Key messages

- The incidence of hip fracture has been increasing, and mortality is often higher than expected for age and sex
- Being older, having a poorer level of activities of daily living, being male, and having a history of cardiovascular disease were important determinants of death
- One of the hospitals had a much higher survival rate. This seemed to be due to an aggregate effect of the total package of care
- Routine thromboembolic prophylaxis is indicated for patients with fractured hip
- Written policies that include prophylaxis should be developed and implemented for this vulnerable group of patients if mortality is to be improved

hospitals used anticoagulant prophylaxis routinely (in nearly all cases), half only in a minority of cases. It is almost certain that the number of emboli we recorded represents underreporting. But we have no reason to believe that the reporting of emboli at postmortem examination was biased between districts. The Thromboembolic Risk Factors Consensus Group recommended use of anticoagulant drugs for patients with a fractured hip; the results of our study again confirm the importance of prophylactic measures to combat venous thromboembolism. Despite considerable evidence of its efficacy, treatment with anticoagulant drugs is by no means used routinely by surgeons throughout the United Kingdom.¹⁴ Risk of thromboembolism becomes appreciable for patients aged 40 or over, and patients with a fractured hip are at high risk: 40-80% will develop deep vein thrombosis, 10-30% proximal vein thrombosis, and 1-10% fatal pulmonary embolism if prophylactic measures are not taken.¹⁴

CONCLUSIONS

The present data, revealing the striking difference between hospitals in mortality after fracture of the hip, were collected with audit methodology. Thus these

data generate a hypothesis rather than test a specific hypothesis. No single variable that we identified explains the protective effect of hospital 6, suggesting that it is an aggregate effect of the total package of care. Further work must be undertaken to identify more fully in what other ways, if any, treatment in hospital 6 differs and whether any specific components account for these clinically important differences.

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Safety and efficacy of combined meningococcal and typhoid vaccine

S H Khoo, J St Clair Roberts, B K Mandal

Immunisation for travel could be made more acceptable by combining compatible vaccines in one injection, provided that the mixture conferred adequate protection and was safe. Countries where meningococcal vaccine is recommended for travel are also areas where typhoid immunisation is advised.¹ Unpublished data from Merieux, which manufactures a typhoid and a meningococcal polysaccharide vaccine for injection, showed that the vaccines were compatible and stable in combination. We investigated the acceptability and serological responses to this combination in a single blind volunteer study.

Subjects, methods, and results

Between December 1991 and March 1992 we allocated 158 volunteers by block permuted randomisation to receive 0.5 ml typhoid polysaccharide vaccine (Typhim Vi, Merieux) intramuscularly (group A);

0.5 ml meningococcal polysaccharide vaccine (Mengivac (A+C), Merieux) intramuscularly (group B); or a mixture of both vaccines, the liquid typhoid vaccine being used to reconstitute the lyophilised meningococcal vaccine (group C). Group A comprised 54 subjects (27 men and women, median age 23 (range 18-56)), group B 50 (21 men, 29 women, median age 21 (18-62)), and group C 54 (24 men, 30 women, median age 22 (18-54)). Exclusion criteria were pregnancy, compromised immune system, fever, receiving any vaccine or immunoglobulin in the preceding three months, typhoid vaccination within the previous three years, previous meningococcal vaccination, and a history of typhoid or meningococcal disease. Volunteers kept a diary for five days recording pain in their arm (0=no pain, 1=pain on pressure, 2=pain on movement, 3=unable to sleep); size of induration and of erythema at injection site (using callipers provided); fever; aches; nausea; headache; itching; and other symptoms.

Subjects were blinded to their treatment until their return 3-6 weeks later, when those in groups A and B were offered the other vaccine; 66 accepted. Venous blood was sampled at both visits. After one year all those who had received both vaccines were invited to provide a further blood sample. We received responses from 40 in the combined groups A and B and 40 in group C. Antibody response to meningococcal A,

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	Antigen		
	Typhoid Vi	Meningococcal A	Meningococcal C
<i>Prevaccination antibody titres (geometric mean (range) (mg/l))</i>			
Group A (n=54)	0.3 (0.1-2.1)	5.2 (2.3-21.0)	2.7 (0.9-22.1)
Group B (n=50)	0.3 (0.1-2.0)	5.1 (2.3-15.0)	3.1 (0.8-3.0)
Group C (n=53)	0.3 (0.1-2.7)	5.4 (2.1-16.0)	3.0 (0.8-21.0)
Difference (95% confidence interval; P value):			
A v C	80 to 130; 0.9	81 to 116; 0.7	83 to 146; 0.5
B v C	75 to 132; 1.0	87 to 126; 0.6	76 to 132; 0.9
<i>Antibody titres at 3-6 weeks (mg/l)</i>			
Group A (n=54)	2.1 (0.3-26.0)	5.3 (2.3-22.0)	2.8 (0.9-22.0)
Group B (n=50)	0.2 (0.1-1.8)	23.3 (5.8-93.0)	34.0 (4.0-420.0)
Group C (n=53)	3.7 (0.3-45.0)	22.2 (5.5-174.0)	31.9 (6.0-520.0)
Difference (95% confidence interval; P value):			
A v C	79 to 182; 0.4	—	—
B v C	—	76 to 142; 0.8	71 to 160; 0.8
<i>Increase in prevaccination titres (range (mg/l) (%))</i>			
Group A (n=54)	1.1-25.1 (804)	-2.0-+1.1 (103)	-1.0-+4.0 (103)
Group B (n=50)	-0.3-+0.7 (101)	1.1-87.0 (452)	1.0-407.0 (1102)
Group C (n=53)	0.1-45.0 (686)	1.3-162.0 (413)	-3.0-+516.0 (1065)
Difference (95% confidence interval; P value):			
A v C	79 to 175; 0.4	—	—
B v C	—	8.3 to 143; 0.5	65 to 165; 0.9
<i>Antibody titres at 1 year (mg/l) *</i>			
Groups A and B (n=40)	0.6 (0.1-15.0)	15.1 (3.9-176.0)	21.2 (1.7-151.0)
Group C (n=40)	0.6 (0.1-11.0)	16.4 (4.9-85.0)	22.6 (5.8 to 241.0)
Difference (95% confidence interval; P value)			
	60 to 168; 1.0	77 to 154; 0.6	70 to 163; 0.8
<i>Difference between titres at 3-6 weeks and 1 year (range (mg/l) (%))</i>			
Group A (n=24)	-10.3-+0.1 (35)	—	—
Group B (n=16)	—	-40.0-+16.8 (77)	51.4-17.5 (79)
Group C (n=40)	-34.4-+0.0 (35)	-89.2-+4.3 (70)	-279.3-+6.9 (62)
Difference (95% confidence interval; P value):			
A v C	70 to 143; 1.0	—	—
B v C	—	73 to 111; 0.3	62 to 97; 0.03

