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sRAGE et asthme : une étude prospective sur 68 enfants âgés de 7 ans

Julie Magnier

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UFR DE MÉDECINE
ET DES PROFESSIONS PARAMÉDICALES
Université Clermont Auvergne

N°

UNIVERSITÉ CLERMONT AUVERGNE

UFR DE MÉDECINE ET DES PROFESSIONS PARAMÉDICALES

THÈSE D'EXERCICE

Pour le

DIPLÔME D'ÉTAT DE DOCTEUR EN MÉDECINE

Par

MAGNIER Julie

Présentée et soutenue publiquement le 23 octobre 2020

TITRE DE LA THÈSE

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LISTES DES ABREVIATIONS

AGEs : advanced glycation end products

AAI : airway inflammation

ARDS : acute respiratory distress syndrome

BAL : broncho alveolar lavage

FeNO : fraction of exhaled nitric oxide

FEF : forced expiratory flow

FEV1 : Forced expiratory volume in 1 second

FVC : forced vital capacity

HMGB1: high mobility group box 1 protein

PEF : peak expiratory flow

MEF : maximum expiratory flow

MMEF : maximum mid-expiratory flow

mRAGE: membrane receptor for advanced glycation end products

Rint : Interrupter resistance

sRAGE: soluble receptor for advanced glycation end products

sRAGE and asthma: A prospective study in 68 children aged 7 years

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ABSTRACT

BACKGROUND: Asthma is a chronic inflammatory disease of the airways common in children. In severe cases it can lead to chronic bronchitis in adulthood. The soluble receptor for advanced glycation end products (sRAGE) is a biomarker of lung injury. Its assay has a prognostic value in acute respiratory distress syndrome (ARDS) and could be useful in asthma. Few studies are currently available in children.

MATERIALS AND METHODS: We conducted a prospective, observational, analytical study at Clermont-Ferrand University Hospital. Our main objective was to measure serum sRAGE levels in asthmatic and healthy children aged 7 years.

RESULTS: Of the 68 children assessed, 15 (22.05%) presented asthma. All presented normal respiratory function. The mean plasma sRAGE level was 1875 pg/mL (SD = 472) in asthmatic children and 1794 pg/mL (SD = 418) in healthy children ($p = 0.525$). Mean plasma sRAGE level was significantly decreased with tobacco exposure during pregnancy: 1478 pg/mL (SD = 296) versus 1870 pg/mL (SD = 422). Lower levels were observed in children living in apartments (1557 pg/mL) than in those living in houses (1863 pg/mL) ($p = 0.031$).

CONCLUSION: No difference was observed in serum sRAGE levels in asthmatic children in our population. Most were well treated and controlled. The use of inhaled corticosteroids at an efficient dose may have normalized serum sRAGE levels in this population. Environmental exposure could have an impact on its levels. Further studies are needed, and concomitant assessment in broncho-alveolar lavage fluid and serum could help to better understand its role.

KEYWORDS: sRAGE Biomarker Asthma Tobacco Children

INTRODUCTION

Asthma is a chronic inflammatory disease of the airways associated with airway wall remodeling.

It is important to evaluate inflammatory status, especially in severe cases, to adapt therapeutics. Currently, the main methods to evaluate airway inflammation include sputum analysis, exhaled breath condensate, and fraction of exhaled nitric oxide (FeNO).[1]

RAGE is a receptor abundantly expressed in the lungs, particularly in alveolar epithelial type I cells.[2,3] It is an important mediator in allergic airway inflammation (AAI) and asthma. RAGE is a protein of the immunoglobulin superfamily.[4] It is found in the body in two main forms: membrane-bound RAGE (mRAGE) and soluble RAGE (sRAGE).[5] Three domains make up the membrane-bound RAGE: an extracellular domain for the recognition and linking of RAGE ligands, a hydrophobic transmembrane domain, and a cytoplasmic domain for intracellular signaling. The best studied ligands are advanced glycation end products (AGEs), high mobility group box 1 protein (HMGB1), proteins from the S100 family, and beta-amyloid peptides.[6] Soluble RAGE contains only the extracellular domain of mRAGE. It is a product of either alternative splicing events[5,7] or the proteolytic cleavage of mRAGE[8] by ADAM10 or matrix metalloproteinase 9.[9,10] It can bind ligands but cannot transduce signals intracellularly, making it a decoy receptor that sequesters RAGE ligands and prevents inflammatory responses[11] (Figure 1[12]).

