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Longitudinal SF_6 multiple breath washout testing in children aged 0-4 years with cystic fibrosis

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INTRODUCTION

Lung clearance index (LCI) from multiple breath washout (MBW) is a feasible (1) and sensitive outcome to assess lung function impairment in children with cystic fibrosis (CF) (2). After the implementation of newborn screening for CF in May 2016, we gradually implemented regular SF_6MBW testing in these children.

AIM

To describe the occurrence and pattern of lung function impairment in CF infants diagnosed with newborn screening

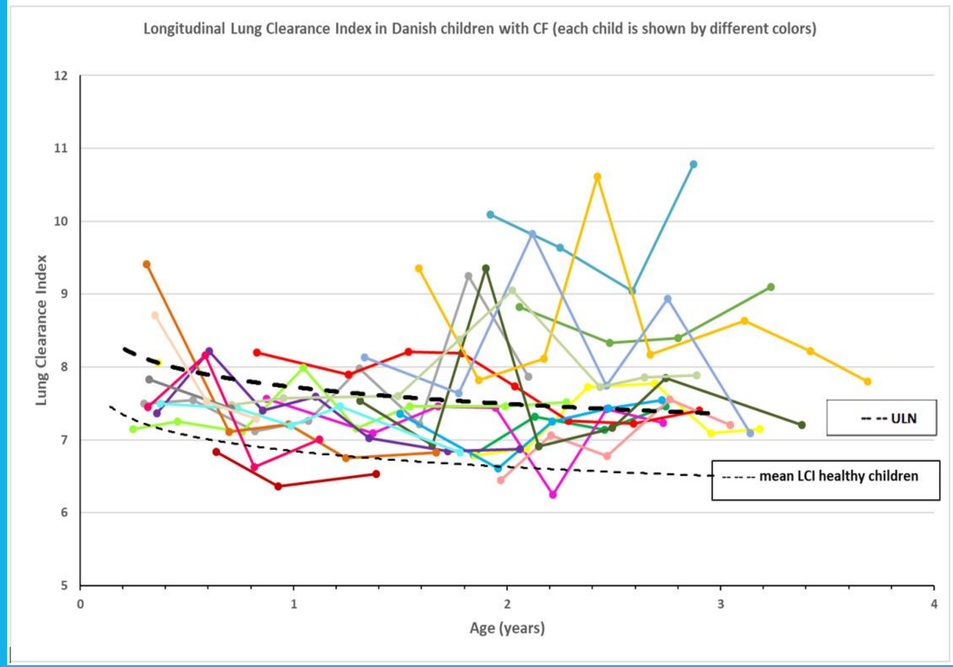
METHOD

SF_6MBW (Exhalyzer® D, ECO MEDICS AG, set 1, Rüsch face mask #1 or #2) was performed quarterly during sleep induced by intranasal dexmedetomidine (3) in children with CF aged 2-45 months followed at CF Center Copenhagen, Denmark. Cross-sectional data from 196 Swedish and Danish healthy infants aged 2-36 months served to predicted mean and upper limit of normal for LCI. Tests were only performed in children without clinical signs of acute upper or lower airway infection (increased cough, fever, or severe rhinitis)

RESULTS

Multiple breath washouts

- Median (range) number of test occasions per child with CF was 5 (1-8)
- MBW sessions in total N = 120



Children with cystic fibrosis

- N = 22, 64% ΔF508 homozygote, 27% ΔF508 heterozygote, 9% others

Treatments

- Pulmozyme® from median (range) age 33 days (16-239)
- Orkambi® from median (range) age 2.3 years (2.1-2.9)
- Antibiotics for CF pathogens found in monthly routine laryngeal suction samples

MBW results

- Eight (36%) children with CF had normal LCI on all occasions, while 9 (41%) children had abnormal LCI in >50% of test occasions and of these, 3 had abnormal LCI on all occasions.
- A linear mixed model analysis demonstrated an annual increase in LCI of 0.22 units/year (p=0.048).

Age groups, months	Cystic fibrosis LCI median (range)	Healthy LCI as-ULN (N)	Cystic fibrosis LCI > as-ULN, N/total test occasions (%)	Cystic fibrosis FRC, mL median (range)	Healthy FRC, mL median (range)
2-6	7.5 (7.1-9.4)	8.3 (24)	5/30 (17%)	106.8 (85.1-124.3)	113.4 (71.3-195.2)
6-12	7.4 (6.4-8.2)	7.7 (90)		173.2 (116.6-235.3)	165.8 (83.3-266.8)
12-18	7.5 (6.5-8.1)	7.5 (53)	16/39 (41%)	209.7 (147.3-276.4)	198.4 (143.0-276.8)
18-24	7.5 (6.5-10.1)	7.5 (15)		251.3 (170.5-339.9)	243.5 (193.3-338.9)
>24	7.6 (6.3-10.8)	7.7 (13)	26/51 (51%)	301.3 (197.4-441.8)	273.7 (251.3-413.5)

Table 1. Presenting LCI and FRC in children with CF alongside reference values derived from age-matched healthy controls (N total =196). Age specific upper limits of normal (as-ULN) were calculated as age-specific means + 1.96*SD.

CONCLUSIONS

Longitudinal SF_6MBW in infants with CF diagnosed by newborn screening demonstrated intermittent lung function impairment in the majority, but also a definite overall gradual worsening. The abnormal trend in the development of LCI calls for an even earlier start of potential effective treatments such as inhaled hypertonic saline and/or CFTR-modulators.

REFERENCES

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