Colonisation of lung allografts with *Pseudomonas aeruginosa* in heart-lung transplant recipients with cystic fibrosis

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Abstract

Six patients (four with cystic fibrosis, two with bronchiectasis) harboured *Pseudomonas aeruginosa* in the lung before heart-lung transplantation. Three of the patients with cystic fibrosis were colonised by strains of different genotype postoperatively, and the colonisation tended to be short lived.

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Cystic fibrosis is characterised by abnormalities in ion transport affecting the epithelia and exocrine glands,[1,2] and this is probably the primary cause of recurrent infections in the lungs.[2] *Pseudomonas aeruginosa* is the predominant pathogen associated with pulmonary infection and mortality in cystic fibrosis.[3]

Heart-lung transplantation is an established treatment for patients with cystic fibrosis with end stage respiratory disease, and colonisation of allografts with *Ps aeruginosa* after heart-lung transplantation may adversely affect lung function. We have determined whether patients were colonised postoperatively with *Ps aeruginosa* strains which were resident before the operation.

Methods

Thirteen consecutive recipients of heart-lung transplantation were studied. Their underlying lung pathology included cystic fibrosis (five), non-cystic fibrosis bronchiectatic lung disease (four). All recipients with cystic fibrosis received appropriate antipseudomonas intravenous antibiotics for two weeks after heart-lung transplantation. Aerosolised colomycin was used as maintenance therapy after heart-lung transplantation and all patients with *Ps aeruginosa* in the lower airways during the first three months were treated with appropriate antibiotics; subsequently only clinical chest infections were treated.

Preoperative nose and throat swabs and sputum samples were taken. After heart-lung transplantation bronchoalveolar lavage via an endotracheal tube adaptor was undertaken weekly for one month and then quarterly or when clinically indicated. Swabs and sputum were collected before bronchoscopy on each occasion.

Nose and throat swabs and sputum specimens were processed by standard bacteriological methods. Lavage fluid was centrifuged and the deposit was treated similarly. Isolates of *Ps aeruginosa* were genotyped with the pCMTox probe.[4]

Results

Of the 13 patients who underwent heart-lung transplantation six were found to be colonised with *Ps aeruginosa* after the operation (one six months after transplantation) and four of these had cystic fibrosis. Each of the patients with cystic fibrosis before operation was positive for *Pseudomonas* in the sputum, and in one case the organism was isolated from a nasal swab at the time of operation. The two non-cystic fibrosis bronchiectatic patients harboured *Ps aeruginosa* solely in the sputum preoperatively.

Three of the four patients with cystic fibrosis (nos 1, 2, and 4, table) were colonised postoperatively by strains of different genotype to those isolated before the operation (figure). Two of these patients had identical strains in both upper and lower airways, while the third harboured at least three distinct genotypes. The remaining patient with cystic fibrosis and the non-cystic fibrosis bronchiectatic patient (no. 5) retained a single strain throughout the sampling period.

Summary of DNA probe analysis of Ps aeruginosa isolates before and after heart-lung transplantation

Patients	*Specimen*	*Weeks before (−) or after (+) HLT*	*Genotype*
No. 1 (CF)	S	0	A
	N	0	A
		HLT	
	L	+1	B
	T/S/L	+3	B
	S	+4	C
	S	+24	B
No. 2 (CF)	S	−6	D
	S	0	E
		HLT	
	L	0	D
	S	+1	F
	L	+1	G
	S	+13	F
No. 3 (CF)	S	−7	H
	S	−4	H
		HLT	
	T/S/L	+2	H
	T	+27	H
	S	+45	H
No. 4 (CF)	S	−2	I
		HLT	
	L	+1	J
	N	+4	J
No. 5 (non-CF)	S	0	K
		HLT	
	S	0	K
	L	+2	K
	T	+3	K
	L	+5	K

CF = cystic fibrosis; HLT = heart-lung transplantation; S = sputum; N = nose swab; L = bronchoalveolar lavage; T = throat swab; A–K = *Ps aeruginosa* strains of different genotypes.