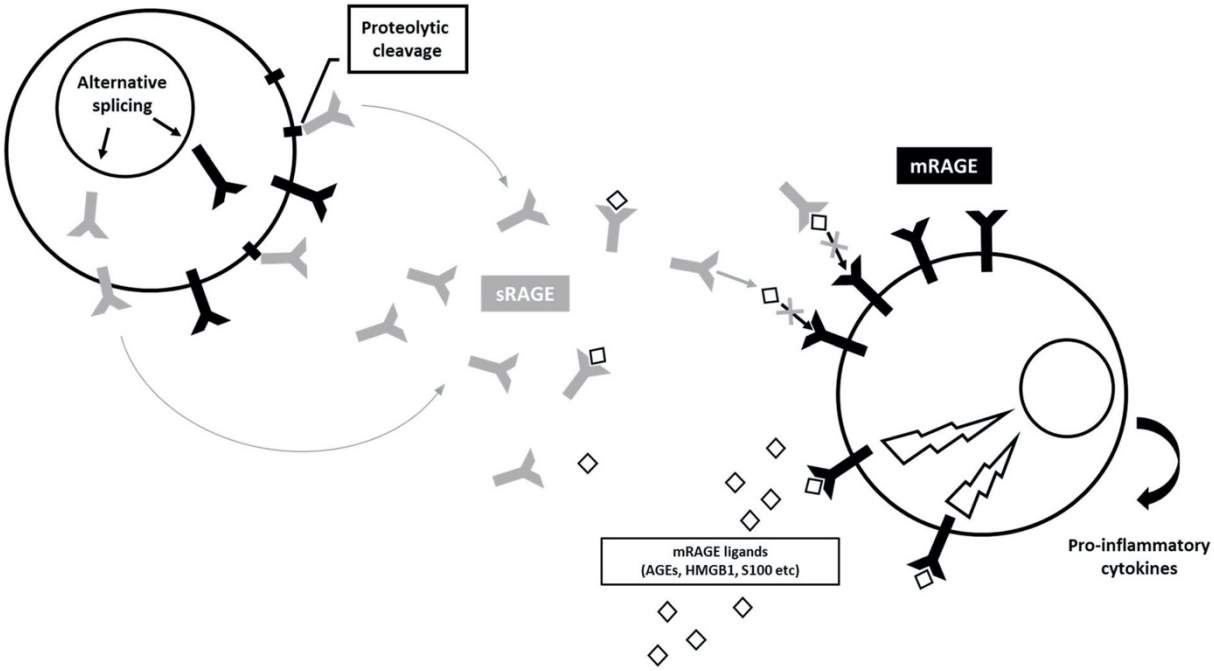

Figure 1. sRAGE arises by alternative splicing mechanisms or through proteolytic cleavage. sRAGE includes the extracellular domain of mRAGE. In the extracellular compartment, sRAGE acts as a decoy by capturing mRAGE receptor ligands and blocking its pro-inflammatory signal

Several human studies argue that sRAGE is a marker of pulmonary damage processes. In both adults and children, plasma sRAGE is associated with severity and prognosis of ARDS.[13,14] As asthma is an inflammatory disease, RAGE and its soluble form might be expected to play a role in its pathogenesis. A study in mouse RAGE knockouts demonstrated that the absence of RAGE abolished most of the typical pathological indicators of asthma, including airway hypersensitivity, eosinophilic inflammation and airway remodeling, suggesting that RAGE might be a principal mediator of asthma pathogenesis.[15] Few studies are available and the correlation between serum sRAGE levels in young children with recurrent wheezing and its severity is still unclear.[16,1] In this study, we assessed serum sRAGE levels in children aged 7 years and evaluated its correlation with asthma.

MATERIALS AND METHOD

STUDY DESIGN

We assessed healthy and asthmatic children from a cohort of children included during an episode of acute bronchiolitis during the 2011-2012 winter epidemic season at the University Hospital of Clermont-Ferrand (Auvergne Rhône-Alpes, France).

ETHICS

All the children and their parents gave written informed consent to take part.

The research protocol for this study was first approved by our institutional review board (*Comité de Protection des Personnes Nord Ouest IV*, France, approval number 2018-A02659-46).

STUDY POPULATION

All children aged 7 years, included prospectively in a cohort during the acute bronchiolitis epidemic season in winter 2011-2012 (at inclusion, were considered all children aged below 1 year presenting at the Pediatric Emergency Department for a first episode of acute bronchiolitis).

