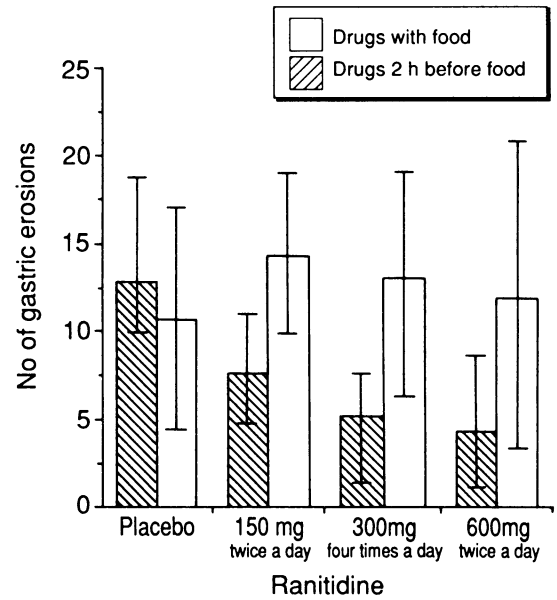
for five days on four different occasions. During each of these four dosing periods the subjects received concurrent treatment with placebo, ranitidine 150 mg twice a day, ranitidine 600 mg twice a day, or ranitidine 300 mg four times a day, each given simultaneously with aspirin. All subjects received each prophylactic regimen. During each treatment period the subjects were allowed to eat only at 9 am, 2 pm, 8 pm, and midnight. Half the subjects always took drugs at the same time as food. The other half always took their drugs two hours before food (at 7 am, midday, 6 pm, and 10 pm). The order in which subjects received the different treatment regimens was randomised by Latin square design. There was a washout period of nine days between each treatment regimen.

Subjects were studied in the morning, approximately eight hours after the last doses had been taken. Spontaneous microbleeding was measured as previously described,[4] followed by unsedated endoscopy with a paediatric endoscope, when erosions in the body, antrum, and duodenum were counted. Statistical analysis was by two way analysis of variance, with treatment and timing of dose in relation to food as the determining variables.

Aspirin increased the number of gastric erosions from none at baseline to a median of 10·6 (drugs given with food) or 12·8 (drugs given before food) (figure). Ranitidine reduced the total number of gastric erosions in a dose dependent fashion when the drugs were taken two hours before food ($p=0·006$), but had no effect when taken with food. Overall, taking drugs before food was associated with a significant reduction in mucosal injury ($p=0·003$) in comparison to taking them with food.



Effect of ranitidine and food on total number of gastric erosions in subjects given 2·4 g aspirin daily. Bars indicate 95% confidence intervals

Comment

Higher doses of ranitidine were more effective than standard doses, but only when the drugs were taken two hours before meals. The most plausible explanation for this finding is that this regimen achieves greater acid inhibition than when the drugs are given with food. However, an alternative explanation—that coadministration of food increases the toxicity of aspirin—remains possible. Although there was no difference in the number of erosions developing in the absence of ranitidine, injury may simply be maximal under these circumstances and differences may become apparent only under the protection of ranitidine. In support of this proposition, rats given indomethacin showed a dose dependent relation between the amount of food ingested and the extent of antral injury.[4] Faecal blood loss in humans taking aspirin with food has been reported to be higher than when aspirin was given without food, though the differences did not reach significance.[5] Thus, conventional advice to take aspirin and possibly other non-steroidal anti-inflammatory drugs with food may in fact be wrong. In any case, ranitidine together with aspirin offers greater mucosal protection if the drugs are taken two hours before meals rather than with food.

1 Ehsanullah RSB, Page MC, Tildesley G, Wood JR. Prevention of gastroduodenal damage induced by non-steroidal anti-inflammatory drugs: controlled trial of ranitidine. *BMJ* 1988;**297**:1017-21.
2 Daneshmend TK, Stein AG, Bhaskar NK, Hawkey CJ. Abolition by omeprazole of aspirin-induced gastric mucosal injury in humans. *Gut* 1990;**31**:514-7.
3 Satoh H, Guth PH, Grossman MI. Role of food in gastrointestinal ulceration produced by indomethacin in the rat. *Gastroenterology* 1982;**83**:210-5.
4 Hawkey CJ, Hawthorne AB, Hudson N, Cole AT, Mahida YR, Daneshmend TK. Separation of the impairment of haemostasis by aspirin from mucosal injury in the human stomach. *Clin Sci* 1991;**81**:565-73.
5 Stephens FO, Milverton EJ, Hamblyck Van der Van EK. The effect of food on aspirin-induced gastrointestinal blood loss. *Digestion* 1968;**1**:267-76.

