

Letter

Ref: Gallstone formation in obese subjects undergoing a weight reduction diet

We read with interest the recent article by Heshka and colleagues¹ who found that weight loss achieved after 16 weeks on a 1200 kcal/d regular food diet with 20 g/d fat (15% of kcal) was not accompanied by a high rate of gallstone formation in moderate obese persons. We conducted a double-blind clinical trial to compare the effect of a rational diet (calculated for each patient according to their energy expenditure—500 kcal) plus ursodeoxycholic acid (UDA) vs a rational diet supplemented with *Psyllium plantago* (*Pp*) for the prevention of gallstones in obese subjects undergoing a weight-reduction diet.² The description of the composite daily intake is shown in Table 1. Patients with a body mass index (BMI) of 30 kg/m² or more and with

normal gallbladder and biliary tree ultrasound were included. Patients were randomly and blindly assigned either to group I (*n* = 18) (diet + 750 mg UDA + fiber placebo) or group II (*n* = 18) (diet + 15 g *Pp* + UDA placebo) and followed the diet for 8 weeks. All patients concluded the 8 week follow-up period. Weight reduction was similar in both groups (group I = 6 ± 2 kg vs group II = 6 ± 3 kg). Gallstones development was observed in one patient of group I (1/18) and two patients of group II (2/18) (*p* > 0.05). All patients with gallstones lost a minimum of 4 kg during the study period (Figure 1) and had a BMI > 32 kg/m² and a waist-to-hip circumference ratio > 0.85³ (Table 2).

Table 1 Diet characteristics and frequency of gallstones formation

Author (ref)	Energy (kcal)	Carbohydrates (g)	Protein (g)	Fat (g)	Subjects with gallstones
Heshka ¹	1200*	190	73.7	20	0
Uribe ²					
Group I	1689 ± 160**	248 ± 31	67 ± 8	48 ± 6	1/18
Group II	1679 ± 187**	247 ± 34	66 ± 10	48 ± 6	2/18

* Regular food diet with approx 20 g/d fat (15% of kcal)

** Basal energy expenditure was calculated by indirect calorimetry

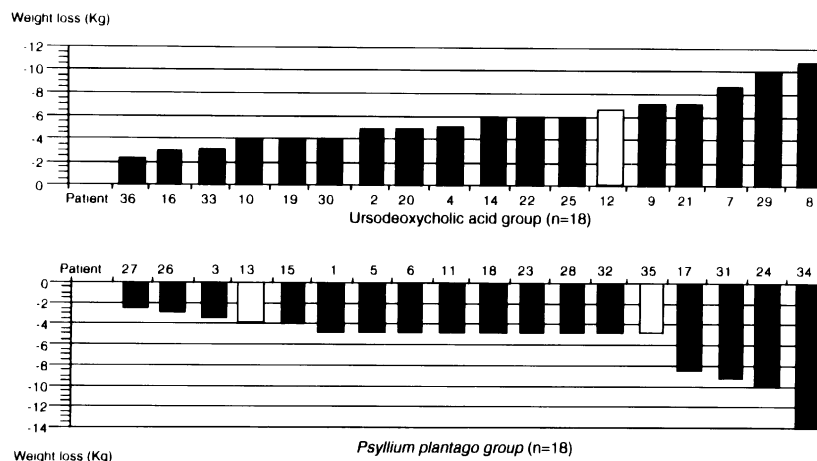


Figure 1 The graphic illustrates weight loss of each patient. Patients who developed gallstones are represented in white bars.

Table 2 Basal characteristics of the patients who developed gallstones disease

Patient	Group	Gender	Age (years)	BMI (kg/m ²)	WHR	Weight reduction (kg)
12	I	Female	23	32.9	0.90	6.7
13	II	Female	22	42.4	0.88	4
35	II	Female	45	38.3	1.00	5

BMI = Body mass index at base line

WHR = Waist-to-hip circumference ratio at base line

Gallstones developed in both groups even when the caloric content allowed was above 1200 kcal (25% of the total energy intake given as fat), and when one group had received UDA. Our contrasting differences in respect to Heshka's study results could be explained in terms of a greater susceptibility of our population to develop gallstones,⁴⁻⁶ which is as well reflected in obese subjects undergoing a weight reduction diet, without overlooking the large drop-out rate seen in Heshka's study. This suggests that the only proven factor for gallstones formation is the weight reduction *per se*. Consequently, more prospective trials to evaluate the degree of energy restriction and fat content as well as the subjects characteristics (ethnic or racial group, age and gender) are needed to establish more precisely the risk of gallstone formation associated with weight reduction.

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Reply to Morán et al

The identification of persons undertaking a weight loss program who are likely to develop gallstones remains an important but elusive goal and we appreciate the additional information provided by Morán et al.

Previous studies have identified numerous personal and dietary factors associated with increased risk, including large body mass index (BMI, kg/m²), high waist/hip ratio, high relative amount and rate of weight loss or BMI change, low fat content in formula diets, high initial serum triglyceride, bilirubin, ALT and AST, and large increases in ALT and AST upon beginning weight loss.¹⁻³ Thus, the higher rate of gallstone formation that Morán et al observed (3/36) compared to that reported in our paper (0/34) might be expected in view of the higher average BMI (minimum BMI in Morán et al 30 kg/m², vs our mean BMI of 28.9 kg/m²) and a greater rate of weight loss (group mean = 0.75 kg/week vs 0.3 kg/week).⁴ Nevertheless, the rate of weight loss, although higher than in our study, did not approach the high-risk threshold of 1.5 kg/week which has been proposed by Weinsier et al.⁵ The waist/hip ratio and BMI were unremarkable and a higher dietary fat content, which stimulates gallbladder contractions, did not have a protective

effect in their study. Regrettably, blood chemistry and lipid values are not available. Thus, it is not easy to account for the seemingly high rate of gallstone formation that they report.

However, comparison with published reports,⁵ as well as our own clinical experience with patients on moderately restricted calorie diets (daily total energy expenditure less 500 kcal), suggests that for unknown reasons their observed rate of gallstone formation is unusually high. Especially so, since half of the subjects were administered ursodeoxycholic acid which has been demonstrated to reduce the rate of gallstone formation during weight loss.⁶ Also puzzling is their report of a mean 6 kg weight loss over an 8 week period with a deficit of only 500 kcal/day. Assuming an energy value of approximately 7000 kcal per kg of weight lost, the expected mean weight loss is only about 4 kg which suggests that subjects may have restricted their energy intake beyond what was prescribed by the investigators.

Finally, we note that although 3 occurrences in a sample of 36 appears to be a high rate, the 95% confidence interval on a sample of this size includes proportions ranging from 0.0175 to 0.2247, and the difference between their result and the result reported

in our study is not statistically significant ($P = 0.24$). A larger sample would be necessary to be certain that Morán *et al* have observed a higher rate of gallstone formation than previously reported.

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FX Pi-Sunyer

References

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