Children with bronchopulmonary dysplasia, history of prematurity under 34 weeks, cystic fibrosis, known immune deficiencies, suspected primary ciliary dyskinesia, congenital heart disease, or acute renal failure were excluded from the study.

COLLECTED DATA

CLINICAL DATA

A clinical questionnaire was administered to assess data on respiratory symptoms (day or night cough, discomfort during exercise, use of salbutamol), respiratory treatments (corticosteroid p.o. or inhaled, long-acting bronchodilator), hospitalization for asthma, wheezing outside viral episodes, personal atopy (presence of atopic dermatitis, eczema, rhino-conjunctivitis, food

anaphylaxis from birth), environmental exposure to tobacco smoke (current or during pregnancy), pets, type of housing, daycare attendance and number of siblings.

Sociodemographic data were also collected, including sex, weight, height and precariousness assessed using the EPICES (Assessment of Precariousness and Health Inequalities in Health Examination Centers) questionnaire.[17] A precariousness threshold of 30 was considered.

Data from physical examination including symptoms of asthma, existence of eczema or signs of rhino-conjunctivitis, or chest deformity were also collected.

Asthma was defined according to the frequency of the following symptoms: asthma symptoms (tachypnea, wheezing, expiratory stridor, respiratory chest retraction), doctor-diagnosed wheezes or the use of anti-asthmatic medication. If ≥3 respiratory symptoms were documented ≥2 times, or if any such episode lasted ≥4 weeks, then the subject was classified as suffering from asthma.[18,19]

PULMONARY FUNCTION TESTING

Spirometry was performed using the Jaeger MasterScreen. The spirometer was calibrated each morning using a 3-liter syringe. A nose clip was applied, and the children underwent a forced vital capacity (FVC) test in accordance with American Thoracic Society/ European Thoracic Society 2005 spirometry standards.[20] For each child, we obtained three FVC maneuvers meeting ATS/ERS acceptability criteria. Forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC), the peak expiratory flow (PEF), maximum mid-expiratory flow (MMEF), forced expiratory flow (FEF), maximum expiratory flow (MEF), and maximum expiratory flow at 25%, 50%, and 75% expiratory volume (MEF 25, MEF 50, MEF 75) were measured.

Interrupter resistance (Rint) was measured using a Spiro Dyn apparatus (Spiro Dyn'R, Toulouse) calibrating daily for flow. Rint was measured during a 100 ms occlusion during expiration. During measurements, the child was seated and asked to breathe quietly, connected

to the flowmeter by a mouthpiece. Measurements were made with the child's head held in the neutral position, cheeks and chin held by a physician.

The examinations were performed with and without bronchodilator. For bronchodilator response, 400 µg of salbutamol was inhaled through the spacer device. Fifteen minutes after administration of the drug, each child underwent further spirometry to evaluate bronchodilator response.

Normal pattern was defined by normal FVC and normal FEV_1/FVC ratio. Significant obstructive ventilator disorder was defined by $FEV_1/FVC < 0.8$.
We considered significant reversibility for an increase of 12% in FEV_1 or a decrease of 35% in Rint.

BIOLOGICAL ASSESSMENT

sRAGE levels were measured in duplicate using purpose-designed commercially available ELISA kits (RAGE Quantikine, R&D Systems, Minneapolis, MN) with a manufacturer-stated detection limit of 78 pg/mL. The personnel responsible for performing sRAGE assays had no knowledge of the clinical setting.

Eosinophilia was defined as levels above 0.300 G/L.[21]

Prick tests were carried out by the same trained clinical research nurse to optimize reproducibility. Skin prick tests included histamine and physiological serum as controls, and the main aeroallergens (*Dermatophagoides pteronyssinus, Dermatophagoides farinae, Alternaria*, timothy grass, birch, cats and dogs), and the main trophallergens (egg, peanut, walnut, almond, hazelnut, soy). Papule diameter was measured at 20 minutes. The prick test was considered positive with a diameter equal to or greater than 3 mm, compared to the control.

Sensitization to aeroallergens and trophallergens was confirmed by unitary assay of specific serum IgE by ImmunoCAP (Phadia 250®, Phadia AB, Uppsala, Sweden). ImmunoCap Phadia 250® provides a quantitative result ranging from 0.1 to 100 kUA/L. We took 0.35 kUA/L as the positive threshold. Multi-sensitization was defined if tests (SPT or IgE assay) were positive for at least two allergens.

