SHORT REPORTS

Meal frequency and duration of overnight fast: a role in gall-stone formation?

Supersaturation of bile with cholesterol is a necessary condition for the formation of cholesterol gall stones.[1] Most normal people have lithogenic bile after an overnight fast,[2] and short-term fasting is associated with a decreased rate of biliary bile-acid secretion and an increase in cholesterol saturation of hepatic and gall-bladder bile.[3-5] Thus meal frequency—that is, the duration of fasting throughout the day—might have an effect on gall-stone formation. We therefore tested this hypothesis by comparing, in a prospective case-controlled study, the duration of overnight fasting in patients with gall stones and controls.

Patients, methods, and results

We studied 380 consecutive women outpatients referred to the department of radiology for oral cholecystography. The main indications for this investigation were pain in the right hypochondrium, dyspepsia, and migraine. The patients were divided into two groups: 115 with radiolucent gall stones and 245 with a normal gall bladder, who served as controls. The control patients were individually matched to patients with gall stones for age (within five years), body weight (5 kg), number of pregnancies, and consumption of lithogenic drugs (oral contraceptives, clofibrate). The final study population consisted of 47 case-control pairs. The mean age and weight of the patients with gall stones and the controls was 50 ± SD 16 years and 61 ± 10 kg, respectively.

The duration of fasting was measured from the end of the last meal of the day (always dinner) until the beginning of the next meal (breakfast or lunch). The precise composition of the breakfast was determined in all subjects. Drinking, on waking, only cup(s) of black or white coffee with or without sugar was considered to be similar to a total fast. We had verified in 10 women volunteers, by real-time ultrasonography, that coffee did not cause gall-bladder emptying. Statistical analysis was carried out using the Wilcoxon signed-rank test for paired samples.

Total fast in the morning was noted in 11 patients with gall stones and five controls. The duration of overnight fasting (mean ± SEM) in the whole group was not significantly different between the patients with gall stones (13 h 30 min ± 36 min) and the controls (12 h 47 min ± 18 min). In the youngest patients (20-35 years), however, total fast was noted in six out of 12 patients and two out of 12 controls. In these young subjects duration of overnight fasting was significantly longer in the patients with gall stones (14 h 41 min ± 48 min) than in the controls (12 h 41 min ± 39 min; $p < 0.05$). We verified by using covariance analysis that no other factor modified the interpretation of this result—for example, mean body weight in the young patients with gall stones and the controls was 60·8 ± 8·8 kg and 60·2 ± 9·2 kg, respectively.

Comment

This study shows that the overnight fast—that is, the interval between dinner and the following meal, be it breakfast or lunch—is significantly greater in young women with gall stones (20-35 years) than in women in the same age range without gall stones. As the patients and their controls were closely matched for the well-known risk factors of cholesterol cholelithiasis these results suggest that reduction in meal frequency and prolongation of overnight fasting might increase the chances of gall-stone formation at least in younger people. In the older age groups this time difference was not found; it is difficult, however, to exclude the possibility that these patients, when younger, had had different dietary habits. In this north-western region of France the times of lunch and dinner invariably ranged from 12 noon to 1 pm and from 7 to 8 pm, respectively. By contrast, there are large individual variations in the existence, time, and composition of breakfast. In young people breakfast is often not eaten or limited to coffee, but presumably it becomes more regular and substantial with aging.

These results agree with several studies showing an increase in the cholesterol saturation of hepatic and gall-bladder human bile after an eight- to 16-hour fast.[3-5] Fasting is associated with the storage of a part of the bile-acid pool in the gall bladder, a decrease in the rate of biliary bile-acid secretion, without a parallel diminution in the biliary secretion of cholesterol, and the hepatic production and secretion of supersaturated bile. This effect might be accentuated by previous bile-acid deficiency or excess cholesterol secretion or both. Finally, if mixing of supersaturated bile in the gall bladder is inadequate or incomplete cholesterol precipitation and crystal growth might occur in localised regions of the gall bladder and promote gall-stone formation.[3]

We conclude that, at least in young women, reduced meal frequency and short-term prolongation of fasting might increase the risk of gall-stone formation.

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Antihistamine treatment: a patient self-assessment method in chronic urticaria

Chronic urticaria is common and intractable. Occasionally an underlying cause is identifiable, but most patients have to await eventual spontaneous remission of this distressing disorder. Systemic antihistamines give some symptomatic relief, though their capricious efficacy and troublesome side effects make them unsatisfactory to both patients and doctors. A current commercial index of proprietary preparations lists 20 separate antihistamines, which reflects the inadequacy of this class of drug. Since people's responses to particular antihistamines vary considerably[1] it is crucial to select the drug best suited to a given patient. A self-assessment questionnaire used in patients with rheumatoid arthritis receiving non-steroidal anti-inflammatory drugs has been described,[2] though no data on its value in practice were given. This method has now been modified for use in patients with chronic idiopathic urticaria who require antihistamine treatment, and I report here results obtained in 18 patients.

Patients, methods, and results

Eighteen adults attending the outpatient department of St John's Hospital for Diseases of the Skin were studied. Chronic idiopathic urticaria was defined as the occurrence of extensive wealing daily for at least three months. Pre-existing drug treatment was withdrawn for at least three days before the start of the study.

Self-assessment questionnaire—Each patient was given a self-assessment questionnaire (figure). Six antihistamines were given in random order, but no attempt was made to carry out the study blind. In a preliminary study a placebo was included: since this had no detectable influence on the severity of the urticaria and was not associated with side effects its use was discontinued. Each drug was taken by number for five days beginning on Monday and ending on Friday. No treatment was given on Saturday or Sunday, to prevent overlap between successive drugs. Patients were warned both verbally and on the questionnaire of the dangers of alcohol consumption while receiving antihistamine treatment, and possible relevant occupational hazards were also discussed. At the end of each treatment day the patient recorded the following information: approximate number of weals; severity