

LETTERS

Efficacy of nebulised colomycin in patients with non-cystic fibrosis bronchiectasis colonised with *Pseudomonas aeruginosa*

Colonisation with *Pseudomonas aeruginosa* is a feature of bronchiectasis and is associated with more severe disease and lower quality of life.¹ Nebulised colomycin, a polymixin, bactericidal antibiotic with potent activity against most Gram-negative organisms, including *P aeruginosa*, is frequently employed in these patients, but evidence is lacking for this approach.

We have retrospectively assessed the efficacy of nebulised colomycin in *P aeruginosa*-colonised patients receiving a minimum of 6 months treatment. Patients who received concomitant prophylactic macrolide treatment for >4 weeks were excluded. Bronchiectasis was confirmed in all patients by standard high-resolution CT criteria, and all received nebulised colomycin 1–2 megaunits twice daily through a standard jet nebuliser and compressor. The annualised frequency of hospital admissions, infective exacerbations requiring rescue antibiotics and sputum positivity for *P aeruginosa* per patient, prior to, and while on, colomycin treatment was compared. Forced expiratory volume in 1 s (FEV₁) and self-reported sputum volume within 6 months of starting treatment and most recent on treatment were also compared. The data were analysed by non-parametric Wilcoxon test (table 1).

Nineteen patients (9 males/10 females), mean age 66 years, were assessed between January 2000 and April 2007. Four patients had idiopathic disease and 15 disease of known cause. The mean length of data collection before commencing colomycin was 23.6 months and the mean duration on treatment was 21.2 months (range 6–39 months) with 17 patients still on treatment at assessment (two patients discontinued treatment, one erroneously and one due to lack of efficacy).

Only one previous study has interrogated the role of inhaled colomycin in this patient group. Steinfert *et al*² retrospectively reviewed the efficacy of nebulised colomycin in 18 patients with chronic bronchial sepsis (14 with bronchiectasis) of whom 14 were colonised with *P aeruginosa*. There was a significant attenuation in decline in FEV₁ and forced vital capacity (FVC), and an improvement in quality of life. *P aeruginosa* was eradicated in three patients but admission and exacerbation frequency were not assessed. Inhaled colomycin is frequently employed in patients with cystic fibrosis chronically colonised with *P aeruginosa*, but there is little evidence to support this. One study, involving 115 patients comparing inhaled colomycin with tobramycin over 4 weeks, demonstrated a significant decrease in the sputum *P aeruginosa* density with both

Table 1 Clinical outcomes pre- and postnebulised colomycin

n = 19	Precolomycin Mean (SD)	Postcolomycin Mean (SD)
Exacerbation frequency/year	7.8 (3.0)	2.7 (2.1)*
Admission frequency/year	3.0 (2.7)	0.95 (1.1)†
<i>P aeruginosa</i> sputum positivity/year	4.2 (2.5)	0.5 (0.5)* (eradication n=3‡)
Sputum volume (ml)	31 (20.8)	14 (13.5)*
FEV ₁ (litres)	1.13 (0.6)	1.14 (0.6)

*p<0.001; †p=0.002.

‡Eradication= \geq 2 negative *P aeruginosa* sputum cultures postcolomycin. FEV₁, forced expiratory volume in 1 s.

treatments but a significant improvement in FEV₁ in the tobramycin group only.³

Several studies have assessed the efficacy of nebulised tobramycin in *P aeruginosa*-colonised patients with non-cystic fibrosis bronchiectasis.^{4–5} Tobramycin consistently reduced sputum *P aeruginosa* density with eradication rates of 13–35%, but resistance emerged in 7–11% of patients. The only study addressing exacerbations demonstrated a significant reduction in admission, but not exacerbation, frequency.⁵ Both studies showed a non-significant decrease in FEV₁ on treatment, probably due to increased bronchospasm, with drug intolerance in up to 10% mainly due to airway symptoms.

In conclusion, nebulised colomycin appeared to reduce exacerbation frequency, hospitalisation, sputum *P aeruginosa* positivity and sputum volume in *P aeruginosa*-colonised patients with bronchiectasis and was well tolerated. These results are encouraging in this severely affected patient group and strengthen the need for a prospective, adequately powered, randomised controlled trial to investigate the efficacy of this treatment further.

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Competing interests None.

Provenance and peer review Not commissioned; externally peer reviewed.

Accepted 5 July 2009

Thorax 2010;65:553.

doi:10.1136/thx.2008.112284

REFERENCES

- Wilson CB, Jones PW, O'Leary CJ, *et al*. Effect of sputum bacteriology on the quality of life of patients with bronchiectasis. *Eur Respir J* 1997;10:1754–60.
- Steinfert DP, Steinfert C. Effect of long-term nebulized colistin on lung function and quality of life in patients with chronic bronchial sepsis. *Intern Med J* 2007;37:495–8.

- Hodson ME, Gallagher CG, Govan JRW. A randomised clinical trial of nebulised tobramycin or colistin in cystic fibrosis. *Eur Respir J* 2002;20:658–64.
- Barker AF, Couch L, Fiel SB, *et al*. Tobramycin solution for inhalation reduces sputum *Pseudomonas aeruginosa* density in bronchiectasis. *Am J Respir Crit Care Med* 2000;162:481–5.
- Drobnic ME, Sune P, Montoro JB, *et al*. Inhaled tobramycin in non-cystic fibrosis patients with bronchiectasis and chronic bronchial infection with *Pseudomonas aeruginosa*. *Ann Pharmacother* 2005;39:39–44.

Maternal smoking during pregnancy decreases Wnt signalling in neonatal mice

Epidemiological studies have shown that maternal smoking during pregnancy is a risk factor for the development of asthma. However, the mechanisms underlying the increased risk of developing asthma are largely unknown. We have shown that maternal smoking during pregnancy increases smooth muscle layer and collagen III deposition around the airways in mouse offspring in association with increased airway hyper-responsiveness.¹ Other factors also appear to contribute to the development of increased airway hyper-responsiveness. We hypothesise that lung development is such a factor. Since genes in the Wnt- β -catenin pathway are essential for lung development and epithelial stem cell differentiation/expansion, we investigated the effects of maternal smoking during pregnancy on Wnt gene expression in lung tissue from neonatal offspring.

Balb/c mice were exposed to fresh air or cigarette smoke from 3 weeks before conception until delivery. Offspring (n = 16 from non-smoking mothers, n = 18 from smoking mothers) were killed 1 day after birth. RNA was isolated from total lung tissue and qRT-PCR was performed using microfluidic card assay.

We found that maternal smoking during pregnancy decreased the expression of *Foxa2*, *Fzd-7*, *Egf*, *Cttnb1*, *Fn1* and *Pdgfra* (encoding forkhead box a2, frizzled receptor 7, epidermal growth factor, β -catenin, fibronectin and platelet-derived growth factor receptor α , respectively) in lung tissue from neonatal offspring (figure 1). Maternal