STATISTICAL ANALYSIS

Statistics were computed using Stata v15 (StataCorp, College Station, Texas, USA). Study sample is described by frequency and percentage for categorical data and by means ± standard deviation for continuous data or by median and interquartile range when data were not normal. Comparisons of sRAGE levels were made using Student's *t*-test for two groups (or ANOVA for three or more groups), or Mann and Whitney's test (or Kruskal-Wallis for three or more groups) when data were not normal. Relationships of sRAGE with continuous data were sought using Pearson's correlation coefficient (or Spearman's when data not normal). All tests were two-sided and a p-value < 5% was considered significant.

RESULTS

Population

In all, 68 children were evaluated at age 7 years. Our sample was composed mainly of boys (63.2%), aged 7.68 ± 0.3 years. Mean body mass index was 15.9 kg/m² (±2.1 SD). Fifty-six children (82.3%) lived in a house. Animals were present at home for 48 (70.6%) of them, cats for 25 (36.8%). Twenty-six children (38.2%) were exposed to tobacco smoking, 10 (14.7%) during pregnancy. Precariousness was suspected by the EPICES score for 7 patients (10.3%).

We found an asthma rate of 22.05% in our population, i.e. in 15 children. Among these 12 (80%) presented persistent asthma since age 3 years and three (20%) developed symptoms at school age. At clinical examination, only one child presented wheezing. None had any chest deformity. All except one used Ventolin (93%) and 11 (73%) followed a background treatment. We noted an atopic family history for 47 patients (69.1%), 17 patients (25 %) presented an atopic dermatitis history, 20 (29.4%) presented respiratory allergic symptoms, and none had a food allergy.

Regarding respiratory functional exploration, none of the children had any obstructive ventilation disorder (FEV_1 104% ± 9.3%, FEV_1/FVC 107% ± 6).We noted reversibility in 29 children (44.6% of our population), observed in five asthmatic patients (35.7%) and 24 of the non-asthmatics (45%), $p = 0.45$.

We highlighted aero sensitization for 16 (20%) children. Eosinophilia was observed for 30 children (44.8%).

sRAGE levels

The main results are reported in Table 1.

Mean levels

The mean plasma sRAGE level was 1812 (± 428 SD) pg/mL at 7 years.

There was no significant difference between plasma sRAGE level according to sex in our population (1842 (±430 SD) pg/mL in girls and 1795 (± 432 SD) pg/mL in boys).

We found no correlation between sRAGE and BMI ($r = 0.17$, $p = 0.17$) or with birth term ($r = -0.08$, $p = 0.53$)

Table I Mean serum sRAGE levels

	Mean serum sRAGE (pg/mL)				
	Yes	*N*	No	*N*	*p*
Asthma 7 years	1875 ± 472	15	1794 ± 418	53	0.525
Patient with inhaled treatment	1893±453	23	1771 ± 414	45	0.271
Personal atopic status					
Aeroallergen sensitization	1908 ± 494	16	1783 ± 406	52	0.309
Eosinophilia	1821± 380	30	1819 ± 465	37	0.981
Environmental exposures					
Tobacco smoking in utero	1478 ± 296	10	1870 ± 422	58	0.007
Passive tobacco smoking	1772 ± 479	26	1837 ± 397	42	0.547
Apartment	1557 ± 372	11	1863 ± 427	56	0.031
Cat	1774 ± 311	25	1834 ± 485	43	0.579

Asthma and atopic status

There was no significant difference in plasma sRAGE levels between asthmatic patients and healthy patients (Figures 2 and 3): 1875 (± 472 SD) pg/mL versus 1794 respectively ($p = 0.525$). sRAGE levels did not differ in patients with significant reversibility (1690 (± 683 SD) versus 1787 ± 381 pg/mL respectively). sRAGE levels were not correlated to eosinophil level

($r = -0.10$, $p = 0.42$), and no difference was observed in eosinophilic versus non-eosinophilic patients (Table 1). In the same way, sRAGE levels did not differ in sensitized versus non-sensitized patients. The same results were observed in the asthmatic population (for aeroallergen sensitization ($p = 0.418$) and eosinophilic status ($p = 1$)).

