Title:

USE OF IBUPROFEN TO ASSESS INFLAMMATORY BIOMARKERS IN INDUCED SPUTUM: IMPLICATIONS FOR CLINICAL TRIALS IN CYSTIC FIBROSIS

Authors:

James F. Chmiel, MDab*, Michael W. Konstan, MDb, Frank J. Accurso, MDc, James Lymp, PhDd, Nicole Mayer-Hamblett, PhDde, Donald R. VanDevanter, PhDb, Lynn M. Rose, PhDde, and Bonnie W. Ramsey, MDe for the Assessment of Induced Sputum in Cystic Fibrosis Study Group

Affiliations:

a Rainbow Babies and Children’s Hospital, 11100 Euclid Avenue, Cleveland, OH 44106 USA
b Case Western Reserve University School of Medicine, 2109 Adelbert Road, Cleveland, OH 44106 USA
c Children’s Hospital Colorado and University of Colorado, 13123 East 16th Avenue, Aurora, CO 80045 USA
d Seattle Children’s Hospital Research Institute and Cystic Fibrosis Therapeutics Development Network Coordinating Center, 2001 Eighth Avenue, Seattle, WA 98121 USA
e Seattle Children’s Hospital and University of Washington School of Medicine, 4800 Sand Point Way NE, Seattle, WA 98105 USA

What was your research question?

This trial aimed to find out if looking for changes in levels of inflammatory markers in sputum (induced by inhaling salt water) before and after one month of ibuprofen treatment could be used to screen anti-inflammatory drugs for use in people with cystic fibrosis (CF) before assessing these drugs in large clinical trials.
Cystic Fibrosis Research News

Why is this important?

People with CF have a large amount of inflammation in their lungs that damages the airways, making breathing difficult. Lessening inflammation with drugs is an essential part of a patient’s treatment plan. Ibuprofen is the only drug recommended for treating inflammation, but it is not widely prescribed. There are potential treatments that can reduce inflammation that may help people with CF. The problem with clinical trials for anti-inflammatory drugs is that they take many months and require large numbers of participants. It would be helpful to have a method for screening anti-inflammatory drugs before testing them in large trials.

What did you do?

Volunteers with CF were split into 2 groups: one group received their usual CF treatments, and the other group received their usual CF treatments plus high-dose ibuprofen. Volunteers who took ibuprofen gave a sputum sample two weeks before and again just before starting ibuprofen, at the end of one month of ibuprofen, and two weeks after stopping ibuprofen. Volunteers in the usual treatment group gave a sputum sample at the same time points. Many different inflammatory markers were measured in sputum and changes in these markers between the beginning and the end of treatment were calculated for all volunteers. We also looked at differences between the different treatment groups.

What did you find?

We tested ibuprofen in this system, and it did not show a benefit. We found no differences in safety measures between the two groups. Of all of the inflammatory markers measured, only IL-6, a molecule which promotes inflammation, was different at the end of treatment compared to the beginning of treatment in the ibuprofen group. When comparing changes in sputum between the ibuprofen group and the usual treatment group, IL-6 was again the only marker that was different.
**Cystic Fibrosis Research News**

**What does this mean and reasons for caution?**

These results probably occurred because inflammation is different in different parts of the lung. One sputum sample may come from a part of the lung that may not have much inflammation, and another time, the sample may come from a different part of the lung that has much more inflammation. Furthermore, one month is probably not long enough to see changes in sputum markers. Ibuprofen has shown benefits on lung function and life-span in other studies. If ibuprofen had been screened in this way using sputum, it may not have gone on to larger trials. This method may not be sensitive enough for CF.

**What’s next?**

A different method for screening anti-inflammatory drugs to work out which of these should go on to larger trials must be found.

**Original Manuscript citation in PubMed**