SHORT REPORTS

Effect of temperature on creamatocrit method

Since the description of the creamatocrit method for estimating the fat concentration and energy in human milk[1] this technique has been used widely for quality control in human milk banks and in various studies. A study was carried out to assess the effect of the temperature to which milk samples are subjected before and during analysis.

Methods and results

The study was designed to simulate the possible range of conditions under which milk fat content might be estimated in different laboratories. The fat content in each of 24 specimens of fresh human milk was estimated by the creamatocrit technique: (*a*) with the centrifuge run in a cold room at 4°C, (*b*) with the centrifuge run at room temperature (18°C), and (*c*) at room temperature with a centrifuge that had been "prewarmed" by being run continuously for 30 minutes before use, as might occur with a centrifuge in regular use. The 24 milk samples were then pasteurised at 62°C for 30 minutes and the fat content again measured under the same conditions. In each case creamatocrit values were calculated by the published formula[1] relating percentage cream (C) to fat content: fat (%)=(C−0·59)/1·46. A subsample of each of the 24 specimens of fresh milk was also analysed for fat content by the Gerber reference method.[2] The creamatocrit values in each group were tested for linear correlation with values obtained by the Gerber method and with values determined in each of the other groups. The mean fat contents of the 24 samples in each group were compared with each other by paired *t* test.

The table shows the mean fat contents of the 24 samples of fresh and pasteurised milk estimated by the creamatocrit and the Gerber reference method. Only samples of fresh milk tested at room temperature had a similar fat content as estimated by the creamatocrit method to that determined by the Gerber method (these conditions approximate to those under which the creamatocrit method was calibrated originally[1]); in all other instances the calculated mean fat values were significantly lower or higher than the standard ($p < 0·001$). Furthermore, at each temperature previous pasteurisation of the milk resulted in a significantly lower estimated fat concentration ($p < 0·001$). Under all conditions studied, however, the creamatocrit values showed a high linear correlation with values determined by the Gerber method ($r = 0·931$ to 0·981, $p < 0·001$).

Mean (SD) milk fat (g/100 ml) measured in 26 samples by creamatocrit method under various conditions and by Gerber method

Creamatocrit method	Fresh milk	Pasteurised milk	Gerber method
Centrifugation at 4°C	3·32 (1·51) (r = 0·931)*	2·99 (1·36) (r = 0·969)	2·66 (1·18) (range 1·0-6·2)
Centrifugation at room temperature	2·73 (1·17) (r = 0·963)	2·21 (1·12) (r = 0·974)	
Prerun centrifuge at room temperature	2·45 (1·14) (r = 0·981)	2·09 (1·12) (r = 0·981)	

*Linear correlation between creamatocrit values and values obtained by Gerber method.

Comment

The creamatocrit method is used often in clinical practice and is especially valuable in assessing nutrient intakes of sick and low birthweight infants fed on banked breast milk. Thus it is important that the results are accurate. In this study, however, the temperature to which milk samples are subjected during centrifugation was found to exert a significant effect on the fat values calculated by the creamatocrit method.[1] The wide variety of temperatures likely to exist in different countries and laboratories together with variation in the usage and condition of the haematocrit centrifuge used (poorly serviced centrifuges are more likely to overheat during use) all result in unacceptably large variations in calculated fat values. Furthermore, many milk banks conduct quality control on pasteurised milk, yet this study showed that calculated fat values were significantly lower in pasteurised than in fresh milk (this conflicts with previous observations, made without controlling environmental temperature[1]). Even at a constant environmental temperature of 18°C, fresh milk samples had a fat content over 30% higher than that of pasteurised milk spun in a centrifuge warmed up by repeated use; and when the environmental temperature was altered considerably greater differences were observed.

These results may be partly explained by the effect of heat in disrupting the fat globule membrane, the released fat occupying less space than cream, which is a suspension of fat in the aqueous phase of milk. Nevertheless, the close linear correlation between fat estimations performed by the Gerber creamatocrit method under all the conditions studied shows the validity of the creamatocrit technique. Clearly, however, the method must be standardised for the conditions that exist in any particular laboratory.

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[2] British Standards Institution. *Gerber method for determination of fat in milk and milk products* (*BS*696). London: British Standards Institution, 1955.

