

Controlling Asthma by Training of Capnometry-Assisted Hypoventilation (CATCH) vs Slow Breathing

A Randomized Controlled Trial

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e-Appendix 1.

Exclusion criteria were clinically significant heart disease, cerebrovascular disease, thyroid dysfunction, out-of-control diabetes, clinically significant chronic obstructive pulmonary disease and emphysema. No oral corticosteroids use in the last 3 months. Psychiatric exclusion criteria were a lifetime history of bipolar disorder, schizophrenia, psychosis, delusional disorders, organic brain syndrome, mental retardation, current substance or alcohol abuse or dependence, or significant suicidal ideation. Patients with prior experience in breathing training were also excluded.

Diurnal variability of peak flow. 6 daily measures were taken in the early morning after waking and before bronchodilator use, late morning (11am-12pm), early afternoon (2-3pm), late afternoon (5-6pm), early evening (8-9pm), and late evening (before going to bed). A pre-programmed internal alarm with a series of tones alerts the patients to the scheduled self-assessment times. The best of three expirations was stored in the electronic memory of the device. Variability was determined as the coefficient of variation across all 3-day measurements. Adherence with PEF measurements was high and did not change significantly throughout the observation period, with the average completed measurements per day being 81.6%-84.9% for 4 or more completed measurements and 69.2%-73.3% for 5 or more. Latest guidelines[1] continue to stress the value of serial PEF measurements for long term monitoring of the disease, in particular when changes through therapy are expected.

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Results

Control variables. No significant changes were observed in the control variables dosage or reported frequency (as indicator of adherence) of inhaled corticosteroid prescription and reported flu symptoms. Cold symptoms fluctuated over time with increases from pre- to post-treatment, decreases at 1MFU, and increases at 6MFU. Leukotriene modifier use was low at pre-treatment, post-treatment, and 6MFU, but somewhat increased at the 1MFU ($p=.029$ for the time effect).

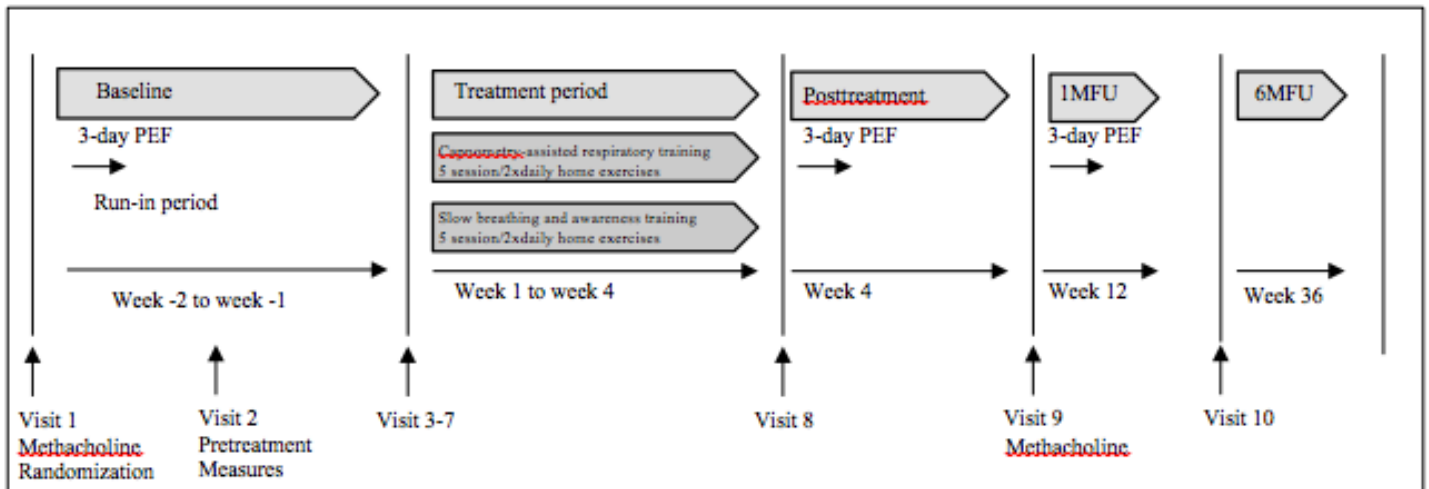
Not-study related, adverse events. As expected in asthmatics, the majority reported having a runny nose, sore throat, sneezing, shortness of breath, wheezing, cough, or seasonal or allergy related issues at one point during the study. Other adverse events included stomach viruses, food poisoning, nose bleeds. Five serious adverse events, none of which being judged to be related to treatment by an independent external medical monitor, were: one patient was hospitalized for colitis (6MFU, CART), two were admitted to ER (broken ankle [run-in, SLOW], allergic reaction to amoxicillin [during treatment, SLOW]), one was hospitalized after a seizure brought on by malnourishment due to an eating disorder (6MFU, CART), and one patient was diagnosed with leukemia (6MFU, CART)

