GULF WAR ILLNESS

Author Correction: Exercise - induced changes in cerebrospinal fluid miRNAs in Gulf War Illness, Chronic Fatigue Syndrome and sedentary control subjects.

Baraniuk JN[1], Shivapurkar N[2].

Sci Rep. **2018 Apr 19**;8(1):6455. doi: 10.1038/s41598-018-23238-0. PMID: 29674668.

Erratum for:

- Exercise - induced changes in cerebrospinal fluid miRNAs in Gulf War Illness, Chronic Fatigue Syndrome and sedentary control subjects. [Sci Rep. 2017]

Abstract:

A correction to this article has been published and is linked from the HTML and PDF versions of this paper. The error has not been fixed in the paper.

This Abstract Appeared in the RAC-GWVI Research Alerts for November 14, 2017:

Exercise - induced changes in cerebrospinal fluid miRNAs in Gulf War Illness, Chronic Fatigue Syndrome and sedentary control subjects.

Baraniuk JN[1], Shivapurkar N[2].

Sci Rep. **2017 Nov 10**;7(1):15338. doi: 10.1038/s41598-017-15383-9.

Abnormal rheological properties of red blood cells as a potential marker of Gulf War Illness: A preliminary study.

Falvo MJ[1,2], Chen Y[1,2], Klein JC[1], Ndirangu D[1], Condon MR[2,3].

Clin Hemorheol Microcirc. **2018**;68(4):361-370. doi: 10.3233/CH-170262. PMID: 29660926.

BACKGROUND: Veterans with Gulf War Illness (GWI) experience chronic symptoms that include fatigue, pain, and cognitive impairment. This symptom cluster may be the consequence of impaired tissue oxygen delivery due to red blood cell (RBC) dysfunction.

OBJECTIVE: The purpose of this preliminary study was to determine whether the microrheological behavior of RBCs is altered in GWI.

METHODS: We recruited 17 cases of GWI (GWI+) and 10 age matched controls (GWI-), and examined RBC deformability and aggregation via ektacytometry along with measurement of complete blood counts.

RESULTS: RBCs were more deformable in GWI+, as indicated by higher elongation indices particularly at higher shear stress values (5.33, 9.49, and 16.89) when compared to GWI-. Aggregation formation, stability and kinetics were similar between GWI+and GWI-. Complete blood counts were also similar, with the exception of mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and RBC distribution width (RDW) which was elevated in GWI+.

CONCLUSIONS: In this preliminary study, we observed increased deformability along with increased MCH, MCHC and RDW in veterans with GWI+, which may contribute to the symptomatology of GWI. Further research is required to confirm our findings and the role of RBC microrheology in GWI.

CHRONIC FATIGUE SYNDROME

Metabolic abnormalities in chronic fatigue syndrome/myalgic encephalomyelitis: a mini-review.

Tomas C[1], Newton J[2,3].

Biochem Soc Trans. **2018 Apr 17**. pii: BST20170503. doi: 10.1042/BST20170503. PMID: 29666214. [Epub ahead of print]

Chronic fatigue syndrome (CFS), commonly known as myalgic encephalomyelitis (ME), is a debilitating disease of unknown etiology. CFS/ME is a heterogeneous disease associated with a myriad of symptoms but with severe, prolonged fatigue as the core symptom associated with the disease. There are currently no known biomarkers for the disease, largely due to the lack of knowledge surrounding the eitopathogenesis of CFS/ME. Numerous studies have been conducted in an attempt to identify potential biomarkers for the disease. This mini-review offers a brief summary of current research into the identification of metabolic abnormalities in CFS/ME which may represent potential biomarkers for the disease. The progress of research into key areas including immune dysregulation, mitochondrial dysfunction, 5'-adenosine monophosphate-activated protein kinase activation, skeletal muscle cell acidosis, and metabolomics are presented here. Studies outlined in this mini-review show many potential causes for the pathogenesis of CFS/ME and identify many potential metabolic biomarkers for the disease from the aforementioned research areas. The future of CFS/ME research should focus on building on the potential biomarkers for the disease using multi-disciplinary techniques at multiple research sites in order to produce robust data sets. Whether the metabolic changes identified in this mini-review occur as a cause or a consequence of the disease must also be established.

HEADACHE and MIGRAINE

Subclinical hypothyroidism is associated with migraine: A case-control study.

