



Bronchodilators and cough in Cystic Fibrosis – longitudinal study

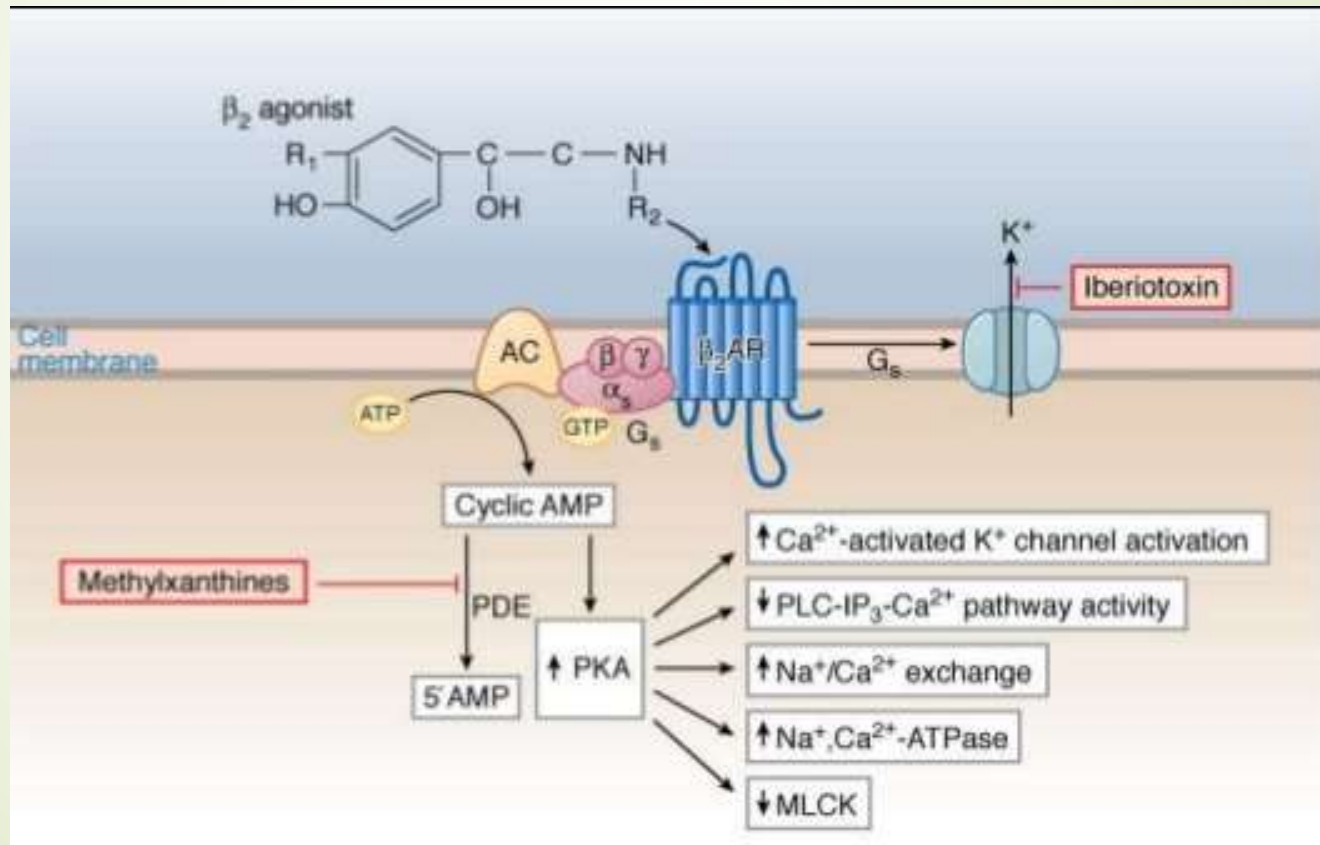
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Introduction

