The case for extra fine particle ICS: to cover the entire lung

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Learning objectives

• To understand importance of the small airways in asthma
• To learn if there is a difference in the inflammatory response between large and small airways
• To determine if consideration of small airway dysfunction is important in selecting medications

No COI or disclosures to report on this topic
Current perspectives

Small-airways dysfunction associates with respiratory symptoms and clinical features of asthma: A systematic review

van der Wiel, E, ten Hacken, N, Postma D, and van den Berge, M.

(JACI 2013;131:646-57)

Anatomic evidence:
Airway Obstruction in Asthma

Courtesy of Bruce Rubin, M.D.

Physiologic reason for extra fine particle ICS
Peripheral Airways Resistance

![Bar graph showing PAR (cm H2O/ ml/min) for asthma and normal subjects.](image)

Wagner, et al ARRD 1990; 141:584

Uncoupling of the Airways

![Diagram illustrating nocturnal inflammation and airflow changes.](image)
The Small Airways: Role in Recurrent Exacerbations in Asthma

Does a difference in proximal vs. distal inflammation support the physiologic findings?

An inflammatory reason
Does particle size of inhaled medication alter lung physiology and inflammation?

Suspension vs Solution Aerosols

Lung Attenuation after 4 weeks of EF ICS vs large particle

EF significantly reduces air trapping compared to large particle (p=0.044)

Median lung attenuation (Hounsfield units)

-600
-620
-640
-660
-680
-700
-720
-740
-760

Pre-Mch
Post-Mch

p = .048
p = .037

EF (n=11)
Large (n=9)

Goldin et al., J Allergy Clin Immunol 104:S258-67, 1999

EF particle ICS and eosinophils

MBP/mm²

0
20
40
60
80
100

Before
After
Before
After

Peripheral Airways
Central Airways


Is there clinical evidence that an extra fine particle size ICS improves drug effectiveness?
US (OptumInsight): Cost-effectiveness EF particle ICS relative to larger particle. Matched cohort 12-80 y/o, n = 10,312

Effectiveness = Overall Control (Risk and Impairment)

Risk = no hospital for asthma, oral corticosteroids, or antibiotics for LRI
Impairment ≥ 2 puffs sabaday

Effectiveness

Less effective
More costly

Effectiveness Diff

Cost Diff

More effective
Less costly

• Is there supporting physiologic and clinical evidence that the central and distal airways are different in asthma? – Yes

• Is there evidence to support a differentiation between central and distal inflammation? – Yes

• Does particle size of ICS alter asthma outcome?
  – EF ICS appears to be equal to or have more effectiveness at a lower cost

See following page for references.
References


