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P101 SURFACE PARASTERNAL INTERCOSTAL ELECTROMYOGRAM (SEMGPARA) AS A MONITORING TOOL IN CYSTIC FIBROSIS

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Lung function has been traditionally accepted as the primary monitoring tool in cystic fibrosis. The rate of change in lung function however, is slowing and is now as low as 1% per annum. Alternative monitoring tools to assess disease severity are therefore required. Measuring neural respiratory drive (NRD) using diaphragm electromyography (EMG) provides a sensitive measure of load on the respiratory system. The invasive nature of this technique limits is application, however measurement of NRD by sEMGpara is non-invasive and has potential clinical application in monitoring respiratory function in cystic fibrosis (CF).

Hypothesis That NRD measured by sEMGpara%max can be used to assess the change of ventilatory mechanics during an infective exacerbation in CF.

Methods Eight patients [median (range) 20 (20–25) years old, three females] with CF, admitted to hospital with an acute chest infection were studied. The studies were performed within 48 h of admission and on the day of discharge. At both time points spirometry and sEMGpara were measured. sEMGpara was recorded from bipolar surface electrodes placed 3 cm bilaterally from the midpoint of the sternum in the second intercostal spaces (positive electrode on the right side of the chest). The reference electrode was placed on the lateral aspect of the clavicle. For EMG analysis the root mean square (RMS) was calculated and peak RMS of the resting EMG was expressed as a percentage of peak RMS of the maximum (EMG % max) obtained during inspiratory capacity manoeuvres.

Results The median (range) length of stay was 10 (5–22) days. There was a significant reduction in median (range) sEMGpara% max between the first measurement and discharge [19.5 (8–28)% vs 13.5(6–18)% p=0.008]. The reduction in sEMGpara%max was coupled with an improvement in FEV_1% predicted [41 (20–62)% vs 46 (34–85)% p=0.02] and VC% predicted [70 (38–79)% vs 74 (45–90)% p=0.033] on discharge.

Conclusion These findings support the hypothesis that NRD measured by sEMGpara%max has potential as a clinical tool to assess changes in ventilatory function in patients with CF following an acute exacerbation.

P102 QUANTITATIVE BIOLOGICAL IMAGING OF PLASMID DNA IN LIVE HUMAN AIRWAY EPITHELIAL CELLS FOLLOWING NON-VIRAL GENE TRANSFER

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We are interested in non-viral gene therapy for cystic fibrosis (CF). It is widely accepted that in addition to extracellular barriers responsible for inefficient uptake, there are key intracellular obstacles to the nuclear delivery of the therapeutic plasmid DNA (pDNA). Thus, we are investigating the intracellular fate of pDNA following transfection, using the clinically relevant cationic Genzyme Lipid (GL) 67 formulation, using three-dimensional Spinning-Disk real-time confocal, combined with transmission electron microscopy (TEM) to track, quantitate and provide high resolution 'snapshots' of pDNA at the single molecule level in transfected primaryhuman airway epithelial cells (AECs) grown at the air–liquid interface (hALI). The pDNA was tagged with fluorescent, photostable semiconductor quantum dots (Qdot-pDNA) or 1.4 nm gold nanoparticles (Au-pDNA) for use in fluorescence or TEM studies, respectively. Both confocal microscopy and TEM experiments demonstrate that Lipid GL67 was able to transfect AECs with Qdot- and Au-pDNA. The number of gold spots in the nuclei of Au-pDNA-transfected AECs compared with those in unconjugated-pDNA-transfected control cells was significantly higher ($p<0.05$, n=5 independent experiments). Approximately 50% of the total internalised pDNA localised to nuclei within 1 h post-transfection in both confocal (123 AECs, eight independent experiments) and TEM (40 AECs, five independent experiments) studies. Thus, within 1 h pDNA is equally distributed between the cytoplasm and the nucleus in well differentiated human ALIs following non-viral-based gene transfer. Experiments are now underway to track the intracellular trafficking of the pDNA at earlier time points.

P103 ORAL CONTRACEPTIVE USE DOES NOT AFFECT CF DISEASE SEVERITY

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Several studies using a variety of in vitro models indicate that sex hormones such as oestrogen can alter ion transport across epithelial cells by either directly affecting CFTR or altering the activity of alternative chloride channels; such effects may in part explain the gender-difference in disease severity observed in some studies. However, published data are inconsistent with several studies postulating beneficial and others detrimental effects of oestrogen on CF ion transport abnormalities. A large proportion of women with CF regularly use oral contraceptives (OC), but the effect of OC use on disease severity has not been systematically studied. Here, we assessed the effects of OC use in a retrospective study. The data included annual follow-up information from 681 women born between 1937 and 1992 of whom 42% have taken OC for varying periods of time. Data regarding OC use is currently available from 1981 to 2010. We performed an *inter-patient* analysis comparing average yearly changes in FEV_1% and body mass index (BMI) and total days of intravenous (IV) antibiotic use over a 5-year period between matched cohorts of OC users (n=57), (median age at start of study period: 23 (16–45), median FEV_1% at start of study period: 56.2 (20.4–111.1)), and OC non-users (n=57) (median age at start of study period: 22 (17–44), median FEV_1% at start of study period: 48.4 (12.8–119.6)). We found no differences between the groups (median change in FEV_1%: users: −1.87 (−11.5 to 10.4), non-users: −1.03 (−11.8 to 17.9); median change in BMI: users: 0.051 (−1.1 to 1.6), non-users: −0.065 (−1.5 to 3.3); median total days on antibiotics: users: 49 (0–308), non-users: 42 (0–378)). We next performed an *intra-patient* analysis of the same outcomes over a 3-year period on and a 3-year period off OC in the same patient (n=23–27), but again did not detect any differences in any of the clinical outcomes studied. In conclusion, OC use in CF females did not affect FEV_1%, BMI or intravenous antibiotic usage in this study; our findings suggest that there is no evidence of a clinically significant effect on CF outcomes.