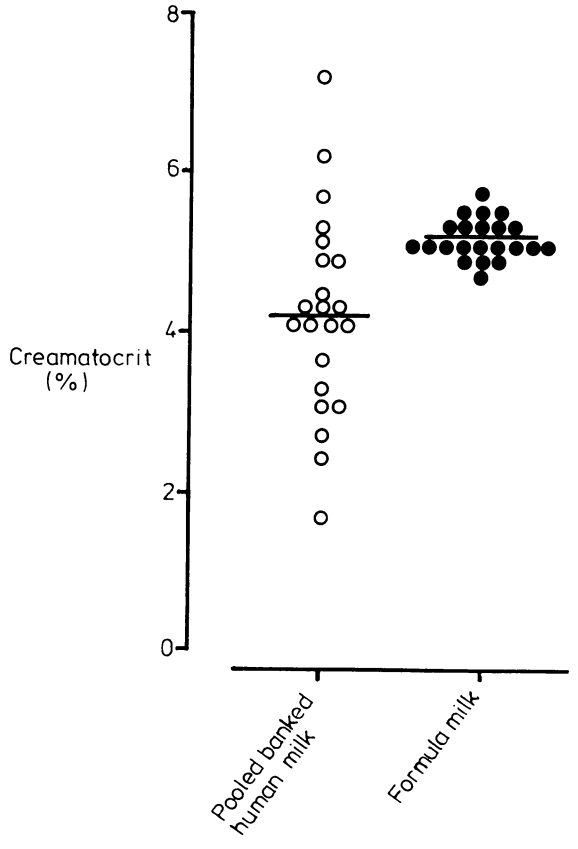
SHORT REPORTS

Fat content and fatty acid composition of pooled banked milk

The amount of fat in human milk is influenced by diurnal variations in fat content, by the stage of lactation, and, more importantly, by the method of milk collection—namely, whether it is expressed or dripped.[1] In human milk banks milk is usually pooled, and pooling is generally assumed to result in a more uniform fat content. We compared the fat contents in pooled banked human milk and a commercially available formula milk. We also analysed the fatty acid composition of pooled banked human milk and compared our findings with those published by the Department of Health and Social Security.[2]

Methods and results

We obtained milk samples from 22 batches of pooled human milk arriving at the special care baby unit from the milk bank, and from SMA ready to feed formula milk for infants. The human milk had been collected by three or four mothers at home over one to five days and stored in the freezing compartment of a domestic refrigerator; after thawing this milk was pooled in 200 ml containers. It consisted of expressed breast milk and milk that had dripped from the opposite breast when the baby was being fed.



Distribution of creamatocrit values in 22 samples of pooled banked milk and 22 of a formula milk. Each value is the mean of three determinations in a single milk specimen. Horizontal lines indicate mean values.

We measured the fat content of the milk by the creamatocrit method.[3] Milk triglycerides were separated by thin layer chromatography, and the fatty acid composition was determined by gas-liquid chromatography.[4] Mean creamatocrit values were compared by Student's t test.

In pooled banked human milk the maximum creamatocrit, 7·26%, was nearly four times greater than the minimum creamatocrit, 1·72%, and a third of the creamatocrit values were below 4% (figure). By contrast, the creamatocrit values in formula milk were distributed over a fairly narrow range (4·75-5·26%). The mean creamatocrit in formula milk (5·16 (SD 0·19)%) was significantly greater than that in pooled human milk (4·21 (1·24)) ($p < 0·001$) (figure).

Comparison of the fatty acid composition of our pooled banked human milk with that of mature human milk analysed by the Department of Health and Social Security[2] showed that our milk contained more linoleic acid and linolenic acid (polyunsaturated fatty acids C18:2 and C18:3) but less lauric acid (saturated fatty acid C12:0). In our 22 specimens of pooled banked milk the mean proportions of linoleic, linolenic, and lauric acids were 11·2%, 1·2%, and 2·7%; the proportions reported by the Department of Health and Social Security were 7·2%, 0·8%, and 5·4% respectively.