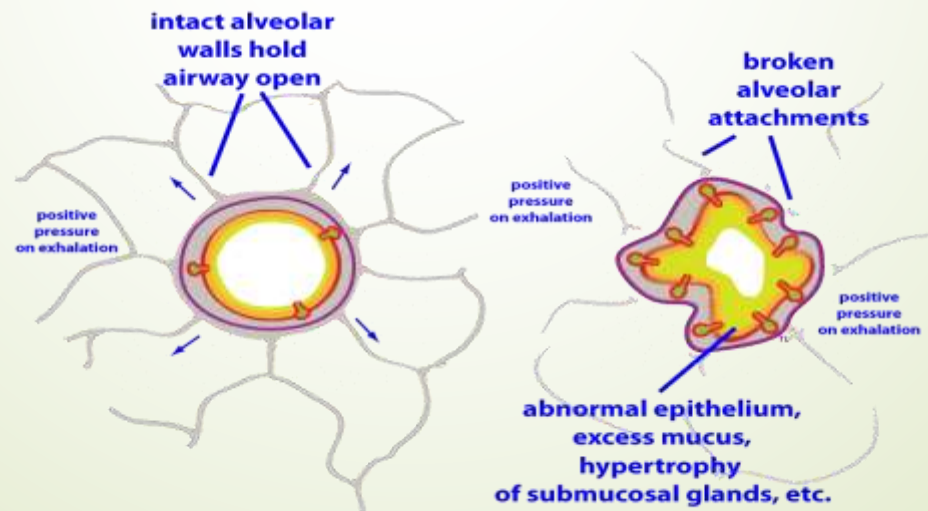
- ▶ The prevalence of "Asthma like" symptoms in CF is higher than in the entire population, rising from 17% to 31.5% (NAECF, EERCF)
- ▶ Bronchodilators (BD) are widely used in patients with CF (Brand. JRSM, 2000)
- ▶ BD are divided to Short acting SABA (e.g Salbutamol) and Long acting LABA (e.g Salmeterol)
- ▶ Variable and inconsistent response

Introduction





- Alongside with the positive effects, BD have the potential to worsen airway function:
- with the absence of normal cartilage tissue around the airway, the airway potency is dependent also on the smooth muscle (Halfhide, Cochrane 2005)
- Erased intra thoracic pressure causes early collapse and reduces cough efficacy





Physiology of Cough

- Irritation
- Inspiration
- Glottic closure
- Compression - Erased intra thoracic pressure
- Explosive - Glottic opening
- Relaxation - Inspiration

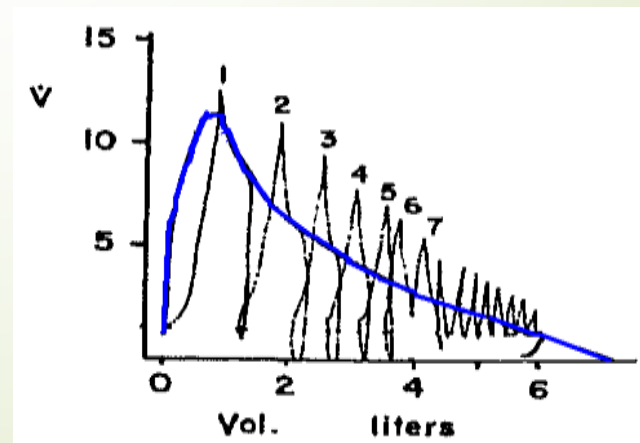


Cough flow Efficiency depend on:

1. Sufficient inspiration volume
2. Proper expiratory flow rates, Threshold 2.6 l/s

Efficient Cough flow volume curve includes:

1. Cough Peak-flow (C-PF). Pre-cough inspired volume of any amount.
2. cough Spikes number 8 - 14





The aim of the study

- to investigate the effect of the long term use of BD lung function and on the efficacy of cough and expectoration in CF patients.



