

Comparison of biomarkers between allergic rhinitis only and allergic rhinitis with concomitant asthma

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Despite many similarities between allergic rhinitis (AR) and allergic asthma (AA), defined in the ARIA guidelines for an integrated diagnostic and therapeutic approach (1), there are still several differences suggestive of distinct phenotypes within the allergic airways disease (2). This *post hoc* analysis was undertaken to further characterize the differences in biomarkers between patients with AR only and patients with AR and concomitant AA (AR & AA). In addition, the relationship between nasal nitric oxide (nNO) and nasal eosinophils in nasal brushings (NAB) was explored, on the analogy of the lower airways in asthmatic patients (3).

Ten patients with AR-only (four M/six F; age 19–43 years) and 10 with AR & AA (six M/four F; age 20–50 years; using short-acting β_2 -agonists $< 2 \times$ pw only) participated in a biomarker validation study. All patients were clinically stable, nonsmokers and not using controller therapy for > 6 weeks. The following baseline data were collected (at the same time of the day, within 2 h) and compared between the two study groups: serum specific IgE (BsIgE, IU/ml);

Pharmacia, Uppsala, Sweden), skin prick tests with six different allergens [wheal response (mm); ALK Abelló, Nieuwegein, the Netherlands; nNo (ppb); Ecomedics CLD 88 SP, Duernten, Switzerland], biomarkers [ECP (μ g/ml), α_2 -macroglobulin (ng/ml), IgE (IU/ml), MUC5AC (AU/ml)] from nasal lavage (NAL) fluid and percentage eosinophils in NAB (% nonsquamous cells). A Wilcoxon sum rank test was performed for nonparametrical comparison of the allergy-related biomarkers between AR-only and AR & AA. All results were expressed as medians [interquartile range]. The correlation between nNO and NAB-eosinophils in all subjects was tested by the Spearman's rank correlation.

There were no statistical differences between the AR-only group (four M/six F; mean age $\pm$ SD = 25.8 ± 8.1 years) and the AR & AA-group (six M/four F; mean age $\pm$ SD = 25.8 ± 8.8 years) in terms of age ($P = 1.00$) and gender

($P = 0.371$). In the AR-only group, there was a significantly larger wheal response ($P = 0.006$) and a higher BsIgE-level to grass pollen ($P = 0.038$) as compared with AR & AA. In contrast, the AR & AA group had higher HDM-specific BsIgE-levels ($P = 0.049$) and overall more allergies ($P = 0.017$) as compared with the AR-only group. All results are shown in Table 1. Because of a large variability, no statistically significant differences could be found in the local biomarkers in this relatively small sample size. Additionally, no correlation could be demonstrated between nNO and NAB eosinophils ($r = -0.222$, $P = 0.426$).

Despite a small sample size, our data underscore and extend previous evidence from pediatric studies (4, 5), suggesting distinct phenotypes of the allergic airways disease. In addition, in contrast with the previously established correlation between exhaled NO and sputum eosinophils within the lower airways of

Table 1. Baseline biomarkers in AR-only vs AR & AA median [interquartile range]

Parameter	AR-only		AR & AA		P-value
	Median	n	Median	n	
SPT – wheal HDM (mm)	4.5 [4.0–7.0]	7	5.75 [5.0–6.25]	8	0.351
SPT – wheal grass (mm)	7.25 [6.75–8.0]	4	4.75 [4.0–5.0]	8	0.006
SPT – wheal trees (mm)	3 [2.5–4.0]	5	5.5 [5.0–6.0]	5	0.116
Multi-atopy status	3 [2.0–4.0]	10	5 [4.0–6.0]	10	0.017
BsIgE HDM (IU/ml)	5.77 [4.89–25.8]	7	40.25 [20.9–50.9]	8	0.049
BsIgE grass (IU/ml)	21.7 [16.95–39.45]	4	4.74 [1.36–7.38]	8	0.038
BsIgE trees (IU/ml)	2.28 [0.50–4.34]	4	12.02 [3.81–27.1]	4	0.083
NAL ECP (μ g/ml)	7.05 [3.5–12.1]	4	3.55 [2.55–7.8]	8	0.394
NAL α_2 -macroglobulin (ng/ml)	78.75 [37.1–181.9]	10	262.05 [198.3–1083.55]	8	0.076
NAL IgE (IU/ml)	5.25 [4.9–5.48]	10	5.2 [5.0–6.43]	10	0.622
NAL MUC5AC (AU/ml)	42.35 [17.2–61.8]	10	53.1 [21.2–59.4]	10	0.762
NAB eosinophils (%)	1 [1.0–6.0]	9	3 [1.0–34.0]	7	0.216
nNO (ppb)	989.7 [844.5–1346.0]	10	834.5 [719.5–848.9]	9	0.072

AR, allergic rhinitis; AA, allergic asthma; SPT, skin prick test; HDM, house dust mite; NAL, nasal lavage; NAB, nasal brush; nNO, nasal nitric oxide.

AA (3), our data point towards a dissociation between baseline values of nNO and NAB eosinophils. Similarly, Hanazawa et al. (6), could not demonstrate any correlation between nNO and eosinophils in NAL in patients with AR. Hence, our findings warrant prospective studies in larger populations including all phenotypes of the allergic airways disease (AR-only, AR & AA and AA-only). Furthermore, our data implicate that proof of efficacy studies with novel treatments in the nose cannot fully predict the situation within the lower airways, and *vice versa*.

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