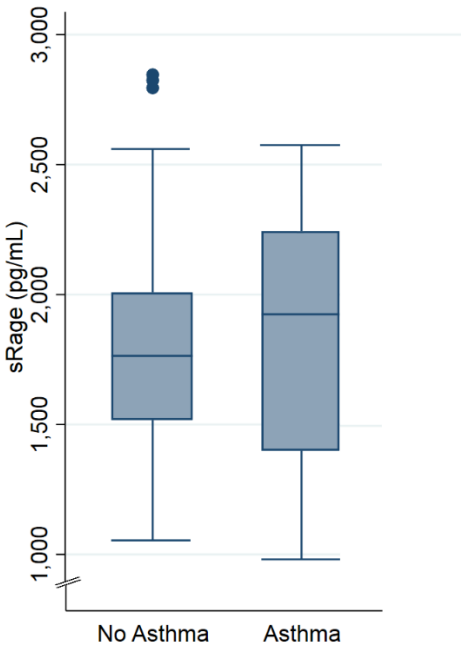

Figure 2. ***Comparison of plasma sRAGE levels in asthmatic and non-asthmatic patients***

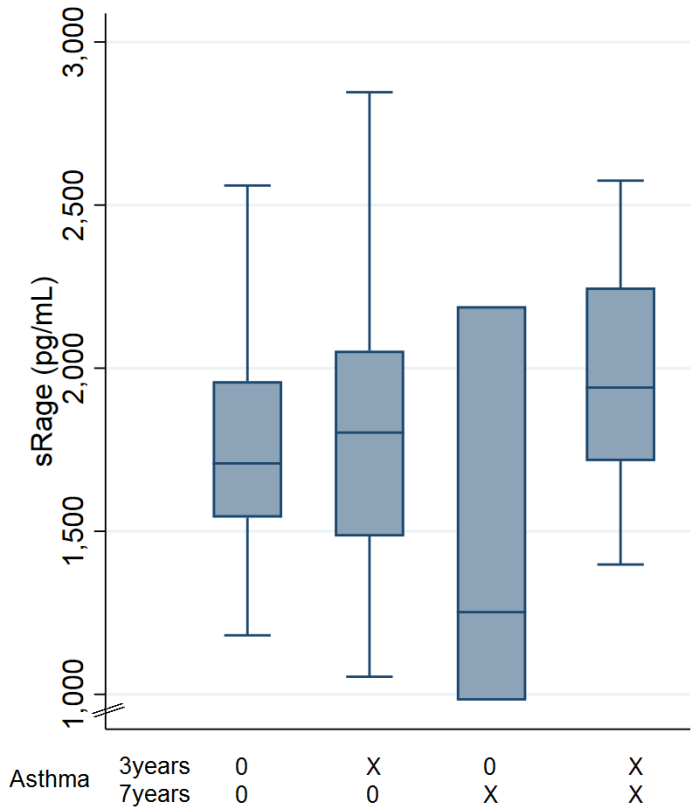

Figure 3. ***sRAGE level according to asthma diagnosis (p = 0.238)***

sRAGE level in pg/mL, − (absence) and × (presence)

Environment

Mean plasma sRAGE levels were significantly decreased in children exposed to tobacco smoking during pregnancy (Table 1). Conversely, current passive tobacco exposure had no impact on its levels ($p = 0.547$). Association of antenatal and current exposure (Figure 4), was associated with decreased levels of SRAGE, but not significantly ($p = 0.053$). In asthmatic patients, sRAGE levels were lowered in children exposed to tobacco during pregnancy (1257± 96 versus 2099 ± 303 pg/mL in none, $p = 0.004$) unlike those exposed to tobacco currently (1686 (± 271 SD) pg/mL versus 1805 (± 388 SD) pg/mL in none, $p = 0.550$).

Lower levels were observed in children living in apartments than in those living in houses (Table 1).

The presence of animals had no impact on sRAGE levels at 7 ($p = 0.322$, especially cats $p = 0.579$).