Rubino E[1], Rainero I[1], Garino F[2], Vicentini C[1], Govone F[1], Vacca A[1], Gai A[1], Gentile S[3], Govone G[1], Ragazzoni F[2], Pinessi L[1], Giordana MT[1], Limone P[2].

Cephalalgia. **2018 Jan 1**:333102418769917. doi: 10.1177/0333102418769917. PMID: 29682977. [Epub ahead of print]

Background: Recent studies suggested a potential association between both overt and subclinical hypothyroidism and migraine. Aims of this study were to estimate the comorbidity of migraine in patients with subclinical hypothyroidism and to evaluate associated clinical characteristics.

Methods: Using a case-control strategy, 151 consecutive subclinical hypothyroidism patients (mean age 48.36 ± 15.86 years) and 150 controls (mean age 50.86 ± 9.19 years) were recruited. In all subjects, migraine characteristics were collected through a direct interview. Clinical and biochemical parameters (thyroid-stimulating hormone, free triiodothyronine, free thyroxine, and anti-thyroid antibodies) were compared between subclinical hypothyroidism patients in comorbidity with migraine and subclinical hypothyroidism patients without migraine.

Results: The prevalence of lifetime migraine was significantly higher in subclinical hypothyroidism patients in comparison with controls (46% vs. 13%, $p < 0.001$; OR 5.80; 95% CI = 3.35-10.34). Both migraine without and with aura were significantly higher in subclinical hypothyroidism patients than controls ($p < 0.001$ and $p = 0.010$, respectively). Thyroid hormones and concentrations of antibodies did not differ between subclinical hypothyroidism patients with and without migraine. Interestingly, a comorbidity for autoimmune diseases was observed in subclinical hypothyroidism patients with migraine in respect to those without migraine ($p = 0.005$).

Conclusions: Our data suggest that migraine is more frequent in patients with subclinical hypothyroidism in respect to controls. Further studies are needed in order to confirm this association.

HEADACHE and MIGRAINE (Continued)

Evaluation of a Janus Kinase 1 inhibitor, PF-04965842, in healthy subjects: a phase 1, randomized, placebo-controlled, dose-escalation study.

Peeva E[1], Hodge MR[1], Kieras E[1], Vazquez ML [1], Goteti K[1], Tarabar SG[2], Alvey CW[3], Banfield C[1].

Br J Clin Pharmacol. **2018 Apr 19**. doi: 10.1111/bcp.13612. PMID: 29672897. [Epub ahead of print]

AIMS: To determine the safety, tolerability, pharmacokinetics and pharmacodynamics of the Janus Kinase (JAK) 1-selective inhibitor, PF-04965842.

METHODS: This was a phase 1, first-in-human, randomized, double-blind, placebo-controlled, combination single- and multiple-dose escalation, parallel design study in healthy subjects (ClinicalTrials.gov, NCT01835197). Subjects received a single dose of placebo or 3, 10, 30, 100, 200, 400 or 800 mg PF-04965842 (single ascending dose phase) and placebo or 30 mg once daily (QD), 100 mg QD, 200 mg QD, 400 mg QD, 100 mg twice daily (BID) or 200 mg BID PF-04965842 for 10 consecutive days (multiple ascending dose phase). The primary objective was to determine the safety and tolerability of PF-04965842.

RESULTS: Seventy-nine subjects were randomized and received study treatments. There were no deaths or serious adverse events (AEs). The most frequent TEAEs were headache (n=13), diarrhoea (n=11) and nausea (n=11). PF-04965842 was absorbed rapidly (median T_{max} generally ≤1 h following either single- or multiple-dose administration) and eliminated rapidly (mean $t_{½}$ 2.8-5.2 h after 10 days of QD or BID administration in the multiple ascending dose phase). Increases in C_{max} and AUC were dose proportional up to 200 mg (single or total daily doses) with an apparent trend towards greater than proportional increases with higher doses. Less than 4.4% of the dose was recovered unchanged in urine. Changes in PD biomarkers were consistent with the known effects of JAK signalling inhibition.

CONCLUSIONS: These results support further evaluation of PF-04965842 for clinical use in patients with inflammatory diseases.

Effects of depression and anxiety on quality of life in five common neurological disorders.

Prisnie JC[1], Sajobi TT[2], Wang M[2], Patten SB[3], Fiest KM[4], Bulloch AGM[3], Pringsheim T[5], Wiebe S[5], Jette N[6].