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Lipoprotein(a) in cirrhosis

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The serum concentration of lipoprotein(a) is a strong independent risk factor for the development of premature coronary heart disease.[1] Studies in patients undergoing liver transplantation suggest that lipoprotein(a) is synthesised in the liver.[2] To determine the influence of liver disease on lipoprotein(a) concentrations we compared concentrations in patients with varying degrees of severity of hepatic cirrhosis, controls, and patients with established coronary heart disease.

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Subjects, methods, and results

Thirty patients (aged 27-71 years) with histologically diagnosed cirrhosis were matched for age and sex with healthy controls (hospital/university staff and relatives, 22-69 years) and patients with established coronary heart disease (26-68 years), all with normal liver function. Cirrhosis was secondary to chronic alcohol intake (24 patients), chronic active hepatitis (five), and haemochromatosis (one), and patients were clinically stable. Concomitant treatment included diuretics (five) and prednisolone (two). The severity of liver disease was assessed independently by using the Child Turcotte classification, with 10 patients in each group—A (mild), B (moderate), and C (severe). Lipoprotein(a) concentrations were determined by an enzyme linked immunosorbent assay (ELISA) (Biopool, Tint Elise) (coefficient of variation 7·6%) on fasting serum samples stored at −20°C. Statistical assessment was by Wilcoxon rank sum and correlation by least square regression analysis.

Lipoprotein(a) concentrations were raised in patients with coronary heart disease and reduced in those with cirrhosis (figure). Concentrations tended to be lower in those with more severe disease but this trend was not significant. Lipoprotein(a) was not

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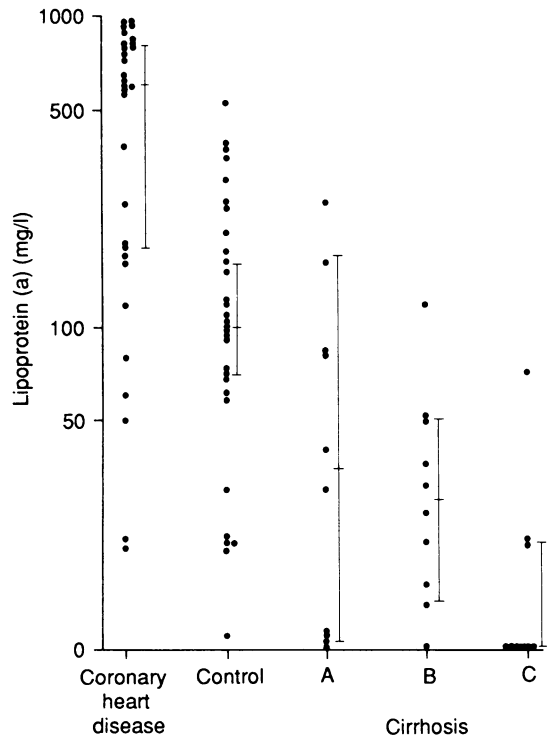
detectable in seven of the 10 patients in group C. There was no difference between those with alcohol related cirrhosis and those with non-alcohol related cirrhosis. In controls and patients with heart disease there was no association between alcohol consumption (based on recall and expressed as units/week) and lipoprotein(a) concentrations.