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e-Figure 1 CART training illustration



e-Figure 2 CATCH Study Design



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e-Table 1 Asthma Symptom Checklist (ASC) subscales

	Mean (SE)				Time effect <i>p</i>	Group x Time effect <i>p</i>	Mean change (95% CI) from baseline to:		
	Baseline	Post	1 MFU	6 MFU			Post	1 MFU	6 MFU
Panic-fear					0.015	0.001			
CART	0.7 (0.1)	0.5 (0.1)	0.6 (0.1)	0.4 (0.1)			-0.1 (-0.3 to 0.0)	-0.1 (-0.3 to 0.0)	-0.3 (-0.4 to -0.1)
SLOW	0.6 (0.1)	0.6 (0.1)	0.4 (0.1)	0.6 (0.1)			-0.0 (-0.2 to 0.1)	-0.2 (-0.4 to -0.1)	-0.0 (-0.2 to 0.2)
Differential change							-0.1 (-0.3 to 0.1)	0.1 (-0.1 to 0.3)	-0.3 (-0.5 to -0.0)
<i>p</i> value							0.310	0.318	0.025
Dyspnea					<0.001	0.014			
CART	1.5 (0.1)	1.0 (0.1)	1.1 (0.1)	0.9 (0.1)			-0.4 (-0.6 to -0.2)	-0.4 (-0.6 to -0.2)	-0.6 (-0.8 to -0.4)
SLOW	1.3 (0.1)	1.0 (0.1)	0.9 (0.1)	1.1 (0.1)			-0.3 (-0.4 to -0.1)	-0.4 (-0.6 to -0.2)	-0.2 (-0.4 to 0.0)
Differential change							-0.2 (-0.4 to 0.1)	0.0 (-0.3 to 0.3)	-0.4 (-0.7 to -0.1)
<i>p</i> value							0.206	0.797	0.010
Irritability					0.640	0.013			
CART	1.0 (0.1)	0.8 (0.1)	0.9 (0.1)	0.7 (0.1)			-0.2 (-0.4 to 0.0)	-0.1 (-0.3 to 0.1)	-0.4 (-0.6 to -0.1)
SLOW	0.9 (0.1)	1.0 (0.1)	0.8 (0.1)	1.0 (0.1)			0.1 (-0.1 to 0.3)	-0.1 (-0.3 to 0.2)	0.1 (-0.1 to 0.4)
Differential change							-0.3 (-0.6 to 0.0)	-0.0 (-0.4 to 0.3)	-0.5 (-0.8 to -0.1)
<i>p</i> value							0.075	0.812	0.010
Congestion					<0.001	0.052			
CART	1.2 (0.1)	0.9 (0.1)	1.1 (0.1)	0.7 (0.1)			-0.3 (-0.5 to -0.1)	-0.1 (-0.3 to 0.2)	-0.5 (-0.7 to -0.3)
SLOW	1.3 (0.1)	1.2 (0.1)	1.0 (0.1)	1.0 (0.1)			-0.0 (-0.3 to 0.2)	-0.2 (-0.5 to 0.0)	-0.3 (-0.5 to -0.0)
Differential change							-0.3 (-0.6 to 0.1)	0.2 (-0.2 to 0.5)	-0.2 (-0.5 to 0.1)
<i>p</i> value							0.122	0.331	0.184
Hyperventilation					0.005	0.454			
CART	0.4 (0.0)	0.4 (0.0)	0.4 (0.0)	0.3 (0.0)			-0.1 (-0.1 to -0.0)	-0.1 (-0.2 to -0.0)	-0.1 (-0.2 to -0.0)
SLOW	0.4 (0.0)	0.4 (0.0)	0.4 (0.0)	0.4 (0.0)			-0.1 (-0.2 to -0.0)	-0.1 (-0.1 to 0.0)	-0.0 (-0.1 to 0.0)
Differential change							0.0 (-0.1 to 0.1)	-0.0 (-0.1 to 0.1)	-0.1 (-0.2 to 0.0)
<i>p</i> value							0.963	0.702	0.174

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Fatigue					0.010	0.423			
CART	1.2 (0.1)	1.1 (0.1)	1.1 (0.1)	0.9 (0.1)			-0.1 (-0.3 to 0.2)	-0.1 (-0.4 to 0.2)	-0.3 (-0.5 to -0.1)
SLOW	1.4 (0.1)	1.1 (0.1)	1.1 (0.1)	1.1 (0.1)			-0.3 (-0.5 to -0.0)	-0.3 (-0.6 to -0.0)	-0.3 (-0.5 to -0.0)
Differential change							0.2 (0.1 to 0.5)	0.2 (-0.1 to 0.6)	-0.0 (-0.2 to 0.6)
<i>p</i> value							0.171	0.355	0.883

Note: 1MFU, 1 month follow-up; 6MFU, 6 months follow-up; CART, Capnometry-assisted respiratory training; SLOW, Slow breathing and awareness training; ASC, Asthma Symptom Checklist; differential change was calculated as the difference in change from baseline for the CART condition versus change from baseline for the SLOW condition.

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