Gen Hosp Psychiatry. **2018 Apr 4**;52:58-63. doi: 10.1016/j.genhosppsych.2018.03.009. PMID: 29684713. [Epub ahead of print]

BACKGROUND: It is unclear whether anxiety and depression impact health-related quality of life (HRQoL) equally across neurological diseases. This study examines the association between anxiety or depression and HRQoL in select neurological disorders.

METHODS: HRQoL was measured using the Short Form Health Survey (SF-12) in neurological patients: epilepsy (n = 279), migraine (n = 268), multiple sclerosis (MS) (n = 222), stroke (n = 204), and Parkinson's disease (PD) (n = 224). Depression and anxiety symptoms were assessed using the Patient Health Questionnaire (PHQ-9) and Hospital Anxiety and Depression Scale (HADS-A), respectively. Multiple linear regression was used to evaluate variables associated with the SF-12 mental health component (MCS) and physical health component scores (PCS). Pratt index was used to estimate the relative importance of anxiety and depression on HRQoL.

RESULTS: Anxiety and depression had the largest contribution to PCS in stroke and to MCS in epilepsy. Overall, anxiety and depression had a larger contribution to MCS as compared to PCS, except in stroke patients. Different patterns were seen across neurological diseases, with mental health variables strongly affecting MCS in all conditions, with also a sizable contribution to PCS in migraine, MS, and stroke.

CONCLUSIONS: Anxiety and depression have varying impacts on HRQoL across neurological diseases. It is important for clinicians to be aware of how these patterns differ in each condition.

HEADACHE and MIGRAINE (Continued)

Nosographic analysis of osmophobia and field testing of diagnostic criteria including osmophobia.

Chalmer MA[1], Hansen TF[1], Olesen J[1].

Cephalalgia. **2018 Jan 1**:333102418771375. doi: 10.1177/0333102418771375. PMID: 29665696. [Epub ahead of print]

Introduction Osmophobia has been suggested as an additional symptom of migraine without aura, and a high prevalence of osmophobia of up to 50% has been reported in the literature. We conducted a nosographic study of osmophobia in all migraineurs and tension-type headache patients and a field testing of suggested diagnostic criteria of osmophobia, presented in the appendix of the second edition of The International Classification of Headache Disorders and suggested by Silva-Néto et al. and Wang et al., in migraine without aura and tension-type headache patients (n = 1934). Materials and methods Each patient received a validated semi-structured interview. All subjects fulfilled the diagnostic criteria of the second edition of The International Classification of Headache Disorders for migraine or tension-type headache. Statistical analyses were performed using statistical software R. The statistical R package "Caret" was used to construct a confusion matrix and retrieve sensitivity, which is defined as the suggested criteria's ability to correctly diagnose migraine without aura patients, and specificity, defined as the suggested criteria's ability to not wrongly diagnose tension-type headache patients. Results Osmophobia was present in 33.5% of patients with migraine with aura, in 36.0% of patients with migraine without aura, and in 1.2% of patients with tension-type headache. All migraineurs with osmophobia also fulfilled the current criteria for migraine by having nausea or photophobia and phonophobia. The appendix criteria had a sensitivity of 0.96 and a specificity of 0.99 for migraine without aura, and a sensitivity of 0.65 and a specificity of 0.99 for probable migraine without aura. Both the criteria by Silva-Néto et al. and Wang et al. had a sensitivity of 0.98 and a specificity of 0.99 for migraine without aura, and a sensitivity of 0.66 and a specificity of 0.99 for probable migraine without aura. Discussion This study demonstrates the remarkable specificity of osmophobia. The criteria by Silva-Néto et al. and Wang et al. both had a higher sensitivity than the appendix criteria for migraine without aura; all three criteria had a low sensitivity for probable migraine without aura. However, neither the appendix criteria nor the criteria by Silva-Néto et al. or Wang et al. added any extra patients that would not have been diagnosed by the current diagnostic criteria for migraine. Osmophobia is a valuable symptom that may be useful to differentiate between migraine without aura and tension-type headache in difficult clinical cases. Conclusion Our results do not suggest that alterations of the current diagnostic criteria for migraine without aura are needed.

CHRONIC PAIN

Twelve year follow up of chronic pain in twins: changes in environmental and genetic influence over time.

Burri A[1,2], Ogata S[3,4], Rice D[1,2], Williams FMK[5].

