A cluster of *Pneumocystis carinii* infections in children

Pneumocystis carinii pneumonia occurs almost exclusively in immunosuppressed patients, particularly those being treated for acute lymphoblastic leukaemia. The mode of transmission of the organism is not clear.¹ Several hospital outbreaks have been reported, and animal to animal transmission has been documented, but convincing evidence is still lacking of person to person transmission. We present a cluster of children currently receiving the United Kingdom Acute Lymphoblastic Leukaemia eight (UKALL 8) regimen for acute lymphoblastic leukaemia who became seropositive for antipneumocystis antibody within a short space of time, providing further evidence for person to person transmission.

Patients, methods, and results

Children currently receiving the UKALL 8 regimen for acute lymphoblastic leukaemia have an indirect immunofluorescence test performed monthly by Coon's technique² for the detection of IgG antibodies to *P. carinii*. Six children in a paediatric ward aged 3½ to 8 years were being so treated, and between November 1983 and May 1984 five of them (who were all previously seronegative) developed antibodies in significant titre to *P. carinii*. Only two of the children developed a pneumonitis clinically and radiologically resembling *P. carinii* infection. Both were admitted and responded promptly to co-trimoxazole. Invasive diagnostic procedures were not performed.

On reviewing retrospectively the remaining three seropositive children we noted that all three had symptoms of upper respiratory tract infection with fever and a dry cough coinciding with the times of rising antibody titre.

One of the children was found to have an extremely high titre of antibodies. She was the only patient in whom IgM antibodies to *P. carinii* were measured, and this titre was also raised. All six children attended an outpatient department simultaneously once a week, spending about an hour together in a small waiting room. All had been admitted to hospital at various stages but never at the same time. No patient had been given prophylactic co-trimoxazole during the previous five to six months. When last measured all the titres were falling.

The figure shows the titres and times of increase of antibodies in the five patients.

Relation of rising pneumocystis antibody titres with respect to time.

Comment

Several workers have found antibodies to *P. carinii* in three quarters to all of the population studied by the age of 4 years.^{3,4} This suggests universal exposure and subclinical infection with *P. carinii*, the disease becoming evident clinically only in immunosuppressed patients.

There have been four major outbreaks of *Pneumocystis* pneumonia reported in patients with malignant disease, all of which occurred in North America.⁵ Two of these were considered to be due to reactivation, probably secondary to highly intensive chemotherapy regimens. In the remaining two, person to person spread was thought to be a possibility.

In our series also cross infection among the patients would be the most likely explanation, for several reasons. Firstly, all five patients had negative titres initially, implying that previous exposure had not occurred (although it may indicate suppression of antibodies⁶ from chemotherapy). The remaining child already had a low titre of antibodies to *P. carinii* and thus may have been protected. Secondly, the rise in titre in all patients was seen over

six months. An interval of four to eight weeks occurred between cases, consistent with the incubation period of *P. carinii* infection. Thirdly, the only patient tested for IgM specific *P. carinii* antibodies had these in high titre, indicating a primary infection.

An alternative but less likely explanation for our findings would be that some common factor might have induced reactivation of latent infection.

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Local anaesthetic infiltration versus Bier's block for Colles' fractures

After recent concern¹ about the safety of Bier's intravenous regional anaesthesia for manipulation of Colles' fractures in outpatients,² we have considered the simpler and quicker method of local anaesthetic infiltration directly into the haematoma of the fracture. A series of 280 patients treated with this method showed good tolerance and absence of pain for 4-24 hours after manipulation.³

Objections to local infiltration are the possibility of infection, a more painful injection, and difficult reduction with less relaxation of muscles. A prospective randomised trial was carried out to test the effectiveness and duration of each treatment and note complications or side effects.

Patients, methods, and results

One hundred consecutive patients requiring manipulation of Colles' fractures and satisfying the following criteria were randomly allocated to receive either Bier's block or local infiltration: aged over 15; normal sensation and circulation of limb; closed injury; no diabetes, epilepsy, or sickle cell disease; and no relevant allergy.

The patient's forearm was prepared with 2% chlorhexidine in spirit and draped with sterile towels. Wearing sterile gloves, the operator injected 10 ml of 2% lignocaine into the cavity of the fracture and around the adjacent periosteum, including the ulnar styloid. The arm was raised for one minute before inflating the upper part of a double cuff to 250 mm Hg; then 30-40 ml of 0.5% prilocaine was injected into a vein on the back of the hand. The lower cuff was inflated and the upper one deflated 20 minutes later. The fracture was manipulated 10 minutes after injection in each group.

Pain scores were recorded on 10 cm linear analogue scales⁴ representing the range from "no pain" to "very severe pain" before beginning the procedure, during injection of local anaesthetic, during manipulation, and when plaster was completed during radiography. The casualty officer recorded his impression of the effectiveness of the technique on a linear analogue scale and noted any difficulties. The times of first consultation, start of procedure, completion of plaster, and release of tourniquet were recorded.

Records of 83 patients were completed adequately and analysed. The groups were comparable in age, sex, dominance of affected wrist, and degree of displacement of fracture. Forty four received Bier's block. Pain scores during manipulation were higher for patients receiving local infiltration (mean 5.53 (SD 3.67)) than for those receiving Bier's block (2.64 (3.02)) ($p < 0.0003$ using Student's *t* test). At other stages the scores were not significantly different between groups. The casualty officer's impression of effectiveness was usually more generous than the patient's but showed the same superiority of Bier's block (7.68 (2.38)) over local infiltration (6.11 (2.84)) ($p < 0.009$).