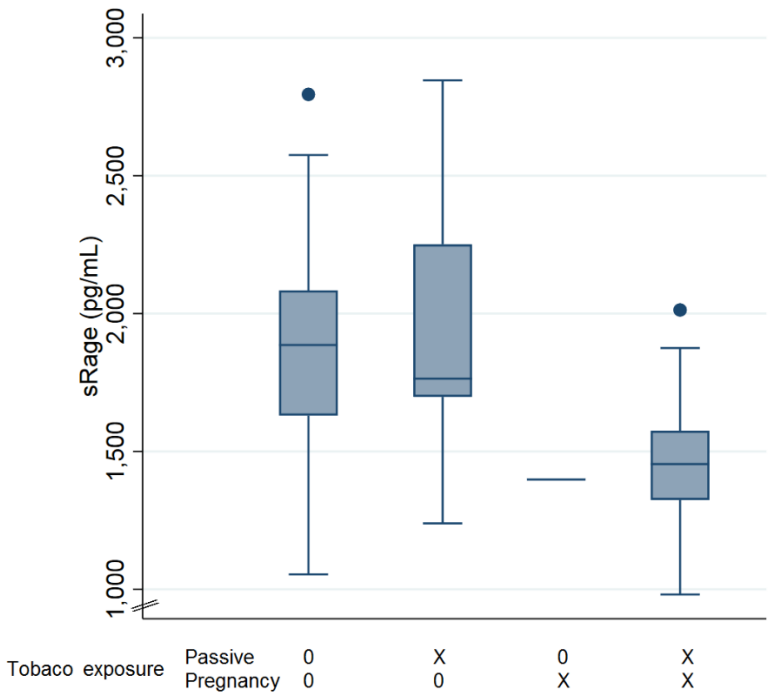

Figure 4. ***sRAGE level according to tobacco exposure (p = 0.053)***

sRAGE level in pg/mL, − (absence) and × (presence)

DISCUSSION

The main objective of this study was to investigate the association between serum sRAGE levels and asthma in children at age 7 years. The study enrolled 68 children: to our knowledge, this is so far the largest cohort of patients in a study of sRAGE levels at age 7 years in healthy children or with asthma.

In children, studies examining the role of sRAGE in the pathogenesis of asthma are limited. Since sRAGE levels have been scantly studied in children, we do not currently have reference values in the literature that are significantly different from adults. The processes of lung maturation and alveolation are thought to explain higher sRAGE levels in infants[3] and we observe a decrement in its levels as alveolation phenomena gradually cease. In our previous study, conducted on infants aged under 1 year, we found a mean serum sRAGE level of 2203 (± 905 SD) pg/mL in the healthy group.[12]. At age 7 years, we observed mean plasma sRAGE level of 1794 (± 418 SD) pg/mL in healthy children. In an adult population[22] the mean plasma sRAGE level significantly decreased compared with 550 pg/mL in controls. However, these observations need to be confirmed given the small number of studies available and the variability in the levels observed.[23,24]

Initially, sRAGE was studied as a marker of lung epithelial injury and alveolar fluid clearance. Several studies showed its utility for evaluating the severity and prognosis of lung injury in acute respiratory distress syndrome (ARDS) in adults and children, with elevated levels. Jabaudon *et al.* provide evidence that alveolar epithelial injury at baseline, as assessed by elevated plasma sRAGE, is an independent variable associated with 90-day mortality in ARDS.[25] In children, sRAGE levels were higher in PARDS non-survivors, correlated with number of non-pulmonary organ failures and associated with mortality in direct lung injury and in immunocompetent children.[26] Median levels observed in these cases were strongly elevated (5000 pg/mL [2600–7200], $p = 0.005$). As sRAGE is more highly expressed in BAL fluid than

in serum[27] (ratio of 4), its serum elevation in ARDS could reflect alveolo-capillary membrane damage with a marked leakage of sRAGE from BAL to serum.

Unlike ARDS, bronchial inflammation seems responsible for decreasing sRAGE levels in adults and pediatric health disorders. Decreased sRAGE plasma levels are associated with increased progression of airflow limitations in COPD patients.[28] In pediatric patients, significant lower sRAGE levels were observed in asthmatic patients and a cut-off value of serum sRAGE levels for asthma diagnosis of 1080.4 pg/mL has been proposed. sRAGE levels could be correlated and used as a severity biomarker, with lowered levels in uncontrolled and severe asthmatic subgroups compared to others.[16] In these conditions, sRAGE could act as a decoy and serve as an anti-inflammatory element to limit the activation of the RAGE cascade. If sRAGE is considered as a "blocker" of the inflammatory cascade, it could be "consumed" by its binding with pro-inflammatory RAGE ligands to control the inflammation and therefore be found in lower quantities in the plasma. Unlike the lesions induced by ARDS, asthma does not reach the alveolo-capillary membrane and we might expect the blood levels to approach the levels found in the BAL fluid with a consumption proportional to that of the inflammation of the airways. Our present study showed sRAGE levels to be conserved in asthmatic patients. This can be explained by the fact that almost all our patients presented controlled asthma, with normal respiratory function, and daily treatment. A well-taken inhaled corticosteroid treatment controls lung inflammation and could therefore normalize serum level of sRAGE. The study of Sukkar *et al*.[29] in clinically stable asthma adult patients demonstrated that the levels could remain relatively stable regardless of the medical therapy used. In addition, the type of inflammation could modify the expected values of sRAGE. Eosinophilic or neutrophilic inflammation may influence sRAGE level.[24] In our study, eosinophilia and sensitization did not impact sRAGE levels, but our asthmatic population was too small to draw any firm conclusion.