*Group A, typhoid vaccine followed by meningococcal vaccine at 3-6 weeks; group B, meningococcal vaccine followed by typhoid vaccine at 3-6 weeks; group C, combined typhoid and meningococcal vaccine.

†For difference in geometric mean titre, values in group C being expressed as percentages of those in group A or B.

‡Mean post titre as percentage of mean pre titre.

§For difference in geometric mean titre, values in group C being expressed as percentages of those in groups A and B.

¶Mean 1 year titre as percentage of mean 3-6 week titre.

meningococcal C, and typhoid Vi antigens was assessed by radioimmunoassay.^{2,3} It was evaluated by unpaired *t* test (two tailed P values are given) comparing the log values of titres and differences in log titres from prevaccination values and between 3-6 weeks and one year.

Groups A, B, and C did not differ significantly ($P > 0.2$; χ^2 test) in the reported frequency or duration of redness (19 patients (35%), 18 (36%), and 27 (50%) respectively) or in the reported frequency of headache (9 (17%), 5 (10%), and 8 (15%)); fever (1 (2%), 1 (2%), and 6 (11%)); nausea (all groups, 3 (6%)); generalised aches (6 (11%), 7 (14%), and 7 (13%)); or itching (2 (4%), 5 (10%), and 6 (11%)). However, volunteers in group A were less likely than those in groups B and C to complain of swelling (7 (13%) v 17 (34%) and 16 (30%) subjects; $P=0.03$, χ^2 test) or to score pain in the arm as 2 or more (12 (22%) v 22 (44%) and 26 (48%) subjects; $P=0.01$, χ^2 test).

There were no significant differences between the three groups in prevaccination titres, in antibody titres at 3-6 weeks, or in the increase in titres after vaccination of antibodies against all three antigens (one subject in group C from whom paired serum samples were not available was excluded) (table). After one year, antibody titres against all three antigens had fallen, but there were no significant differences in titres achieved or in the rise from prevaccination values between separate and combined vaccination. In some subjects from group C, however, the fall in titres between 3-6 weeks and 1 year was greater; it was significant only for antibodies to meningococcal C antigen ($P=0.03$), although the geometric mean titre was still over sevenfold greater than prevaccination values.

Comment

Mixing both vaccines did not increase adverse events, which were similar to those reported previously,² or significantly affect the antibody response. Nevertheless, postvaccination titres of typhoid antibodies were slightly lower than those seen in other comparable studies,^{2,3} possibly reflecting differences in age, previous exposure, ethnic group, or radioimmunoassay. After one year all three titres had fallen from their peak at 3-6 weeks, in keeping with other studies.⁴ The fall tended to be greater for antibodies to meningococcal C antigen in group C, but titres were still high compared with prevaccination values and absolute titres after one year were not different from those in the other groups. Whether these differences mean a more rapid loss of efficacy of the combined vaccine in the longer term (requiring more frequent boosters) needs further study. Our findings suggest that the combination is an acceptable alternative to separate vaccinations before travel.

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Abnormality rates on barium meal examination in different racial groups

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Barium meal examination of the upper gastrointestinal tract is a widely performed investigation readily available to general practitioners and hospital outpatient departments. In central Birmingham a high proportion of the population is of Asian (from the Indian sub-continent) descent. We investigated differences in rates of abnormality on barium meal examination in Asian and white patients attending our departments.

Patients, methods, and results

The reports of barium meal examinations of patients attending two radiology departments in central Birmingham during 1992 were retrospectively analysed. Racial origin was indicated on the request form at the time of examination and was recorded in all patients. All retrievable radiological reports of Asian patients and a comparable number of white patients were studied. Reports were classified as showing (a) normal findings, including small amounts of gastro-oesophageal reflux; (b) minor abnormalities, including conditions such as hiatus hernia, gastric erosions, and duodenitis; and (c) major abnormalities including malignancy or suspected malignancy and gastric or duodenal ulceration.

The data were analysed using χ^2 tests, and subgroups were also compared according to age, sex, and source of referral.

See p 890.

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