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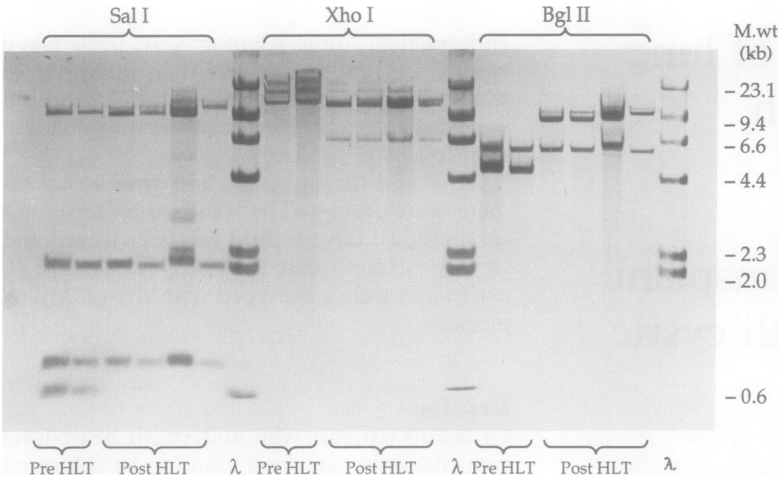

DNA hybridisation patterns of Ps aeruginosa strains from patient with cystic fibrosis (no. 1 in table) before (pre) and after (post) heart-lung transplantation (HLT). Six positive isolates were digested by three restriction endonucleases, Sal I, Xho I, Bgl II (Gibco, Middlesex, UK). Complementary restriction fragment length polymorphisms were expressed in kilobases (kb) with reference to standard molecular weight markers, labelled as lambda (λ) Hind III fragments. The isolates before and after heart-lung transplantation gave different strains of Ps aeruginosa.

There was no significant difference between the mean FEV_1 % predicted in the four patients with *Ps aeruginosa* colonisation at six and 12 months after heart-lung transplantation compared with non-cystic fibrosis patients not colonised by the organism (88·3% and 91·6% respectively).

Discussion

Heart-lung transplantation has been successfully performed in patients with cystic fibrosis and end stage respiratory disease,[5 6] with the transplant procedure itself removing the major source of *Ps aeruginosa*. However, colonisation of the lung allografts, predominantly with *Ps aeruginosa*, has been reported in patients with cystic fibrosis during the early postoperative period and this probably reflects the prevalence of this organism in their upper airways.[7]

During the first month after heart-lung transplantation three of the five cystic fibrosis patients in our study had *Ps aeruginosa* in both the upper and lower airways, and one acquired this organism in the lower airways only. In contrast, patients with emphysema and pulmonary vascular disease did not become colonised with *Ps aeruginosa*. Our finding of *Ps aeruginosa* colonisation of the transplanted lungs in cystic fibrosis during the early postoperative period was not associated with increased episodes of clinical infection. Smyth *et al*[8] also found that the incidence of bronchitis and pneumonia with this organism was similar between recipients of heart-lung transplants with and without cystic fibrosis.

The native cystic fibrosis upper airways which retain the ion transport defect are a potential source of *Ps aeruginosa* contamination of the transplanted lower airways. The early use of aerosol and oral antipseudomonas antibiotics[9] to prevent chronic *Ps aeruginosa* colonisation of lung allografts is supported by this study, as colonisation was found to be short lived.

The change in the *Pseudomonas* population after heart-lung transplantation shown in some patients with cystic fibrosis in this study may reflect a lack of sensitivity of the preoperative sampling methods used and we may simply have failed to isolate all preoperative strains that were present – for example, the intestinal tract, which is known to be a potential source of *Ps aeruginosa* in cystic fibrosis,[10] was not sampled.

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