Interleukin-6, is it an inflammatory biomarker in asmathatic children with and without respiratory atopy?

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Background

IL-6 is a pleiotropic cytokine that can be produced by many cell types (immune and non immune cells) in response to a wide array of inflammatory stimuli and cytokines. It is becoming evident that IL-6 is not simply a proinflammatory marker, but an active factor that contributes to the pathogenesis of certain inflammatory and autoimmune diseases such as rheumatoid arthritis, and a successful target for some of these diseases.

As a chronic inflammation of the lower respiratory system, asthma expresses several inflammatory markers. The interleukin-6, , was recently well identified as a potential biomarker in several immune pathologies, including adult asthma. However, the involvement of IL-6 in asthma, especially its pediatric form, remains unclear.

Objective

This work aimed to evaluate the variation of IL-6 plasma levels in asthmatic children with different degrees of severity, and with and without respiratory atopy, in order to investigate the potential use of IL-6 as an inflammatory biomarker in pediatric asthma.

Patients and Methods

1. Study cohort

This prospective observational case-control study included 32 asthmatic children aged 5-15 years (mean age(SD) 7.72(3.07)) and 30 age matched Healthy controls. The demographic and clinical characteristics of the study cohort are summerized in **fig.1** and **Table 1**

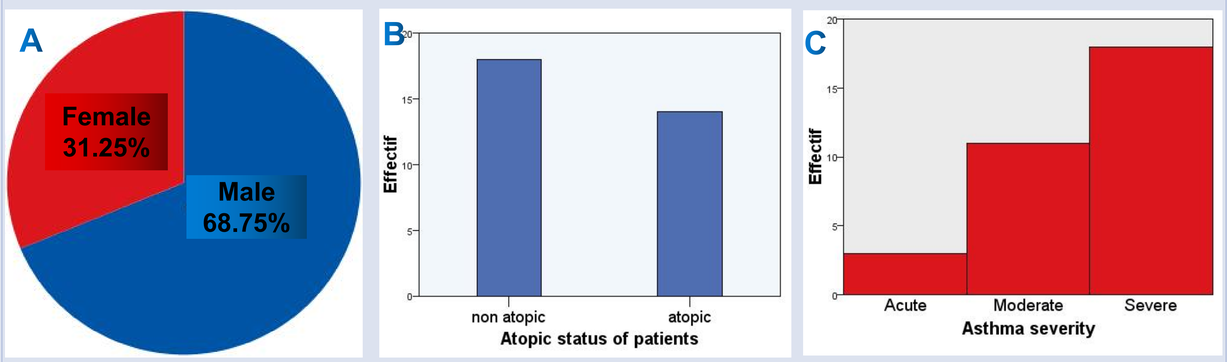

Fig.1 Demografic and clinical characteristics of asthmatic children. (A) Sexe poucentages of the study cohorte. **(B)** Atopic and non atopic patients effectifs. **(C)** Acute, moderate and severe asthma patients effectifs

Table 1. Demographic and clinical characteristics of patients

	Asthmatic children (N=32)			
	All patients N=32	Mild n= 3 (9.4 %)	Moderate n=11 (34.4%)	Severe n= 18 (56.2%)
Age (years)	7.72(3.07)	6.67(5.69)	7.27(2.83)	7.81(2.79)
Sexe				
Male	22/32(68.75%)	2/3(66.67)	7/11(63.6)	5/18(27.78)
Female	10/32(31.25%))	1/3(33.33%)	4/11(36.4)	13/18(72,22)
Sex-ratio	22/10(2.2)			
sIgE plasma levels (UI/ml)	14/32(43.75%)	2/3(66.67)	6/11(18,38%)	6/18(33.37)
sIgE+	18/32(56.25%)	1/3(33.33%)	9/11(81.62%)	12/18(66.67)
sIgE-				

Data are expressed as mean ± SD or n/N (%), where N is the total number of patients with available data

2. IL-6 plasma levels measurement

About 4 ml of heparinized total peripheral blood was collected from each participant. Plasma was immediately separated and plasma levels of IL-6 were quantified during the 3 hours right after sampling by chemiluminescence

Results

Our analysis, showed no significant difference between patients' IL-6 plasma levels compared to controls (Table 2, **Fig 2A**); between the 3 groups of asthmatic children: acute , moderate, and severe; and between sIgE+ patients and the sIgE- group.

