycemic episodes: mean (range) 1.3 (0–4) with alcohol vs. 0.6 (0–2) with placebo, \( P = 0.02 \) using Wilcoxon’s test]. There were no reported episodes of severe hypoglycemia requiring the assistance of another individual. Carbohydrate intake was not different during the 24 h in either group [average (range) 418 g with alcohol (195–1,350) and 369 g (180–1,000) with placebo, \( P = 0.15 \) using Student’s t test]. Overall, the average interstitial glucose level was 1.2 mmol/l (95% CI 0.8–1.6) lower with alcohol compared with placebo [7.4 mmol/l (7.1–7.7) vs. 8.6 mmol/l (8.2–9.0), \( P = 0.02 \) using Student’s t test]. While this varied with time and magnitude throughout the 24-h period (Fig. 1), it was the prevailing glucose that determined the risk of hypoglycemia. This translated into an increased risk of interstitial hypoglycemia throughout the 24-h period, with a persistent risk of hypoglycemia continuing into the next day.

**CONCLUSIONS** — There is a lack of consistent advice given to patients concerning alcohol and the potential risk of low blood glucose levels. In this study, ingestion of modest amounts of alcohol with an evening meal was associated with an increased risk of delayed hypoglycemia in patients with type 1 diabetes. Alcohol may be associated with hypoglycemia in a number of ways. First, ingestion of even small amounts may impair the ability of the individual to detect the onset of hypoglycemia at a stage when they are still able to take appropriate action, i.e., eat carbohydrates. Second, hypoglycemia per se may be mistaken for intoxication by third parties with legal as well as health consequences. Third, alcohol has been shown in some studies to directly impair the hormonal counter-regulatory responses to low blood glucose levels (4). Fourth, recent data indicate that small amounts of alcohol can aug-
ment the cognitive deficits associated with hypoglycemia in individuals with type 1 diabetes (5).

In this study of free-living patients, we have confirmed previous observations from a controlled laboratory-based study (2) that alcohol use may be associated with a delayed effect, increasing the risk of next-day hypoglycemia. There are, however, limitations to the study. In free-living patients with type 1 diabetes, the frequency of hypoglycemia may vary according to a variety of different factors such as prior hypoglycemia, antecedent exercise, varying insulin absorption, and duration of diabetes. While efforts have been made to account for a number of these influences (e.g., continuing similar routines in both arms of the study and alcohol/placebo phase randomization to reduce confounding factors), interpatient variability still accounts for the largest variation in events. However, despite these concerns, our study confirms the suspicion of an immediate and prolonged hypoglycemic effect of alcohol. Education of health care professionals and knowledge for the patient of periods of risk need to be improved as, despite modern intensive treatment regimens, hypoglycemia continues to be an important problem for patients with type 1 diabetes. This study, the first to examine the prolonged effects of alcohol on free-living patients with type 1 diabetes, provides information for patients (and their health care professionals) on the potential periods of risk for hypoglycemia. This may enable patients to be proactive and adjust insulin appropriately, with the aim to reduce the overall risk of hypoglycemia associated with alcohol.

Acknowledgments—We thank MiniMed Medtronic for providing the CGMS sensors used in this study.

References