Pattern of Respiratory Pathogen Nasal Colonization in the first year of life in Healthy Infants and Infants with Cystic Fibrosis

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Background

- Respiratory infections play a major role in morbidity and mortality, especially in early childhood and infancy
- PCR analysis of nasal swab material is an established diagnostic method in healthy infants
- However, little is known about pathogen colonization in infants with chronic respiratory diseases like cystic fibrosis (CF)

Aims:

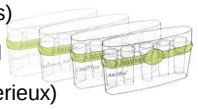
1. To investigate feasibility and quality of parental collected nasal swab material for respiratory diagnostics
2. To analyze possible differences in viral colonization in healthy infants and compare it to infants with CF

Methods

- 31 infants with Cystic Fibrosis from the SCILD* Cohort; 32 unselected, healthy infants from the BILD** Cohort
- Followed prospectively from the age of 6 weeks to 12 months

* SCILD (Swiss cystic fibrosis infant lung development cohort); **BILD (Bern Basel infant lung development cohort)

- Biweekly nasal FLOQSwabs™ (n=1398), placed in viral transport media, were collected by parents (after instruction by study nurses)
- Nucleic acids were extracted (NucliSENS® easyMAG® (bioMérieux, Marcy l'Etoile, France) from 400 µl of sample and eluted in 100 µl
- RNA and DNA analyzed by real-time PCR (combination of 7 duplex Respiratory Multi Well System r-gene® assays, ARGENE®, bioMerieux)
- Sample quality check: HPRT1 cellular gene control (CC) assay (evaluating the quantity of human epithelial cells in the sample) (ARGENE®, bioMerieux)



Results

- Cellular gene control CC was positive in 93% of the samples (1294/1398)
- 98% and 87% were positive in healthy and CF infant groups, respectively
- No difference for:

  - Semiquantitative analysis of positive CC
  - Analyses of the CT values (with and without inclusion of low quality swabs)

- Viral colonization was similar in healthy (43%) and CF infants (42%)
- HRV* was the most frequent virus (healthy: 57% and CF: 46%)
- PIV* was more frequent in healthy infants (11%) than CF (6%); p = 0.038
- hBoV* was less frequent in healthy infants (6 %) than CF (23%); p < 0.001

* HRV (human Rhinovirus), PIV (Parainfluenza Virus), hBoV (Bocavirus)

Viral colonization in healthy infants and infants with CF

samples	positive samples* (%)		positive samples accompanied with symptoms** (%)	
	CF	healthy	CF	healthy
any virus	238 (41)	312 (43)	88 (37)	155 (50)
> 1 virus	53 (9)	46 (6)	16 (30)	28 (61)
Human Rhinovirus	110 (19)	179 (25)	35 (42)	75 (52)
Human Coronavirus	42 (7)	52 (7)	8 (26)	10 (28)
Adenovirus	28 (5)	43 (6)	4 (57)	10 (40)
Parainfluenza Virus	15 (3)	35 (5)	5 (63)	14 (64)
Bocavirus	56 (10)	18 (3)	9 (48)	4 (36)
Respiratory Syncytial Virus	21 (4)	17 (2)	7 (41)	8 (53)
human Parechovirus	8 (1)	8 (1)	0 (0)	2 (40)
Human Metapneumovirus	5 (1)	5 (0.5)	2 (50)	2 (67)
Mycoplasma pneumoniae	9 (1)	4 (0.5)	2(29)	1 (33)
Influenza B	2 (0.5)	2 (0)	0 (0)	0 (0)
Influenza A	0 (0)	1 (0)	0	1 (100)
Chlamydia pneumoniae	1 (0)	0 (0)	0 (0)	0 (0)

Table 1: Infants with CF (n=31, samples n=576); healthy infants (n=32, samples=718), total number of samples (%), Coinfections are excluded if investigated symptomatic samples

*nasal swab with viral colonization irrespective of symptoms, **nasal swab with viral colonization and respiratory symptoms

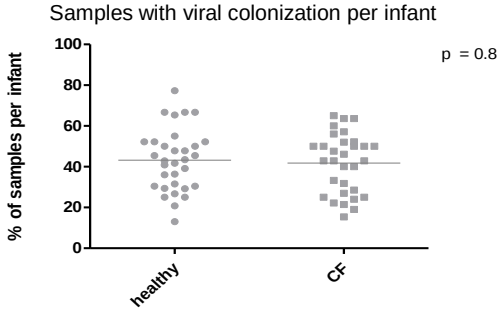


Figure 1: overall viral colonization per infant per year

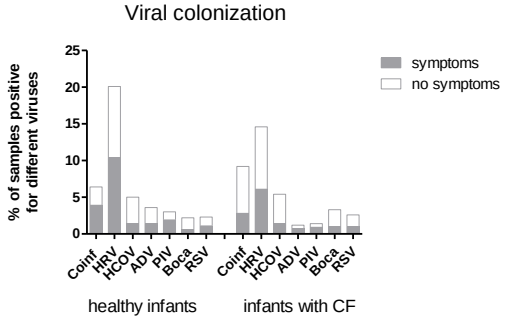


Figure 2: symptomatic and asymptomatic viral colonization(% of samples) in both study groups

Conclusions

This study demonstrated that parental collection of nasal swabs from healthy and CF infants provided easy and adequate material for testing. Although the number of low quality swabs was slightly higher in the CF group, sensitivity analysis showed that this did not bias the results. Possible reasons for lower quality may be more careful swabbing by parents of infants with CF or viscous mucus in the nose. Interestingly, while viral colonization in general was similar in healthy and CF infants, there were clear differences in viral species, a finding of importance for future treatment options and understanding disease development.