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Massive digoxin overdose: successful treatment with intravenous amiodarone

Massive digoxin overdosage is difficult to treat and has a mortality of 10-20%. Atropine may be useful in mild overdosage but is of little value in severely poisoned patients. Phenytoin is effective in moderately poisoned patients, but in severe cases conventional antiarrhythmics including lignocaine, phenytoin, practolol, procainamide, and verapamil seem to be ineffective.[1] Antigen binding fragments of digoxin specific antibodies, though effective,[2] are not widely available. Even cardiac pacing may be unsuccessful in severely poisoned patients. We report on a patient with intractable ventricular fibrillation after digoxin overdosage who was successfully treated with intravenous amiodarone over 24 hours.

Case report

A previously well 26 year old man was admitted to hospital 18 hours after ingesting 100 0·25 mg digoxin tablets. On admission he was conscious but complained of unsteadiness and blurred vision. Examination showed a sinus bradycardia of 50 beats/min, and an electrocardiogram showed considerable ST depression and second degree heart block (PR interval 0·36 s). Blood pressure was satisfactory at 115/70 mm Hg, and there were no other abnormalities. Electrolyte concentrations were normal apart from the serum potassium concentrations, which subsequently rose from 5·1 mmol(mEq)/l to 6·2 mmol/l.

Activated charcoal was administered in the casualty department after gastric lavage. One hour after admission to the coronary care unit he developed ventricular tachycardia with rapid progression to ventricular fibrillation. He was intubated and ventilated with 100% oxygen and in addition received intravenous sodium bicarbonate 8·4% and external cardiac massage. Several attempts at cardioversion, increasing from 100 J to 400 J, failed to induce defibrillation. After intravenous lignocaine (up to 200 mg) a further attempt at cardioversion resulted in asystole, which responded satisfactorily only to intracardiac adrenaline. Pacing facilities were not available, and he was too ill to be moved.

The sequence of events was repeated with further episodes of prolonged ventricular fibrillation unresponsive to defibrillation. After 30 minutes of resuscitation amiodarone 300 mg was administered intravenously over 20 minutes while external cardiac massage and ventilation were continued. One hour after the start of resuscitation he was successfully defibrillated

and no further episodes of ventricular fibrillation occurred. Arterial blood gas tensions at this time were pH 7·3, oxygen pressure 50·7 kPa (380 mm Hg), and carbon dioxide pressure 6·4 kPa (48 mm Hg); standard bicarbonate concentration 21·5 mmol(mEq)/l; and base excess −2·5 mmol(mEq)/l.

Amiodarone was continued as an intravenous infusion with 600 mg in 5% dextrose over 12 hours and 300 mg in 5% dextrose for a further 24 hours, during which time an electrocardiogram showed varying degrees of heart block and nodal rhythms. His clinical state improved, and he required only intravenous atropine on two occasions for bradycardia. Serum digoxin concentration was above 5 μg/l on admission, but the sample was not retained for more accurate determination. Digoxin concentrations did not fall into the therapeutic range until day 5, when a concentration of 1·4 μg/l was recorded. As the plasma half life in overdosage is about 13 hours[3] the peak digoxin concentration would have been over 40 μg/l.

Comment

Serum digoxin concentrations were not obtained accurately in this patient, although he was undoubtedly severely poisoned and had intractable ventricular fibrillation unresponsive to a class I anti-arrhythmic drug. Use of a beta blocker was thought too hazardous because of the absence of pacing facilities and the previous asystole. Amiodarone is a class III antiarrhythmic drug that prolongs the action potential in ventricular muscle, lengthens the refractory period of the myocardium, and reduces the maximum rate of repolarisation. Drugs exhibiting class III antiarrhythmic properties reverse arrhythmias induced with ouabain in animals.[4]

Although amiodarone increases digoxin concentrations when given by mouth and this may produce digoxin toxicity after chronic administration,[5] this phenomenon should not exclude use of amiodarone in digoxin overdosage, as shown by this case. Further work should be undertaken to confirm the usefulness of amiodarone in digoxin overdosage. We believe that its ability to reduce excitability at all levels probably contributed to the survival of this patient, who was discharged fit and well eight days after admission.

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[2] Rozkovec A, Coltart DJ. Treatment of digoxin overdosage with antigen-binding fragments of digoxin-specific antibodies. *Br Med J* 1982;**285**: 1315-6.