Eur J Pain. **2018 Apr 20**. doi: 10.1002/ejp.1233. PMID: 29676837. [Epub ahead of print]

BACKGROUND: While genetic influences on chronic pain have been repeatedly demonstrated, we do not know whether these effects are stable or dynamic over time.

AIMS: To determine the temporal pattern of genetic and environmental effects to individual differences in chronic pain over 12 years, using a sample of N = 961 female twins.

METHODS: Data on chronic pain was collected in 2004 (T1) and 2016 (T2) using the same comprehensive body map which divides the body into 31 distinct anatomical areas. Multivariate twin analyses for repeated measures were conducted to track changes in genetic and environmental influences.

RESULTS: Heritability for chronic pain was 63% at baseline and 55% at follow-up. The best-fitting AE Cholesky model revealed one genetic factor explaining 62% of variance in chronic pain at T1 and 11% at T2. No additional genetic factors explaining the variance in chronic pain at T2 could be detected. Furthermore, a unique environmental factor (E1) explaining 37% of the variance in chronic pain at T1 and 12% at T2 and an additional environmental factor (E2) explaining 77% of the variance at T2 was found.

CONCLUSION: We demonstrate for the first time that the same genetic influences are operative over time and that novel environmental factors are important in pain maintenance. The findings highlight the value of more in depth exploration of these non-shared environmental influences that could provide clues to the mechanisms behind remittance and/or maintenance of chronic pain. The identification of important environmental influences could point to novel therapeutic interventions in future.

CHRONIC PAIN (Continued)

Effectiveness of fixed-site high-frequency transcutaneous electrical nerve stimulation in chronic pain: a large-scale, observational study.

Kong X[1], Gozani SN[1].

J Pain Res. **2018 Apr 9**;11:703-714. doi: 10.2147/JPR.S156610. PMCID: PMC5898590. eCollection 2018.

Objective: The objective of this study was to assess the effectiveness of fixed-site high-frequency transcutaneous electrical nerve stimulation (FS-TENS) in a real-world chronic pain sample.

Background: There is a need for nonpharmacological treatment options for chronic pain. FS-TENS improved multisite chronic pain in a previous interventional study. Large observational studies are needed to further characterize its effectiveness.

Methods: This retrospective observational cohort study examined changes in chronic pain measures following 60 days of FS-TENS use. The study data were obtained from FS-TENS users who uploaded their device utilization and clinical data to an online database. The primary outcome measures were changes in pain intensity and pain interference with sleep, activity, and mood on an 11-point numerical rating scale. Dose-response associations were evaluated by stratifying subjects into low (≤30 days), intermediate (31-56 days), and high (≥57 days) utilization subgroups. FS-TENS effectiveness was quantified by baseline to follow-up group differences and a responder analysis (≥30% improvement in pain intensity or ≥2-point improvement in pain interference domains).

Results: Utilization and clinical data were collected from 11,900 people using FS-TENS for chronic pain, with 713 device users meeting the inclusion and exclusion criteria. Study subjects were generally older, overweight adults. Subjects reported multisite pain with a mean of 4.8 (standard deviation [SD] 2.5) pain sites. A total of 97.2% of subjects identified low back and/or lower extremity pain, and 72.9% of subjects reported upper body pain. All pain measures exhibited statistically significant group differences from baseline to 60-day follow-up. The largest changes were pain interference with activity (-0.99 ± 2.69 points) and mood (-1.02 ± 2.78 points). A total of 48.7% of subjects exhibited a clinically meaningful reduction in pain interference with activity or mood. This proportion increased to 57.1% for the high utilization subgroup.

Conclusion: FS-TENS is a practical option for treating multisite chronic pain. The greatest impact is on pain interference with activity and mood. FS-TENS utilization and effectiveness exhibit a dose-response association, suggesting that daily use maximizes pain relief.

Genetic Association and Expression Analyses of the Phosphatidylinositol-4-Phosphate 5-Kinase (PIP5K1C) Gene in Alcohol Use Disorder - Relevance for Pain Signaling and Alcohol Use.

Lee JS[1], Sorcher JL[1], Rosen AD[1], Damadzic R[2], Sun H[2], Schwandt M[2], Heilig M[3], Kelly J[4], Mauro KL[1], Luo A[1], Rosoff D[1], Muench C[1], Jung J[5], Kaminsky ZA[4], Lohoff FW[1].