No difference was noticed in the period of postoperative painlessness between the groups: Bier's block 3.7 (3.0) hours; local infiltration 4.0 (3.0) hours. The

duration of each procedure was similar: Bier's block 21.1 (7.9) minutes; local infiltration 20.3 (12.5) minutes, but after Bier's block patients required radiography before the tourniquet was released (20.0 (9.2) minutes) and were observed for a further 20 minutes. For Bier's block staff were committed for twice as long (41 (11) minutes), and patients waited longer before the procedure began (89 (52) minutes) than did those receiving local infiltration (67 (37) minutes).

No patient suffered significant complications or side effects. Inadequacy of reduction of the fracture was rare and not related to the technique.

Relative merits of Bier's block and local infiltration. (Values are scores)

	Bier's block	Local infiltration
Complications	4	1
Effectiveness	3	2
Simplicity	2	3
Speed	1	4

Comment

For patients with fresh Colles' fracture local anaesthetic infiltration was more popular among accident service staff (table), giving satisfactory anaesthesia, being simpler and quicker to perform, and avoiding risks of a large intravenous dose of local anaesthetic agent reaching the general circulation. No documented reports exist of infection after its use. Unfortunately, objective comparison of the efficacy of the technique with the widely used and tested Bier's block has shown it to be inferior.

We thank the casualty officers and nursing staff of the Accident Service, John Radcliffe Hospital, for their help in conducting this trial in 1984.

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Do β blockers cause arthropathy? A case control study

Savola described 18 patients with arthritis that he attributed to treatment with β blocking drugs, particularly metoprolol, and he suggested that arthritis is a common adverse reaction to treatment with β blockers.¹ We investigated this hypothesis in a case-control study.

Patients, methods, and results

All patients with both hypertension and arthropathy affecting peripheral joints who had attended the Sheffield Hypertension Clinic during the three years 1980-2

were identified by a search of the formal problem lists used routinely in the clinic. When a specific diagnosis (for example, osteoarthritis) was stated on the problem list this was accepted to avoid importing bias into the study. When no specific diagnosis was stated the clinical and laboratory findings were reviewed. Patients with acute gouty arthritis and lupus induced by hydralazine were excluded because these conditions might have biased the choice of antihypertensive drugs. Each patient in the study was matched for age (same decade) and sex with two control patients who had hypertension but no arthritis and had attended the clinic during the same year. Patients aged over 80 could not be matched and were excluded. The use of β blockers by patients with arthritis and controls was compared. The approximate relative risk and 95% confidence limits were calculated as described by Armitage.²

We identified 127 patients with arthritis (80 women, 47 men; mean age 61.4 years). The 254 controls were well matched for age and sex. There was no association between arthritis of all types and the use of β blockers (approximate relative risk 1.14, 95% confidence limit 0.74-1.77) (table). For atenolol, the β blocker used most commonly, the approximate relative risk was 1.00 (95% confidence limit 0.65-1.54). Osteoarthritis, rheumatoid arthritis, and other specific arthropathies were not associated with use of a β blocker (table).

In 42 patients the cause of the arthritis had not been determined. These patients were no more likely than their controls to be taking a β blocker (69% v 64%). Seventeen patients had been investigated in depth in the clinic, but arthritis had remained unclassified despite this. These patients were no more likely than their controls to be taking a β blocker (approximate relative risk 1.13, 95% confidence limit 0.33-3.91). Arthritis had developed during treatment with a β blocker in only five of this group of patients.

Comment

In this study the use of β blockers was not associated with arthropathies in general or with unclassified arthritis. The 17 patients with arthritis that had remained unclassified despite investigation corresponded most closely to the patients described by Savola,¹ but they were no more likely than control patients to be taking a β blocker. Our study had insufficient power to exclude completely an association between use of β blockers and arthropathy (as shown by the upper 95% confidence limits in the table), but it does not lend support to the suggestion that arthritis is a common adverse reaction to β blockers. The observations differ in two important respects from those of Savola.¹ In his series of cases metoprolol was the drug implicated most often. Few patients in our study population were taking metoprolol, and it remains possible that arthritis is related specifically to this β blocker. It is, however, most unlikely that there is an association between atenolol, or β blockers in general, and arthropathy. The second important difference between the two sets of observations is that Savola's series was uncontrolled. It is often difficult to be certain of cause and effect when assessing possible adverse reactions, and the data reported by Savola did not remove all doubt, as others have pointed out.³

We conclude that arthritis that cannot be classified is not uncommon in hypertensive patients, but there is no evidence that β blockers are responsible for it.

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Use of β blockers by patients with arthritis and controls

	No of patients		No (%) taking a β blocker*		Approximate relative risk	95% confidence limits
	Cases	Controls	Cases	Controls		
All arthritis	127	254	80 (63)	152 (60)	1.14	0.74-1.77
Osteoarthritis	58	116	32 (55)	69 (59)	0.84	0.44-1.59
Rheumatoid arthritis	19	38	13 (68)	21 (55)	1.75	0.55-5.58
Other arthropathies†	8	16	6 (75)	8 (50)		
Unclassified arthritis	42	84	29 (69)	54 (64)	1.24	0.56-2.74

* β Blockers taken were (cases/controls): atenolol 55/110, oxprenolol 11/16, propranolol 5/14, metoprolol 2/6, acebutolol 2/3, sotalol 2/0, timolol 1/1, pindolol 1/1, labetalol 1/1.

†Ankylosing spondylitis (five patients), Still's disease (one), polymyositis with arthralgia (one), and polymyalgia rheumatica (one).