Table 2. IL-6 plasma levels in patients and healthy controls

	Healthy controls N=30	All patients N=32	P	Mild asthma group n=4	Moderate asthma group n=10	Severe asthma group n=18	P	sIgE+ group n= 14	sIgE- group n=18	P
IL-6 plasma level (pg/ml)	0(0-4.3)	0(0-1200)	**0 .13**	2(0-57.7)	2.21(0-1200)	0(0-834)	**0.053**	0(0-1200)	0(0-834)	**0.18**

Data are presented as medians and interquartile ranges. P-values comparing patients to healthy controls, and sIgE+ patients to sIgE- are from independent groups' Mann-Whitney U-test. P value comparing the 3 asthma severity groups mild, moderate, and severe is from the Kruskal-Walis' test.

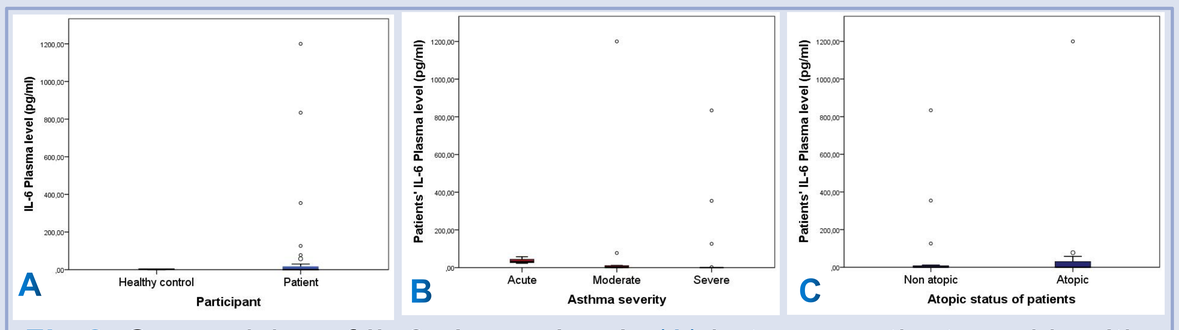

Fig 2. Comparision of IL-6 plasma levels (A) between patients and healthy controls; **(B)** between the three groups : acute, moderate and severe asthma; (C) between sIgE+ group (atopic) and sIgE- group (non atopic)

Discussion

Our analysis showed no variation in IL-6 plasma levels in children with asthma regardless their atopic status and disease severity. It has been demonstrated that corticosteroid therapy can repress IL-6 secretion by reducing IL-6 mRNA integrity **[1],[2]**. So,we suggest that these outcomes may be the consequence of the repressive effect on IL-6 expression. These data are in contrast to the results of Peters et al that indicated an increase in baseline circulating interleukin-6 (IL-6) levels of 1pg/ul in severe asthma patients [**3**]. Furthermore, Jevinkar et al have demonstrated a positive correlation between elevated IL-6 levels and the risk of asthma exacerbations [**4**].

Conclusion

This work indicated no important variation in plasma IL-6 levels in children with asthma despite their atopic status and disease severity. These outcomes are not concluant on the possibility of using IL-6 plasma level as a reliable systemnic inflammatory biomarker. . We suppose that another study on an indentical cohort who went through a one-month therapeutic break may be at the origin of more representative and concluant results about the variation of IL-6 secretion in pediatric asthma .

References

[1] Jevnikar Z, Östling J, Ax E, Calvén J, Thörn K, Israelsson E, et al. Epithelial IL-6 trans-signaling defines a new asthma phenotype with increased airway inflammation. Journal of Allergy and Clinical Immunology. 2019 Feb 1;143(2):577–90.

[2]Quante T, Yee CN, Ramsay EE, Henness S, Allen JC, Parmentier J, et al. Corticosteroids Reduce IL-6 in ASM Cells via Up-Regulation of MKP-1. https://doi.org/101165/rcmb2007-0014OC [Internet]. 2012 Dec 20 [cited 2024 Oct 12];39(2):208–17. Available from: www.atsjournals.org

[3]Peters MC, McGrath KW, Hawkins GA, Hastie AT, Levy BD, Israel E, et al. Plasma interleukin-6 concentrations, metabolic dysfunction, and asthma severity: a cross-sectional analysis of two cohorts. Lancet Respir Med. 2016 Jul 1;4(7):574–84.

[4] Jevnikar Z, Östling J, Ax E, Calvén J, Thörn K, Israelsson E, et al. Epithelial IL-6 trans-signaling defines a new asthma phenotype with increased airway inflammation. Journal of Allergy and Clinical Immunology. 2019 Feb 1;143(2):577–90.