Alcohol Clin Exp Res. **2018 Apr 18**. doi: 10.1111/acer.13751. PMID: 29667742. [Epub ahead of print]

BACKGROUND: The gene encoding Phosphatidylinositol-4-Phosphate 5-Kinase (PIP5K1C) has been recently implicated in pain regulation. Interestingly, a recent cross-tissue and cross-phenotypic epigenetic analysis identified the same gene in alcohol use disorder (AUD). Given the high comorbidity between AUD and chronic pain, we hypothesized that genetic variation in PIP5K1C might contribute to susceptibility to AUD.

METHODS: We conducted a case-control association study of genetic variants in PIP5K1C. Association analyses of 16 common PIP5K1C single nucleotide polymorphisms (SNPs) were conducted in cases and controls of African (427 cases and 137 controls) and European Ancestry (488 cases and 324 controls) using standard methods. In addition, given the prominent role of the opioid system in pain signaling, we investigated the effects of acute alcohol exposure on PIP5K1C expression in humanized transgenic mice for the mu-opioid receptor that included the OPRM1 A118G polymorphism, a widely used mouse model to study analgesic response to opioids in pain. PIP5K1C expression was measured in the thalamus and basolateral amygdala (BLA) in mice after short-term administration (single 2g/kg dose) of alcohol or saline using immunohistochemistry and analyzed by two-way ANOVA.

RESULTS: In the case-control association study using a NIAAA discovery sample, eight SNPs in PIP5K1C were significantly associated with AUD in the African ancestry group ($p < 0.05$ after correction; rs4807493, rs10405681, rs2074957, rs10432303, rs8109485, rs1476592, rs10419980, and rs4432372). However, a replication analysis using an independent sample (N= 3801) found no significant associations after correction for multiple testing. In the humanized transgenic mouse model with the OPRM1 polymorphism, PIP5K1C expression was significantly different between alcohol and saline-treated mice, regardless of genotype, in both the thalamus ($p < 0.05$) and BLA ($p < 0.01$).

CONCLUSIONS: Our discovery sample shows that genetic variants in PIP5K1C are associated with AUD in the African ancestry group, and acute alcohol exposure leads to upregulation of PIP5K1C, potentially explaining one mechanism underlying the increased risk for chronic pain conditions in individuals with AUD.

OTHER RESEARCH OF INTEREST

MEG Working Memory N-Back Task Reveals Functional Deficits in Combat-Related Mild Traumatic Brain Injury.

Huang MX[1,2], Nichols S[3], Robb-Swan A[2], Angeles-Quinto A[2], Harrington DL[1,2], Drake A[4], Huang CW[5], Song T[2], Diwakar M[6], Risbrough VB[1,7,8], Matthews S[9], Clifford R[1,7,8], Cheng CK[10], Huang JW[11], Sinha A[12], Yurgil KA[1,8,13], Ji Z[2], Lerman I[1], Lee RR[1,2], Baker DG[1,7,8].

Cereb Cortex. **2018 Apr 13**. doi: 10.1093/cercor/bhy075. PMID: 29668852. [Epub ahead of print]

Combat-related mild traumatic brain injury (mTBI) is a leading cause of sustained cognitive impairment in military service members and Veterans. However, the mechanism of persistent cognitive deficits including working memory (WM) dysfunction is not fully understood in mTBI. Few studies of WM deficits in mTBI have taken advantage of the temporal and frequency resolution afforded by electromagnetic measurements. Using magnetoencephalography (MEG) and an N-back WM task, we investigated functional abnormalities in combat-related mTBI. Study participants included 25 symptomatic active-duty service members or Veterans with combat-related mTBI and 20 healthy controls with similar combat experiences. MEG source-magnitude images were obtained for alpha (8-12 Hz), beta (15-30 Hz), gamma (30-90 Hz), and low-frequency (1-7 Hz) bands. Compared with healthy combat controls, mTBI participants showed increased MEG signals across frequency bands in frontal pole (FP), ventromedial prefrontal cortex, orbitofrontal cortex (OFC), and anterior dorsolateral prefrontal cortex (dlPFC), but decreased MEG signals in anterior cingulate cortex. Hyperactivations in FP, OFC, and anterior dlPFC were associated with slower reaction times. MEG activations in lateral FP also negatively correlated with performance on tests of letter sequencing, verbal fluency, and digit symbol coding. The profound hyperactivations from FP suggest that FP is particularly vulnerable to combat-related mTBI.

Elderly Persons Without Dementia.