Subjects & Methods

- **Study design:** Retrospective longitudinal study, 6-18 years period
- **Inclusion criteria:**
 - CF patients
 - treatment with LABA and inhaled corticosteroids > 2-years period.
 - Prior positive response to BD
- Included data:** age, body mass index (BMI) percentile for gender, genetics
- **Source:** The clinical archive of the National CF Center at Safra's Children's Hospital



Lung function:

1. Spirometry
 2. Cough flow volume maneuvers.
- Spirometry tests were performed prior to and 15 minutes after inhalation of BD
 - A positive response to bronchodilators (BD) of 12% elevation from baseline FEV1 (according to the global criteria) at the first spirometry
 - Cough maneuvers were performed 15 minutes after BD inhalation.



Results

Baseline vs. end of study anthropometric data and spirometry

N=25

	1 st test	12±6 yrs later	P value
Age (yrs)	16 ±8	28 ±9	0.0001
BMI kg/m ² (percentil)	19 ±18	21 ±20	NS
Spirometry (%predicted values)			
FVC	78 ±18	65 ±20	0.0011
FEV1	63 ±19	52 ±18	0.0001
PEF	71 ±25	61 ±27	0.0618
FEF25-75	41 ±22	24 ±29	0.0012



Response to BD

	<u>1st test</u>	<u>12±6 yrs later</u>	<u>P value</u>
Responders	10	7	NS
FVC	6.4 ±9.7	4.4± 9.5	NS
FEV1	14.2± 9.0	5.4 ±8.5	0.0082
PEF	14.0 ±16	3 ±15	0.0216
FEF25-75	20±28	9±18	0.0350



The Cough flow/volume curve maneuver indices (%predicted) for the 25 patients using regularly BD at the end of 12 years

	<u>Responders</u> <u>N=7</u>	<u>Non-Responders</u> <u>N=18</u>	<u>P value</u>
Age	28 ±9	28 ±10	NS
Peak Cough Flow (PCF)	63 ±24	60 ±21	NS
FEV1	48±16	55±18	NS
PCF/PEF ratio	1.13±0.19	1.04±0.27	NS
Cough vital capacity (C-VC)	47 ±25	48 ±24	NS
%fall in C-VC from FVC	-37 ±21	-39 ±22	NS
2 nd Spike (l/s)	3.9 ±1.4	2.6 ±1.4	0.0449
Patients having at least 4 spikes (%)	7 (100)	6 (33)	0.029



Discussion

- The positive response to BD is diminishing with the advancement of the disease.
- There are few suggested mechanisms
 - Reduced production of beta adrenergic receptors
 - Loss of normal epithel tissue including beta adrenergic receptors
 - Down regulation of the receptors



Discussion

- CF patients who present "asthma like" symptoms and are using BD for years may also present A paradoxical effect of BD
- Possible mechanisms :
 - Airways with malacia due to loss of cartilage
 - Dependence on smooth muscle tone



Discussion

- In comparison with responders, non responders have lower number of cough spikes and lower 2nd cough spike after administration of BD.
- We assume that in non responders it is possible that the harmful effect is bigger than the positive one
- Suggested mechanism is the malacia in the airways.
- Opening for a future study



Conclusions

- Response to BD should be evaluated every year
- Prescribing BD in CF patients should be precarious



Limitations

- No cough maneuver was performed pre BD
- Small number of patients



קצת הדתה - חרב פיפיות במקורות

➤ "יעלזו חסידים בכבוד, ירננו על משכבותם. רוממות אל בגרונם ו**חרב**

פיפיות בידם" תהילים קמ"ט

➤ "וַיַּעַשׂ לוֹ אֱהוֹד חֶרֶב, וְלָהּ שְׁנֵי פִיּוֹת--גָּמַד אָרְכָּהּ; וַיַּחַגֵּר אוֹתָהּ מִתַּחַת

לְמַדְיוֹ, עַל יָרֵךְ יְמִינוֹ. וַיִּקְרַב, אֶת-הַמִּנְחָה, לְעַגְלוֹן, מֶלֶךְ מוֹאָב; וְעַגְלוֹן,

אִישׁ בָּרִיא מְאֹד" שופטים, ג', ט"ו



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