

Reduced Serum Levels of Innate Immune Molecules in Subjects with Frequent Asthma Exacerbations

ET Gardner, C Sheen, LM Stierman, B Jovanovic, JJ Shannon, CA Saltoun, LC Grammer, RP Schleimer, Feinberg School of Medicine, Northwestern University, Chicago, IL; John H. Stroger, Jr. Hospital of Cook County, Chicago, IL
The research reported on this poster was supported by UO1HL72478 and the Ernest S Bazley Trust to Northwestern University & Northwestern Memorial Hospital



ABSTRACT

Rationale. Innate immune molecules are the first line of defense during encounters with organisms that may lead to infection. Upper respiratory infections are a common cause of exacerbations of asthma. In this study we evaluated whether deficiencies in innate immune molecules, which can lead to an increased incidence of infections, are more prevalent in adults who have higher asthma exacerbation rates. We examined serum levels of mannan binding lectin (MBL), C-reactive protein (CRP) and surfactant protein D (SP-D) in inner city subjects with infrequent and frequent asthma exacerbations.

Methods. Serum samples were obtained from 140 subjects derived from the Chicago Health Initiative to Raise Asthma Health Equity (CHIRAH) study. Subjects were classified as either having a low or high rate of exacerbation based on criteria that included number of hospital admissions, prednisone courses, and ER visits. MBL, CRP and SP-D levels were determined using ELISA assays. Deficiency was defined as less than 100 ng/ml, 300 ng/ml and 370ng/ml for MBL, CRP and SP-D respectively.

Results. Preliminary analysis revealed an increased frequency of MBL deficiency in African-American asthmatics with high exacerbation rates ($p \leq 0.05$). There was no difference in the frequency of CRP or SP-D deficiency in asthmatics who were African-American or in MBL, SP-D or CRP deficiency in asthmatics of other races.

Conclusion. In African-American subjects, deficiency of innate immune molecules may contribute to a higher rate of asthma exacerbations.

BACKGROUND

Asthma is an inflammatory disorder of the airways that is characterized by reversible airway obstruction that can lead to recurrent episodes of wheezing, shortness of breath, chest tightness or cough. Triggers for this obstruction include common allergens and upper respiratory infections both of which can lead to high exacerbation rates and symptoms in individuals with this disease.

The innate immune system is often the first line of defense during encounters with organisms that may lead to infection. This innate resistance is provided by proteins whose levels of expression are determined by genetic factors.

Collectins are among the many molecules that serve as effector proteins of the innate immune system. Mannan binding lectin and surfactant protein D are among eight identified collectins that belong to the super-family of mammalian C type lectins. C-reactive protein is also an important protein that plays a role in innate immunity.

RATIONALE

It is well known that upper respiratory infections are a common cause of exacerbations of obstructive respiratory diseases. It has also been shown that deficiencies in innate immune molecules are associated with increased respiratory symptoms leading to uncontrolled disease. In this study we evaluated whether deficiencies in innate immune molecules, which can be expected to lead to an increased incidence of infections, are more prevalent in adults who have higher exacerbation rates of asthma.

METHODS

- >The study group consisted of adults who were subjects in the CHIRAH study. Subjects were given questionnaires through which an extensive medical history was obtained.
- >Patients who indicated a diagnosis of asthma and were taking an inhaler to treat asthma were classified as either having a low or high rate of exacerbation based on certain criteria.
 - o **High exacerbators:** 1 or more hospital admission for asthma or at least one emergency room visit and two or more courses of prednisone in the past twelve months.
 - o **Low exacerbators:** No hospital admissions or emergency room visits, and no more than one course of prednisone in the past twelve months.
- >Serum was analyzed for MBL, SP-D, and CRP using commercially available enzyme-linked immunosorbent assay kits and following each manufacturer's protocol
- >Deficiency was defined as less than 100 ng/ml, 300 ng/ml and 370ng/ml for MBL, CRP and SP-D respectively. Fisher's exact test was used to compare the two groups which were ultimately further subdivided by race.