[3] Hobson JD, Zettner A. Digoxin serum half life following suicidal digoxin poisoning. *JAMA* 1973;**223**:147-9.

[4] Singh BN, Williams EMV. A third class of anti-arrhythmic action. Effects on atrial and ventricular intracellular potentials and other pharmacological actions on cardiac muscle, of MJ 1999 and AH 3474. *Br J Pharmacol* 1970;**39**:675-87.

[5] Moysey JO, Jaggarao NSV, Grundy EN, Chamberlain DA. Amiodarone increases plasma digoxin concentrations. *Br Med J* 1981;**282**:272.

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Failure of increased use of endoscopy to influence complication rate in peptic ulcer disease

In an attempt to rationalise the increasing use of upper gastrointestinal endoscopy, we and others have described a direct referral open access endoscopy service for general practitioners.[1-3] Although the service is popular with general practitioners and may reduce referrals to hospital, it does result in a considerable increase in the number of endoscopies being performed,[2] which is time consuming and expensive. To justify this it is therefore important to document carefully any effects of this increased use of endoscopy on the course of gastrointestinal disease. By comparing three different areas with varying endoscopic practices we have shown that open access endoscopy is unlikely to influence the prognosis of gastric cancer, as the proportion of early lesions found is not increased.[4] We now report its effect on hospital admissions for the major complications of peptic ulcer disease.

Patients, methods, and results

We compared the hospital admission rates for two specific, easily identifiable complications of peptic ulcer disease in three district general hospitals in Wessex with differing endoscopic practice (table). In centre A there was an open access general practitioner endoscopy service, in centre B a freely available hospital based service, and in centre C a limited hospital service only. The yearly numbers of endoscopies performed in these centres were roughly 1130, 540, and 150 per 100 000 population served. The mean admission rates a year for the major complications of peptic ulcer disease (perforation or haemorrhage) were obtained from the Hospital Activity Analysis for the five years before the increased use of endoscopy (1968-72) and for five years after it had been established (1976-80).

Admission rates for complications of peptic ulcer disease per 100 000 population served by each centre. Values shown are for haemorrhage (values for perforation given in parentheses)

Centre	Endoscopic practice	Approximate No of endoscopies performed/ 100 000 population	Duodenal ulcer		Gastric ulcer	
			1968-72	1976-80	1968-72	1976-80
A	General practitioner plus outpatient	1130	17·9 (9·1)	22·5 (11·2)	9·9 (2·1)	9·9 (2·1)
B	Outpatient	580	8·0 (7·0)	7·7 (7·5)	5·1 (1·5)	5·5 (1·5)
C	Limited outpatient	150	5·0 (6·8)	5·6 (7·1)	3·8 (2·2)	4·6 (1·4)

Although the frequency of haematemesis and perforation varied between centres, presumably secondary to the characteristics of the populations served, within each centre the complication rate remained remarkably constant, and there was no evidence that the increased use of endoscopy had any effect on the complication rate of peptic ulcer disease (table). Retrospective review of 100 patients admitted with these complications showed that although 65 of them had a history of diagnosed peptic ulcer disease, only 35 had symptoms at the time of admission and only eight had been given specific antiulcer treatment before admission. Indeed, fewer than 10 had visited their general practitioner in the four weeks before hospital admission with the major complication.

Comment

Although in many instances the Hospital Activity Analysis may not be accurate, as it depends on correct documentation at the time of hospital admission, the analysis for such major complications as haemorrhage and particularly perforation should be reasonably correct because of their ready confirmation and the accuracy of diagnosis.[5] Within these limitations the evidence presented does not suggest that the increased use of endoscopy which results from the introduction of an open access endoscopy service is likely to influence the incidence of such major complications of peptic ulcer disease. One explanation of this emerged from the study of patients admitted with these complications, as it became clear that few of these patients had attended their general practitioners in the weeks before admission and thus were not likely to benefit from more freely available endoscopic services.

The years covered by this report also saw the introduction of H_2 antagonists, and the results might suggest that these also had no major effect on the complication rate, probably for the same reasons discussed above.

This study, together with our previous ones, suggests that the provision of an open access endoscopy service in its present form has little to offer in terms of altering disease course. The best approach towards reducing the complication rate in peptic ulcer disease is probably one directed at encouraging those patients at risk—for example, those with known peptic ulcer disease—to seek help earlier if their symptoms recur.

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