Comment

Our study shows that pooling specimens of human milk whose fat content is not known may not result in milk with a uniform fat content. Newborn infants cannot be assured of an adequate energy intake from any one specimen of pooled human milk owing to the variability in fat content. In this respect formula milk has a clear advantage as its fat content is standardised. Pooled milk might be improved by routine measurement of the fat content in donated human milk. The milk might then be mixed to ensure that the fat content is within an acceptable range.

The change in the fatty acid composition of human milk coincides with a trend towards inclusion in the diet of more fat from vegetable sources than from animal sources. Vegetable fat contains a larger proportion of unsaturated fatty acids, and it appears that this change in intake of fatty acids has altered the fatty acid composition of human milk.[5]

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Effect of digoxin and vitamin E in preventing cardiac damage caused by doxorubicin in acute myeloid leukaemia

The anthracycline antibiotics doxorubicin and daunorubicin are widely used to treat acute leukaemia and solid tumours, but their usefulness is limited by myocardial damage related to dosage above 550 mg/m^2 body surface area.[1] The cause is uncertain, but vitamin E, a powerful antioxidant that limits lipid peroxidation, has inhibited cardiac damage in mice[2] and strophanthin has reduced cardiac damage in dogs and rabbits,[3] perhaps by competitive inhibition with doxorubicin at cardiac receptor sites.

Patients, methods, and results

We studied 63 patients with newly diagnosed acute myeloid leukaemia but without known heart disease who had not previously received digoxin. They were randomised to serve as controls or to receive digoxin (average 0·25 mg daily) or vitamin E (200 mg thrice daily). These drugs were given throughout the study, and patient compliance was confirmed by regular measurements of plasma concentrations. Patients were then given induction treatment for leukaemia of cytarabine 50 mg/m^2 by continuous intravenous infusion for five days, thioguanine 100 mg/m^2 by mouth twice daily for five days, and doxorubicin 30 mg/m^2 intravenously over five minutes on the fifth and sixth days. Induction treatment was repeated once or twice every 10 days. Maintenance treatment with doxorubicin (45 mg/m^2 intravenously) was given monthly for at least one year. No patient received radiotherapy to the mediastinum.

Systolic time intervals were measured before and two weeks after each doxorubicin treatment by simultaneously recording the electrocardiogram, phonocardiogram, and carotid pulse tracing with a multichannel photographic system.[4] The ratio of the pre-ejection period to the left ventricular ejection time was used to evaluate left ventricular function, and an increase in ratio greater than 0·08 above the ratio recorded before treatment with doxorubicin indicated cardiac damage.[4 5]

None of the patients studied showed clinical or cardiographic changes or important changes in systolic time intervals at dosages of doxorubicin below 400 mg/m^2. Only 41 patients entered remission, of whom 25 survived to receive a total doxorubicin dose above 400 mg/m^2. The table shows the maximum change in the ratio of the pre-ejection period to the left ventricular ejection time from the baseline reading in these 25 patients. Analysis of covariance, which allowed for different total dosages of doxorubicin between patients, showed a significant difference ($p < 0·05$) between the control group and the group treated with digoxin but no significant difference between the control group and the group treated with vitamin E.

Changes in ratio of pre-ejection period to left ventricular ejection time in patients receiving total dosages of doxorubicin above 400 mg/m^2

Case No	Maximum change in ratio*	Total dosage of doxorubicin (mg/m^2)	No of systolic time intervals recorded at dosages above 400 mg/m^2
		Controls	
1†	0·143	620	8
2†	0·168	585	7
3	0·117	482	6
4	0·01	480	3
5	0·132	569	2
6	0·090	559	5
7	0·132	1016	11
8	0·076	612	6
		Patients given digoxin	
9	0·035	426	2
10	0·073	445	3
11	0·08	468	3
12	0·072	413	1
13	0·063	581	5
14	0·058	775	8
15	0·048	659	6
16	0·080	742	7
17	0·038	794	7
18	0·017	625	5
		Patients given vitamin E	
19	0·120	642	8
20	0·137	470	3
21	0·035	485	3
22†	0·151	749	9
23	0·030	478	3
24	0·031	572	5
25	0·025	530	3

*Increase in ratio above baseline ratio measured before treatment with doxorubicin began.
†Doxorubicin withdrawn because of large increases in ratio (cases 1 and 22) or heart failure and large increase in ratio (case 2).