Environmental exposure such as to atmospheric pollution and tobacco smoke can cause bronchial inflammation. Decreased sRAGE levels were observed in children living in apartments. We can reasonably assume that this type of housing corresponds to urban living. Exposed to urban pollution, these children may thus have underlying inflammation of the lower airways responsible for sRAGE consumption. The same results were observed with tobacco exposure. Cigarette smoke is known to increase the formation of AGEs and the expression of RAGE.[30] However, the effect of cigarette smoking on sRAGE is inconsistent across the literature. Decreased, elevated, and unchanged levels of sRAGE have been found in different studies, as reviewed by Prasad and colleagues.[31]Mostly confirmed our results, with reduced sRAGE levels. Duration and time of the exposure could be determinant. Recently, Pouwels *et al*.[32] showed that smoking immediately and severely decreased serum sRAGE levels. The time lag between tobacco exposure and blood testing should be taken account. We did not analyze the time lag and intensity of prior smoking exposure in our study, which could be a source of bias. However, *in utero* exposure appeared to impact sRAGE levels more strongly than postnatal exposure. Children with high early-life exposure were more likely than unexposed children to have early transient and persistent asthma and a reduction in FEV1/FVC in adulthood.[33,34] As sRAGE is correlated to alveolation processes, we can expect persistent consequences of tobacco smoking during pregnancy on sRAGE levels in children exposed.

To address the questions raised in this pilot study, a new study is planned on inflammatory biomarkers in serum and BAL fluid in children undergoing endobronchial fibroscopy, to clarify the mechanism of sRAGE anti-inflammatory action and analyze the correlation of its levels in the different fluids.

CONCLUSION

Our study showed no significant difference between the serum levels of sRAGE in healthy and asthmatic children. Most of the asthmatic children were well treated and controlled. By reducing bronchial inflammation, the use of inhaled corticosteroids at an efficient dose may have normalized serum levels of sRAGE in our population. Active airway inflammation was correlated with low sRAGE levels, as shown in children exposed to tobacco smoking and urban pollution. This argues for an anti-inflammatory action by blocking the RAGE inflammatory cascade in the lungs. Further studies are needed, and concomitant assessment in BAL fluid and serum could help to better understand its role.

CONCLUSION

UFR DE MÉDECINE
ET DES PROFESSIONS PARAMÉDICALES
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CONCLUSION

Bien que nos résultats ne montrent pas de différence significative sur les taux sériques de sRAGE entre les enfants sains et asthmatiques, sRAGE semble être un biomarqueur d'inflammation bronchique intéressant y compris chez l'enfant. Les patients asthmatiques de notre population étaient traités et contrôlés expliquant nos résultats. Une nouvelle étude chez l'enfant asthmatique avec évaluation concomitante des taux de sRAGE dans le lavage broncho alvéolaire et sériques devrait nous aider à approfondir l'intérêt du dosage de ce biomarqueur.

Clermont-Ferrand, le 30.9.2020
Pierre CLAVELOU
Doyen - Directeur

Clermont-Ferrand, le 23/09/20
Le Président du Jury,
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SERMENT D'HIPPOCRATE

Au moment d'être admise à exercer la médecine, je promets et je jure d'être fidèle aux lois de l'honneur et de la probité.

Mon premier souci sera de rétablir, de préserver ou de promouvoir la santé dans tous ses éléments, physiques et mentaux, individuels et sociaux.

Je respecterai toutes les personnes, leur autonomie et leur volonté, sans aucune discrimination selon leur état ou leurs convictions. J'interviendrai pour les protéger si elles sont affaiblies, vulnérables ou menacées dans leur intégrité ou leur dignité. Même sous la contrainte, je ne ferai pas usage de mes connaissances contre les lois de l'humanité.

