161 Use of different preparations of tobramycin solution for inhalation (TSI) in the UK

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TSI is recommended for CF patients chronically infected with Pseudomonas aeruginosa, since it improves lung function and reduces pulmonary exacerbations. Despite this, its uptake (both TOBI® and isotonic Bramitob®) in the UK is poor.
To study this, we surveyed 30 specialist UK CF centres, looking at reasons for TSI use, type and regime used, funding issues, whether a trial of therapy was considered and side-effects (SEs): 23 (77%) responded.
Although 16 (70%) used TSI, 12 (75%) only did so when nebulised colomycin failed or was not tolerated. Of these, 10 (65%) only used TOBI® and of those 6 who used both, Bramitob® was first line in 1 (17%). As regards prescription, 13 (57%) followed the licensed alternate month regime, 2 (9%) alternated with colomycin, and the remainder a variable frequency including continuous use.
TSI was funded by primary care in 13 (57%), secondary care in 3 (13%), but the remainder were unclear. Funding was dealt with by the pharmacy in 9 (39%), the finance team in 3 (13%), and in 3 (13%) by the CF team. As regards a therapy trial, 11 units did so with objective measures, but only 2 units carried out reviews at 3 and 6 months respectively. Overall, TSI tolerability was good but common SEs included; bad taste, chest tightness, bronchoconstriction and haemoptysis: these were more common with TOBI®.
Throughout the UK there seems to be a wide variation in the use of TSI in CF units, and funding streams are not clear – this is particularly worrying considering its cost. Since more expensive nebulised therapies are likely to become available in the near future, a coordinated approach to their use and funding is merited within the CF community.

162 Effect of saline concentration on the minimum inhibitory concentration of colistimethate sodium and tobramycin

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Hypertonic saline has been used to facilitate the clearance of mucus from the lungs in patients with cystic fibrosis (CF). Part of the clinical benefit attributed to hypertonic saline might be due to NaCl affecting motility and growth of *P. aeruginosa*. The aim of this study was to determine the effect of NaCl upon the minimum inhibitory concentration (MIC) of colistimethate sodium and tobramycin. *P. aeruginosa* or *E. coli* were used with iso-sensetest broth to prepare inoculum solutions. The broth contained 0.3% NaCl, the lowest concentration of NaCl used in the tests. Sterile tubes were prepared with the concentration ranges, 128–0 mg/L for colistimethate sodium and 32–0 mg/L for tobramycin, with added NaCl concentrations of 0.3%, 0.9%, 2.3% or 4.05%. An inoculum of either *P. aeruginosa* or *E. coli* was added and the tubes then incubated at 35–37ºC for 18–20 h. This process was performed in triplicate for each antibiotic/NaCl/bacteria combination.
The addition of NaCl to the test solution had a synergistic effect on the MIC of colistimethate sodium needed to prevent growth of *P. aeruginosa* at the 4.05% concentration and *E. coli* at all concentrations. NaCl had an antagonistic effect on the MIC of tobramycin at all concentrations; this was most marked against *E. coli*.
The addition of NaCl to the growth environment had a synergistic effect upon the MIC of colistimethate sodium against *P. aeruginosa* and *E. coli* growth, in contrast to an antagonistic effect upon the MIC of tobramycin. The effect was concentration dependent for both bacteria. These results may have implications for the timing of inhaled saline-based treatments in patients with CF using certain antibiotic formulations.

163 Investigation of Colifin® (1 and 2 million international units colistimethate sodium, CMS) for aerosolisation in the eFlow®*rapid* and PARI LC SPRINT® nebuliser

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Aims: This study reports on *in-vitro* delivery performance data of Colifin® (1 and 2 million I.U. colistimethate sodium) by the eFlow®*rapid*, and the PARI LC SPRINT® nebuliser most recently approved via a decentralized approval procedure (DCP) in the United Kingdom, Netherlands, and Germany.
Methods: *In-vitro* nebulisation efficiency of 1 and 2 million I.U. Colifin supplied by PARI Pharma, Starnberg, Germany, dissolved in 3 ml and 4 ml saline, each, was investigated by breath simulation tests mimicking an adult breathing pattern (15 breaths/min, 500 ml tidal volume, inh:exh = 1/1) and aerodynamic particle size assessment by a next generation impactor operated at 18ºC and controlled environmental conditions at 23±2ºC, 50±5% r.H. and a flow rate of 15 l/min. Sample solutions were assayed by a validated HPLC-method and UV detection. The Delivered Dose (DD), Respirable Dose (RD) = drug in droplets <5 and 3.3 µm, Mass Median Aerodynamic Diameter (MMAD) and Geometric Standard Deviation (GSD) were calculated by the Copley CITDAS Version 2.0 software. All tests were carried out with 3 nebulisers in quadruplicate (n = 12 each) using the PARI LC SPRINT powered by a PARI BOY S compressor and the eFlow *rapid*.
Results: See the table.

Summary of aerosol characteristics (n = 12, values are mean±SD)

	DD		Neb. time	RD [mg]		MMAD	GSD
	[mg]	[%]	[min]	<5 µm	<3 µm	[µm]	
LC SPRINT 1 mio IU	26.7±3.6	33.7±4.5	6.2±1.0	15.9±2.4	10.2±1.6	4.0±0.4	2.2±0.1
LC SPRINT 2 mio IU	65.7±3.6	41.6±2.2	11.0±0.7	39.2±2.9	24.6±2.2	4.1±0.2	2.1±0.1
eFlow®rapid 1 mio IU	26.6±2.9	33.6±3.6	3.8±0.3	17.6±2.0	8.0±1.0	4.1±0.1	1.6±0.0
eFlow®rapid 2 mio IU	57.8±2.8	36.6±1.7	6.2±0.7	39.9±2.0	18.2±1.5	4.0±0.1	1.6±0.0

Conclusions: DDs and RDs were comparable for the PARI LC SPRINT and eFlow®*rapid*. However, nebulisation time was shorter for eFlow®*rapid* helping to improve both, quality of life of CF patients and most probably drug adherence, as well.

164 Tolerability of nebulised vancomycin in adults with cystic fibrosis

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Background: Our standard protocol for eradication of MRSA from respiratory culture, in adults with cystic fibrosis (CF) includes nebulised Vancomycin 250 mg twice daily for five days. All patients are pre-treated with a bronchodilator and have pre and post lung function to ensure that the drug is tolerated.
Method: We performed an audit on all patients with first isolation of MRSA between January 2006 and January 2010 to establish the tolerability of nebulised vancomycin in this patient group.
Results: A total 22 patients (median (range) age 26.0 (18.5–46.3) years; FEV_1 52% (27–108), had been eligible for treatment over the study period. One patient refused treatment, another received IV antibiotics instead of standard eradication therapy due to co-existing respiratory exacerbation, while a further patient was not tested due to multiple intolerance to other nebulised antibiotics. Out of 19 patients who received a test dose of vancomycin (250 mg) post bronchodilator, only one was intolerant (FEV_1 –21%; FVC –30%; $FEF_{25–75}$ –10%) and did not commence therapy. The remaining 18 patients tolerated the test dose (see table 1) and subsequently completed 5 days of treatment.

Table 1

	median (range)
FEV_1	0% (–11% to +10%)
FVC	–2% (–29% to 33%)
$FEF_{25–75}$	–1% (–30% to +21%)

Discussion: Nebulised vancomycin appears to be well tolerated although significant bronchoconstriction can occur in some patients. It is important to administer a test dose and monitor respiratory function before commencing treatment.