RESULTS

DEMOGRAPHICS # OF EXACERBATIONS

| | LOW | HIGH |
|---------------------------------|------|-----------|
| AFRICAN AMERICANS (AA) | | |
| Number of Respondents | 34 | 44 |
| Mean Age (years) | 32.1 | 30.1 |
| Female/Male | 30/4 | 37/7 |
| Sensitization to Dustmite (DM) | 14 | 26 |
| Sensitization to Cockroach (CR) | 15 | 29 |
| Sensitization to DM and CR | 9 | 23 |
| # Hospital Admits (SEM) | 0 | 1.3 (1.8) |
| # ER Visits (SEM) | 0 | 2.6 (2.0) |
| Inhaled Corticosteroids | 20 | 30 |
| FEV1% | 76.6 | 71 |

OTHER RACES

| | | |
|----------------------------|-------|-----------|
| Number of Respondents | 39 | 24 |
| Mean Age (years) | 30.9 | 33.9 |
| Female/Male | 26/13 | 15/8 |
| Sensitization to DM | 18 | 9 |
| Sensitizations to CR | 16 | 8 |
| Sensitization to DM and CR | 12 | 2 |
| # Hospital Admits (SEM) | 0 | 0.69(.87) |
| # ER visits (SEM) | 0 | 2.6 (4.6) |
| Inhaled Corticosteroids | 20 | 19 |
| FEV1% | 91 | 84 |

Figure 1

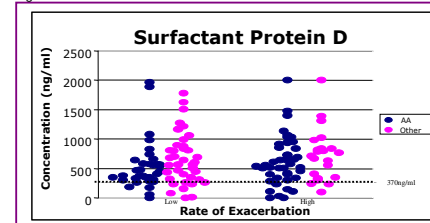


Figure 2

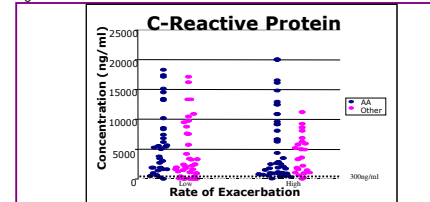


Figure 3

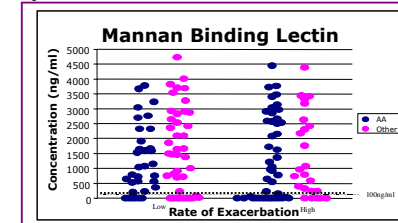
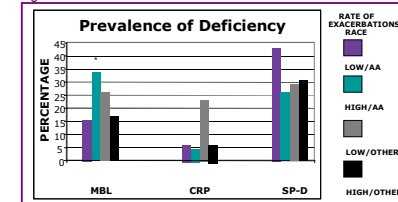


Figure 4



Eighteen of 67 high exacerbation rate subjects were deficient in SP-D, while 26 of 73 low exacerbation rate subjects were deficient in SP-D (Fig.1). We found no difference in the prevalence of SP-D deficiency between the two groups. Four high exacerbation rate subjects were deficient in CRP where as only 11 low exacerbators were CRP deficient (Fig. 2). Again, there was no difference in the prevalence of CRP deficiency between these two groups. Nineteen high exacerbators were MBL deficient and 15 low exacerbators were MBL deficient (Fig. 3). There was no difference in the prevalence of MBL deficiency in these two groups. *However, African-American subjects classified as high exacerbators were more likely to be MBL deficient (15 of 44 subjects) than African-American subjects with low exacerbation rates (5 of 34 subjects)($p \leq 0.05$).

CONCLUSIONS

- >There is no difference in the frequency of CRP or SP-D deficiency between asthmatics who have high exacerbation rates of asthma and those with low exacerbation rates.
- >African-Americans with high exacerbation rates were more likely to be MBL deficient than African-American subjects with low exacerbation rates. Therefore, a deficiency in mannan binding lectin may contribute to a higher rate of asthma exacerbations in these patients.