Comment

Systolic time intervals provide a simple yet sensitive measurement of myocardial damage[4] and have been used previously to assess patients receiving doxorubicin.[5] Our results show that doxorubicin may be given safely to a high total dosage if systolic time intervals are monitored regularly. Although nine patients showed evidence of heart damage (table), we were able to continue using doxorubicin in their treatment with frequent monitoring of the ratio of the pre-ejection period to the left ventricular ejection time. Three patients (one of whom had mild clinical left ventricular failure) showed progressive increases in this ratio, which returned slowly to normal when doxorubicin was stopped.

Patients treated with digoxin before doxorubicin was started did not develop significant changes in the ratio of the pre-ejection period to left ventricular ejection time, suggesting that digoxin may protect the heart against damage by doxorubicin. Digoxin may, however, simply be masking changes caused by doxorubicin, and absolute confirmation of digoxin's protective role must await pathological studies. If digoxin was masking damage to the heart by reducing changes in the ratio, the ratio would be expected to increase when digoxin was withdrawn. Three patients completed treatment for acute myeloid leukaemia and stopped both doxorubicin and digoxin. Subsequent serial readings of systolic time intervals in all three patients did not show any appreciable increase in the ratio.

The search for anthracycline drugs that do not cause cardiac damage continues, but for the moment it seems prudent to treat patients receiving anthracyclines with digoxin and to monitor their cardiac function carefully by measuring systolic time intervals or by echocardiography.

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Danger of dead space in U100 insulin syringes

"Dead" space in a syringe is defined as the volume of a solution retained in the hub and needle when the plunger of the syringe is fully depressed. It is a potential source of error when two different fluids are drawn out, measured, and mixed in the same syringe, as in the case of insulin mixtures. With the recent changeover to U100 insulin any dead space in glass insulin syringes will be more important, and this problem has been assessed in Australia and the United States, where U100 insulin is already used.[1 2] We report a case of hypoglycaemia which was probably caused by incorrect dosage due to the dead space in the syringe. We subsequently measured the dead space in BS 1619 glass syringes and disposable plastic insulin syringes.

Case report and subsequent investigation

Case report—A 40 year old man who had had diabetes for 17 years started having attacks of hypoglycaemia in the late morning and before his evening meal after changing to the new U100 strength insulin. He had been receiving a mixture of 10 units of neutral insulin and 10 units of isophane insulin, drawing the neutral insulin up first. He noticed that when the plunger was retracted after taking in the neutral insulin 14 units were present in the syringe, and he realised that this would alter the ratio of the short acting to long acting types of insulin. After a reduction of the neutral and an increase of the isophane insulin the hypoglycaemic attacks stopped.

Investigation and results—We used the specific gravity of aniline to measure the dead space in insulin syringes. We weighed an empty syringe, drew up aniline to a graduated mark, excluding all air bubbles, and reweighed the syringe. The difference in weights divided by the specific gravity of aniline gave the volume actually drawn up, and the difference between this and the nominal graduation mark gave the volume of the dead space. This procedure was repeated for the major graduation marks of four types of syringe, and the table shows the results. The dead space in the new BS 1619 glass syringes had a volume equivalent to around 5 units of U100 insulin whether the 0·5 ml or 1 ml size was used, whereas the old BS 1619 glass syringe had dead space equivalent to 1·26 units of U20 insulin, 2·52 units of U40 insulin, and 5·04 units of U80 insulin. In contrast, 1 ml plastic disposable U100 syringes had a negligible dead space.