Comment

As expected, lipoprotein(a) concentrations were raised in our patients with established coronary heart disease,[1] but we also found them reduced in patients with cirrhosis. Lipoprotein(a) concentrations are under strong genetic control[1] and are not influenced by age, gender, diet, or smoking. Relatively few drugs affect lipoprotein(a), though nicotinic acid has been shown to lower concentrations through reduced hepatic synthesis.[3]



Lipoprotein(a) concentrations (median and 95% confidence intervals) in matched patients with coronary heart disease, controls, and patients with varying degrees of cirrhosis (Child's stage A-C). Coronary heart disease>control>cirrhosis (p<0·01)

An earlier study reported low lipoprotein(a) concentrations in heavy drinkers (more than 200 g alcohol/day for several years)[4] with none having a concentration over 450 g/l, and suggested that alcohol lowered serum lipoprotein(a) concentration. In contrast, among five of our patients with such a level of alcohol intake and coronary heart disease three had serum concentrations greater than 450 mg/l. In the remaining patients with coronary heart disease and the controls there was no relation between alcohol consumption and lipoprotein(a) concentration. Possibly the low lipoprotein(a) concentration found in drinkers in the earlier study was partly mediated through hepatic damage and reduced synthesis. Support for this view comes from the progressive fall in lipoprotein(a) concentrations with the increasing severity of liver disease and our finding that concentrations were equally reduced in patients with non-alcohol related cirrhosis. We could not detect lipoprotein(a) in seven of the 10 patients with severe liver disease. A low concentration of lipoprotein(a) may be one reason why patients with cirrhosis are less prone to coronary heart disease.[5]

1 Utermann G. Liproprotein (a): a genetic risk factor for premature coronary heart disease. *Current Opinion in Lipidology* 1990;1:404-10.
2 Kraft HG, Menzel HJ, Hoppichler F, Vogel W, Utermann G. Changes of genetic apolipoprotein phenotypes causes by liver transplantations: implications for apolipoprotein synthesis. *J Clin Invest* 1989;**83**:137-42.
3 Carlson LA, Hamsten A, Asplund A. Pronounced lowering of serum levels of lipoprotein Lp(a) in hyperlipidaemic subjects treated with nicotinic acid. *J Intern Med* 1989;**226**:271-6.
4 Marth E, Cazzolato G, Bittolo Bon G, Avogaro P, Kostner CM. Serum concentrations of Lp(a) and other lipoprotein parameters in heavy alcohol consumers. *Ann Nutr Metab* 1982;**26**:56-62.
5 Sherlock S. *Diseases of the liver and biliary system.* 8th ed. Oxford: Blackwell Scientific, 1989: 418.

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Do senior registrars have adequate management training?

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It is recognised that consultants will have an increased management role in the future, but there have been few attempts to examine the extent to which senior registrars are being prepared for this work.[1] Lack of information on senior registrars' present management experience and lack of consensus on appropriate management training[2-4] make it difficult to assess training requirements. This study examines the management experience of senior registrars in several clinical disciplines in one region and their perceptions of this training.

Subjects, methods, and results

In autumn 1990 questionnaires, piloted on psychiatrists,[5] were sent, with one reminder, to all 189 senior registrars in major clinical disciplines in the west midlands. A total of 153 (81%) responded, comprising 47 of 54 physicians, 44 of 54 surgeons, 25 of 31 anaesthetists, 24 of 31 pathologists, and 13 of 19 radiologists. Similar proportions in each discipline had completed higher training: overall, 91 (60%) had completed one to three years and 32 (21%) over three years.

Of the 58 (38%) who had attended a theoretical management course, a greater proportion of pathologists and radiologists (who receive single specialty courses) attended than other trainees (23 (62%); $\chi^2=10{\cdot}2$, df=1, $p<0{\cdot}01$). Only nine (6%) senior registrars had received training in a management skill (leadership, team motivation, budgeting, planning, information technology, chairmanship, recruitment, or conflict management).

Few senior registrars had attended a regional or district level management meeting (16 (11%) and 21 (14%) respectively); 88 (58%) had attended divisions, anaesthetists 21 (84%) more than other disciplines ($\chi^2=7{\cdot}33$, df=1, $p<0{\cdot}001$); 29 (19%) senior registrars had attended medical staff committees, five (3%) unit management group, and four (3%) planning meetings; none had attended budget meetings. Thirty one senior registrars had never attended a regional, district, or unit management meeting.

Those who had organised an operational management task were significantly more likely to rate the task as an important part of training than were those who had not had this experience (table). The proportion with organising experience varied from 73% to 19% according to task. A greater proportion of surgeons had organised duty rotas (40 (91%); $\chi^2=12{\cdot}82$, df=1, $p<0{\cdot}001$), audit meetings (35 (80%); $\chi^2=22{\cdot}32$, $p<0{\cdot}001$), teaching programmes for juniors (35 (80%);