93* Hypertonic saline: effect on mucus rheology and spirometry

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We studied the effect of NaCl 7% (HS) on sputum rheology and lung function in stable CF patients.
Measurements (T0) of mucus rheology (Elasticity G′, Viscosity G″), FEV_1 and FVC were done in 36 patients. Patients with a decrease in FEV_1 of 8% after HS were enrolled in the control group. 10 control (20±10 y) and 21 study patients (23±8 y) were included. FEV_1 was 76±21% and 62±22%, FVC 95±11% and 82±17% ($p = 0.04$) in the control and the HS group respectively.
At T1 after one inhalation with HS, measurements were repeated. The HS group was treated with 4 ml HS twice daily, the control group with 4 ml NaCl 0.9% (NS). After 4 weeks (T2) measurements were repeated.
A single inhaled dose of HS reduced mucus visco-elasticity in 78% of the patients. Mean decrease of elasticity and viscosity was 52±23% and 44±22% respectively ($p < 0.001$). FVC and FEV_1 decreased with respectively 7% (CI 4.1 to 10.5, $p < 0.001$) and 6.5% (CI 3.9 tot 8.4, $p < 0.001$).
At T2 a decrease in G′ and G″ was measured in 63% of the patients in the HS group and 75% of the NS group: G′ and G″ in the HS group were 50±23% and 48±22% respectively, in the NS group 23.5±15% and 18±15% respectively. On T2 no significant decrease of mucus viscosity and elasticity was observed in the HS group. FVC decreased in 75% of the HS group (3.5%, CI 0.8 to 6.2, $p = 0.015$) and in 71% of the NS patients (2.7%, CI −2.6 to 8.1, $p = 0.24$). FEV_1 decreased in 70% of the HS patients (4.2%, CI 0.6 to 7.7, $p = 0.026$) and in 63% of the NS patients (NS).
A single inhaled dose of HS decreased mucus viscosity and elasticity significantly but had adverse effects on spirometry. After 4 weeks therapy with HS we noticed a trend towards decreased sputum viscosity and elasticity, however a significant decrease in FVC and FEV_1 was observed.

94* β-adrenergic stimulation alters sweat gland potential difference in cystic fibrosis (CF) patients but not healthy controls

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Background: New therapies aiming to overcome the basic CFTR defect are hampered by the lack of a practical, sensitive and reliable in vivo test of CFTR function. We recently described a novel method of measuring the transglandular potential difference (ESPD) in sweat glands following cholinergic stimulation which shows promise as outcome measure in clinical trials.
Method: In this study we compared the effects of cholinergic (pilocarpine 1%) and cholinergic plus β-adrenergic (aminophylline 0.8% and isoproterenol 1%) stimulation on sweat gland function, by measuring: 1) ESPD using an ECG electrode, 2) potential difference in single sweat droplets (SPD), 3) sweat rate and 4) sweat chloride concentration.
Results: Addition of β-adrenergic agonists had no effect on sweat rate or sweat chloride concentration. However, cholinergic plus β-adrenergic stimulation resulted in significant reduction in ESPD and SPD in pancreatic sufficient (CFPS) and insufficient (CFPS) patients, but not in healthy controls or obligate heterozygotes. The Table shows mean difference between paired experiments,±standard error (number of subjects), and student t-test with $p < 0.001$(*).
Conclusion: The exact mechanism for these observations remains to be elucidated. However, ESPD measurements with cholinergic and β-adrenergic agents may be a useful in vivo test of CFTR function.
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	Healthy	Hetero	CFPS	CFPI
ΔSweat rate (μl/min)	0.43±0.24 (10)	−0.25±0.17 (8)	0.34±0.19 (10)	0.13±0.37 (7)
ΔSweat chloride (mmol/L)	0.2±2.1 (10)	1.1±1.8 (8)	0.9±4.2 (8)	−1.6±2.1 (8)
ΔSPD (mV)	−7.9±4.4 (7)	−5.5±5.6 (5)	−14.8±3.8 (8)*	−6.8±6.9 (6)
ΔESPD (mV)	−1.3±2.2 (8)	−0.14±1.8 (8)	−18.3±2.6 (10)*	−20.7±3.7 (8)*

*$p < 0.001$.

95 The effect of N-acetylcysteine on chloride efflux from airway epithelial cells

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Defective chloride (Cl^-) transport in epithelial cells decreases mucus viscosity and leads to recurrent infections and oxidative stress among Cystic Fibrosis (CF) patients. We investigated whether N-acetylcysteine (NAC), a well known mucolytic and antioxidant drug, could also stimulate Cl^- efflux from CF and non-CF epithelial cells.
CF bronchial epithelial cells (CFBE) were treated with 1mM, 5mM, 10mM or 15mM NAC and normal bronchial epithelial cells (16HBE) with 10mM NAC, for 2 h at 37°C.
MQAE fluorescence assay: Cells were loaded with the fluorescent probe MQAE for 2 h prior to analysis. Cover slips were placed as bottom in a perfusion chamber on the stage of an inverted microscope. The effect of NAC on Cl^- transport was measured by exposure to a Cl^- free buffer.
X-ray microanalysis (XRMA) of the intracellular elemental content: The CFBE and 16HBE cells were seeded on titanium mesh grids, treated with NAC as described above, frozen and freeze dried. XRMA of the intracellular elemental content was performed in a Hitachi H7100 electron microscope at 100 kV accelerating voltage. Cl^- efflux from CFBE cells was stimulated by NAC in a dose-dependent manner. 10mM NAC caused a significant increase in Cl^- efflux with nearly 80%. This corresponded to about 40% of the efflux in 16HBE cells. Moreover, the intracellular Cl^- concentration in CFBE cells was significantly decreased up to 60% after 2 h treatment with 10mM of NAC. NAC did not affect Cl^- efflux from 16HBE cells.
The stimulation of Cl^- efflux in CF airway epithelial cells induced by NAC could improve hydration of the mucus and might be beneficial for the treatment of CF patients.

96 Preliminary results of oxidative status change in cystic fibrosis (CF) and oral addition with cysteine

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Oxidative status has a role in the progressive lung damage in CF. Glutathione is a defence from pro-antioxidant agents and it is reduced in CF. Cysteine is the amino-acid that gives to glutathione the antioxidant status.
The objective of this study is to reduce the oxidative status in CF with a daily oral addition of whey protein isolate with high content of cysteine.
Oxidative status is estimated on a blood sample with d-ROMs test and BAP test that can measure oxidative stress and antioxidant status respectively. Patients will be checked every three months. We recruited 32 patients still now.
All cases show a pathological condition of oxidative status. Oxidative stress is increased in all patients and in the 52% of cases is very serious. Antioxidant status is normal in the 46% of cases and the 14% show a high deficiency. Five patients deserted the study for a bad compliance to the administration of cysteine.
In 9 compliant patients we have done the first control after three months from the recruitment. No adverse effect has been reported. All these cases show an improved oxidative status. Oxidative stress has become normal in one patient. Antioxidant status has become normal in 5 cases. Respiratory and nutritional conditions are stable in 5 cases and improved in 4. Collected data confirm a high level of oxidative status in CF. Oral addition of cysteine seems efficacious to improve the oxidative status. Oxidative status improvement could correlate to a clinical improvement. These observations coming from preliminary data must be confirmed. We think useful to continue the valuation of the efficacy of oral addition of cysteine and we consider antioxidant therapy potentially important in CF.