Abnormal Respiratory Physiology and Capnometry Guided Respiratory Intervention for Anxiety, Panic, and PTSD

Saturday, April 7: 3:30 PM - 5:00 PM  
336R 
Symposium 
Credits: 1.5 

Anxiety disorder, panic disorder and posttraumatic stress disorder (PTSD) are common and debilitating conditions that have been associated with dysfunctional respiratory physiology. Carbon dioxide (CO2) sensitivity is recognized as a biomarker of panic vulnerability, related to a hypothesized 'suffocation alarm'. The presence of chronic breathing irregularities in individuals with anxiety and panic, particularly in the form of hyperventilation and subsequent hypocapnia, has led to the development of an FDA-cleared digital therapeutic instrument providing real-time feedback of respiratory rate and end-tidal CO2 within a structured, four-week, use-at-home protocol. This capnometry guided respiratory intervention (CGRI) normalizes respiratory physiology reducing panic attack frequency, intensity, and related avoidance behaviors. This symposium will summarize the literature regarding the role of hyperventilation in panic, with an emphasis on CO2 sensitivity. The author of a multi-center clinical trial utilizing CGRI for the treatment of panic disorder will report on the results measured post-treatment and at intervals extending to one-year post-treatment. Data reported from this four-week treatment will include symptom change, treatment adherence and changes to physiological markers. A second efficacy presentation will report clinical and financial outcomes from use of CGRI in a Health System Quality Improvement Program (QIP). Data from this QIP demonstrate clinical outcomes similar to those seen in published clinical trials as well as significant medical cost reduction (more than 50%) in the year following treatment. Finally, data from an ongoing trial of CGRI for PTSD will be presented, showing a significant reduction in PTSD symptoms at post-treatment through 2-month follow-up.

Learning Objectives

1. Describe the study design and outcomes from a multi-center clinical trial utilizing CGRI for the treatment of panic disorder.
2. Evaluate clinical and cost data from a program offering CGRI to health plan participants with panic disorder and compare the results with prior studies.
3. Describe the study design and outcomes from a clinical trial of CGRI for the treatment of PTSD.

Chair 

David Tolin, PhD, The Institute of Living and Yale University 

Discussant 

Stefan Hofmann, PhD, Boston University 

Audience Level 

Intermediate/Advanced 

Demographic 

Adults 

Diversity/Content
A Multi-Center Open Trial of Capnometry-Guided Respiratory Intervention in the Treatment of Panic Disorder

Objective: This presentation reports on the treatment of 69 panic disorder patients enrolled in a multi-center study of Freespira, an FDA-cleared digital therapeutic. Method: The Freespira system comprises a sensor measuring endtidal CO2 (EtCO2) and respiratory rate (RR), with a Bluetooth-connected tablet and App providing real-time EtCO2 and RR feedback within a protocol used to attain normal levels of EtCO2 at weekly decreasing target respiration rates (13, 11, 9, 6 breaths/min). Patients with a clinical diagnosis of panic disorder were educated on hyperventilation and respiratory irregularity and trained on the use of the System, followed by use of the protocol at-home for four weeks (twice daily sessions) with weekly therapist review. The primary study outcome measure was Panic Disorder Severity Scale (PDSS). Secondary outcome measures included Clinician's Global Impression (CGI-S), Beck Depression Inventory (BDI), Sheehan Disability Scale (SDS), Anxiety Sensitivity Index (ASI), and Mobility Inventory for Agoraphobia (MI). The EtCO2 and RR from each session and the number of weekly panic attacks were also recorded. Measures, including physiologic measures of EtCO2 and RR were taken at baseline, immediately post-treatment, 2 months and 12 months post-treatment. Results: 48 patients completed treatment and were available for assessment after the 4-week protocol. At this interval, statistically significant reductions from baseline PDSS, ASI, BDI, SDS and CGI scores and number of prior week panic attacks were seen, with large effect size. At 12 months post-treatment, 82% of available treatment completers exhibited significant response (>40% reduction in PDSS scores), 70% of completers were in remission (PDSS <5) and 79% reported experiencing no panic attacks in the prior week. Mean EtCO2 levels increased significantly from 35 to 39 mmHg at conclusion of active treatment. At 12 months, 82% of patients completing a 0-4-point satisfaction survey (where 3 = would, and 4 = would definitely recommend) reported 3 or 4. Conclusion: Use of the Freespira system within a structured protocol, using EtCO2 and RR, was effective in reducing panic severity symptoms, anxiety sensitivity, work/life disruption, and significantly decreased panic attacks.

Presenter

David Tolin, PhD, The Institute of Living and Yale University
Baseline Respiratory Abnormality Predicts Outcome and Dropout from Cognitive Behavioral Therapy for Anxiety and Related Disorders

Low baseline levels of end-tidal pCO2 – a biological indicator of chronic hyperventilation - are commonly found in individuals with anxiety disorders. We present data from two studies examining baseline end-tidal pCO2 as a predictor of treatment outcome or treatment dropout from cognitive behavioral therapy (CBT) for anxiety disorders, OCD, and PTSD. In the first study, sixty-one individuals with a principal anxiety disorder diagnosis completed an assessment of baseline end-tidal pCO2 and were then randomly assigned to complete twelve sessions of either CBT or acceptance and commitment therapy (ACT). Baseline self-reported anxiety symptoms and quality of life were assessed at pre-treatment, post-treatment, and 6- and 12-month follow-up. Lower pre-treatment baseline pCO2 was a predictor of poorer overall treatment outcome, with individuals with lower pCO2 levels reporting higher anxiety symptoms and lower quality of life at follow-up. The second study examined end-tidal pCO2 as a predictor of treatment dropout in a naturalistic clinical setting. Sixty-nine individuals completed an assessment of baseline end-tidal pCO2 prior to beginning CBT in an outpatient, hospital-based clinic. End-tidal pCO2 was a significant predictor of treatment dropout, with lower pCO2 predicting greater risk of dropout. Additionally, results suggested that individuals with lower end-tidal pCO2 levels who dropped out were not responding well to treatment prior to dropout. Together, these studies suggest that low baseline end-tidal pCO2 indicates a poorer prognosis from CBT and may warrant treatment that directly targets respiratory dysregulation.