J'informerai les patients des décisions envisagées, de leurs raisons et de leurs conséquences. Je ne tromperai jamais leur confiance et n'exploiterai pas le pouvoir hérité des circonstances pour forcer les consciences.

Je donnerai mes soins à l'indigent et à quiconque me les demandera. Je ne me laisserai pas influencer par la soif du gain ou la recherche de la gloire.

Admise dans l'intimité des personnes, je tairai les secrets qui me seront confiés. Reçue à l'intérieur des maisons, je respecterai les secrets des foyers et ma conduite ne servira pas à corrompre les mœurs.
Je ferai tout pour soulager les souffrances. Je ne prolongerai pas abusivement les agonies. Je ne provoquerai jamais la mort délibérément.

Je préserverai l'indépendance nécessaire à l'accomplissement de ma mission. Je n'entreprendrai rien qui dépasse mes compétences. Je les entretiendrai et les perfectionnerai pour assurer au mieux les services qui me seront demandés.

J'apporterai mon aide à mes confrères ainsi qu'à leurs familles dans l'adversité.

Que les hommes et mes confrères m'accordent leur estime si je suis fidèle à mes promesses ; que je sois déshonorée et méprisée si j'y manque.

MAGNIER, Julie Signature

SERMENT D'HIPPOCRATE

En présence des Maîtres de cette FACULTE et de mes chers CONDISCIPLES, je promets et je jure d'être fidèle aux lois de l'Honneur et de la Probité dans l'exercice de la Médecine.

Je donnerai mes soins gratuits à l'indigent et je n'exigerai jamais un salaire au-dessus de mon travail. Admis dans l'intérieur des maisons, mes yeux ne verront pas ce qui s'y passe, ma langue taira les secrets qui me seront confiés et mon état ne servira pas à corrompre les mœurs ni à favoriser le crime.

Respectueux et reconnaissant envers mes MAÎTRES, je rendrai à leurs enfants l'instruction que j'ai reçue de leurs pères.

Que les HOMMES m'accordent leur estime si je suis fidèle à mes promesses. Que je sois couvert d'OPPROBRE et méprisé de mes confrères si j'y manque.

MAGNIER, Julie Signature

sRAGE et asthme : une étude prospective sur 68 enfants âgés de 7 ans

Résumé :

CONTEXTE L'asthme est une pathologie inflammatoire chronique des voies aériennes fréquente chez l'enfant. Son pronostic à long terme est lié au remodelage bronchique, faisant le lit de la bronchite chronique de l'adulte. L'utilisation de biomarqueurs d'inflammation bronchique semble séduisante dans l'espoir d'évaluer et de traiter au mieux ces jeunes patients. Le récepteur soluble pour les produits finaux de glycation avancée (sRAGE) est un biomarqueur de lésions pulmonaires, avec une valeur diagnostique et pronostique désormais reconnue dans le syndrome de détresse respiratoire aiguë (SDRA) de l'adulte, et semble également impliqué dans la pathogenèse d'autres maladies respiratoires comme l'asthme. Peu d'études sont disponibles actuellement chez l'enfant

OBJECTIF Évaluer le taux de sRAGE sérique chez des enfants asthmatiques et sains à l'âge de 7 ans

METHODE Nous avons mené une étude prospective, observationnelle et analytique au CHU de Clermont-Ferrand dont l'objectif principal était d'évaluer le taux de sRAGE sérique chez des enfants asthmatiques et sains à l'âge de 7 ans

RESULTATS Sur les 68 enfants évalués, 15 (22,05%) étaient asthmatiques à 7 ans. Aucun enfant ne présentait de trouble ventilatoire obstructif. Le taux plasmatique moyen de sRAGE était de 1875 (±472 SD) pg/mL chez les enfants asthmatiques et de 1794 (±418 SD) pg/mL chez les enfants sains p= (0.525).

CONCLUSION Bien que nos résultats ne montrent pas de différence significative sur les taux sériques de sRAGE entre les enfants sains et asthmatiques, sRAGE semble être un biomarqueur d'inflammation bronchique intéressant y compris chez l'enfant. Les patients asthmatiques de notre population étaient traités et contrôlés expliquant nos résultats. Une nouvelle étude chez l'enfant asthmatique avec évaluation concomitante des taux de sRAGE dans le lavage broncho alvéolaire et sériques devrait nous aider à approfondir l'intérêt du dosage de ce biomarqueur.

Mots-clés :

- Asthme
- sRAGE
- Tabac
- Enfant
- Biomarqueur