Saliva secretion in F508del mice: contribution of adrenergic and cholinergic pathways

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Aim

This work aimed at dissecting the contributions of cholinergic and β-adrenergic pathways in the regulation of saliva secretion in CF mice.

Methods

Female F508del mice (FVB/129 genetic background) were compared to wild-type (WT) and to heterozygous congeneric mice (n = 5 for each group). Animals, aged 7-11 weeks and fasting for one day, were anesthetized by ip injection of 100µl/10g body weight of a solution of 0.5mg/ml midazolam and 10mg/ml ketamine. Saliva was collected on strips of filter paper weighed before and after collection and placed on the inner face of the stimulated cheek. Saliva secretion flow, expressed as total secreted mass by duration of collection by animal body weight, was assessed in basal conditions, after blocking the cholinergic pathway with 10^{-3} M atropine, and after stimulation with 10^{-4} M isoprenaline, a β-adrenergic agonist.

Results

Saliva secretion flow in basal conditions did not significantly vary with genotype. As expected, isoprenaline response was nearly null in F508del as compared to WT mice (median 3.2 vs 27.9 µg/min/g; $p<0.02$); intermediate values were found in heterozygous mice (28.3 µg/min/g; $p<0.02$). Surprisingly, atropine response was increased in F508del mice with median secretion flow twice as low in F508del than in WT mice (4.8 vs 8.5 µg/min/g; $p<0.04$). Again, intermediate median values were found in heterozygous mice (7.6 µg/min/g; $p<0.04$).

Discussion and conclusion

Saliva secretion test in mice is a noninvasive test to study *in vivo* CFTR function, to dissect the contribution of cholinergic and β-adrenergic pathways, and to evaluate the potential of new drug therapies in CF. Our data confirm that the cholinergic pathway predominates in the nervous control of secretion, and that, in CF the β-adrenergic pathway is refractory to stimulation by an agonist agent. The increased response to atropine in CF could suggest either an increased activity of the cholinergic pathway, or complex interactions between the two pathways.