Presenter
Carolyn Davies, Ph.D., Institute of Living

Evaluating the Impact of a Capnometry Guided Respiratory Intervention on Panic Disorder Patients’ Health and Healthcare Costs within the Allegheny Health Network (25 minutes)

Panic Disorder (PD) is a common debilitating condition that drives medical spending 3-5 times higher than for medically matched controls. Excess resources are consumed in the ED, PCP and specialist visits, prescription (Rx) and tests more than in behavioral health settings. Freespira is an FDA-cleared digital therapeutic for panic. The Freespira treatment is done twice-daily at-home for four weeks under clinician supervision. Clinical trials have demonstrated reduction/elimination of panic attacks and symptoms lasting 12-months post-treatment. Objective: This abstract reports results from a Quality Improvement Program at Allegheny Health Network tracking clinical outcomes and costs to determine if treating PD patients with Freespira would reduce medical costs over a 12-month period. Method: Psychological assessments measured clinical symptoms and improvement. Respiratory rate and levels of exhaled carbon dioxide were captured for every breathing session. Pre-and post-treatment Medical Claims data is reported as median total per member/per month (PMPM) medical costs, ED costs, and medication costs. Results: 50 subjects were enrolled (66% female). Average age was 40 with 10 years mean PD duration. At enrollment, mean CGI-S was
4.4 (moderately / markedly ill), mean PDSS was 14.5 and mean PA frequency/week was 1.74 (range 0-5). Immediately post-treatment, mean CGI-S, PDSS and weekly PA frequency declined to 2.7 (borderline / mildly ill, 4.5 (below the remission threshold of 5) and 0.2 (range 0-2) respectively, all significant at p<0.001. For patients available six months post-treatment, 90% reported PDSS decrease of ≥40% (clinically significant) and 89% were PA free. At the one-year, mean CGI-S, PDSS and PA remained low at 2.6, 5.7, and 0.2 respectively. 92% reported PDSS decrease of ≥40% and 81% were PA free. Median total allowed monthly member claim cost for the pre-treatment 12-months was $480, reduced to $240 PMPM at 12 months post-treatment with Freespira. A 64% reduction in ED costs was recorded. Rx costs were reduced 53% one-year post-treatment. Conclusions: High rates of remission and symptom reduction were achieved, consistent with earlier studies. Meaningful cost savings in overall medical spending, ED, and Rx costs were achieved since majority of patients were panic attack free and/or reduced their symptoms and avoidance behaviors.

Presenter
Alicia Kaplan, MD, Allegheny General Hospital

Investigation of a Non-Invasive Capnometry Guided Respiratory Intervention in the Treatment of PTSD

Objective: To investigate a noninvasive, biofeedback device (Freespira, Palo Alto Health Sciences, Inc.) that allows for the integration of expired EtCO2 (end tidal CO2), respiration rate (RR), and real-time display of these measurements with the goal of increasing EtCO2 and decreasing interoceptive signals associated with anxiety. It is cleared by the FDA for use in panic disorder, but it is not known whether such the device would be of benefit for the treatment of PTSD. We report interim results from a study of this device in patients with PTSD to determine whether it reduces overall Clinician-Administered PTSD Scale for DSM-5 (CAPS-5) scores. Method: Subjects with a primary DSM-5 diagnosis of PTSD, a CAPS-5 score >30 and Clinical Global Impression – Severity scale (CGI-S) score >4 are eligible for this 4-week trial of open-label, capnometry guided respiratory intervention administered for 17 minutes twice-daily. Assessments are completed at baseline, weekly during treatment, end of treatment and 2- and 6-months post-treatment. Physiological data (respiratory rate and EtCO2) is captured. The primary outcome is a reduction in CAPS score of >6 in at least 50% of subjects at 2 months post-treatment. Planned enrollment at end of study is 55 subjects. Results: Eighteen subjects have been enrolled to date. Baseline CAPS- score is 55 (SD 9.6). and mean CGI-S is 4.8. Mean age is 51, of which 72% are male. Within the last 12 months, 33% had presented to the ER and 22% were hospitalized. At end of treatment (n=11), mean CGI-S declined from 4.8 to 3.7 (p<0.05) and mean CAPS-5 scores declined from 55 to 40 (p<0.001) with 91% achieving a >6-point CAPS-5 score reduction (response) and 9% reporting remission (CAPS-5 <25). For subjects who have completed 2-months post-treatment (n=4), mean CGI-S declined to 3.5 and the mean CAPS-5 score declined further to 34 with 75% of patients reporting a >6-point decrease and 50% reporting remission. Conclusions: Interim data from this trial of the this non-invasive, capnometry guided respiratory device in a relatively ill, predominantly male cohort with a primary diagnosis PTSD
suggests that it may be effective for reducing CAPS-5 scores and overall severity at end of treatment and that benefits persist at 2-month follow up.

Presenter

Michael Ostacher, MD, MPH, Stanford University School of Medicine