Carvalho DZ[1], St Louis EK[1], Knopman DS[1], Boeve BF[1], Lowe VJ[2], Roberts RO[1,3], Mielke MM[1,3], Przybelski SA[3], Machulda MM[4], Petersen RC[1], Jack CR Jr[2], Vemuri P[2].

JAMA Neurol. **2018 Mar 12**. doi: 10.1001/jamaneurol.2018.0049. PMID: 29532057. [Epub ahead of print]

Importance: Aging is associated with excessive daytime sleepiness (EDS), which has been linked to cognitive decline in the elderly. However, whether EDS is associated with the pathologic processes of Alzheimer disease remains unclear.

Objective: To investigate whether EDS at baseline is associated with a longitudinal increase in regional β-amyloid (Aβ) accumulation in a cohort of elderly individuals without dementia.

Design, Setting, and Participants: This prospective analysis included participants enrolled in the Mayo Clinic Study of Aging, a longitudinal population-based study in Olmsted County, Minnesota. Of 2900 participants, 2172 (74.9%) agreed to undergo carbon 11-labeled Pittsburgh compound B positron emission tomography (PiB-PET). We included 283 participants 70 years or older without dementia who completed surveys assessing sleepiness at baseline and had at least 2 consecutive PiB-PET scans from January 1, 2009, through July 31, 2016, after excluding 45 (13.7%) who had a comorbid neurologic disorder.

Main Outcomes and Measures: Excessive daytime sleepiness was defined as an Epworth Sleepiness Scale score of at least 10. The difference in Aβ levels between the 2 consecutive scans (ΔPiB) in Aβ-susceptible regions (prefrontal, anterior cingulate, posterior cingulate-precuneus, and parietal) was determined. Multiple linear regression models were fit to explore associations between baseline EDS and ΔPiB while adjusting for baseline age, sex, presence of the apolipoprotein E ε4 allele, educational level, baseline PiB uptake, global PiB positivity (standardized uptake value ratio ≥1.4), physical activity, cardiovascular comorbidities (obesity, hypertension, hyperlipidemia, and diabetes), reduced sleep duration, respiratory symptoms during sleep, depression, and interval between scans.

Results: Of the initial 283 participants, mean (SD) age was 77.1 (4.8) years; 204 (72.1%) were men and 79 (27.9%) were women. Sixty-three participants (22.3%) had EDS. Baseline EDS was significantly associated with increased regional Aβ accumulation in the anterior cingulate (B coefficient = 0.031; 95% CI, 0.001-0.061; P = .04), posterior cingulate-precuneus (B coefficient = 0.038; 95% CI, 0.006-0.069; P = .02), and parietal (B coefficient = 0.033; 95% CI, 0.001-0.065; P = .04) regions. Association of EDS with longitudinal Aβ accumulation was stronger in participants with baseline global PiB positivity in the anterior cingulate (B coefficient = 0.065; 95% CI, 0.010-0.118; P = .02) and cingulate-precuneus (B coefficient = 0.068; 95% CI, 0.009-0.126; P = .02) regions.

Conclusions and Relevance: Baseline EDS was associated with increased longitudinal Aβ accumulation in elderly persons without dementia, suggesting that those with EDS may be more vulnerable to pathologic changes associated with Alzheimer disease. Further work is needed to elucidate whether EDS is a clinical marker of greater sleep instability, synaptic or network overload, or neurodegeneration of wakefulness-promoting centers. Early identification of patients with EDS and treatment of underlying sleep disorders could reduce Aβ accumulation in this vulnerable group.

OTHER RESEARCH OF INTEREST (Continued)

Effects of yogic exercises on functional capacity, lung function and quality of life in participants with obstructive pulmonary disease: a randomized controlled study.

Papp ME[1], Wändell PE[2], Lindfors P[3], Nygren-Bonnier M[4,5].

Eur J Phys Rehabil Med. **2017 Jun**;53(3):447-461. doi: 10.23736/S1973-9087.16.04374-4. PMID: 27830924. Epub 2016 Nov 10.

BACKGROUND: Knowledge of hatha yogic exercises, the most used yoga style, for increasing functional capacity in patients with obstructive pulmonary diseases remains limited.

AIM: The aim was to evaluate the effects and feasibility of hatha yoga (HY) compared to a conventional training program (CTP) on functional capacity, lung function and quality of life in patients with obstructive pulmonary diseases.

DESIGN: Randomized clinical trial.

SETTING: The study was performed at the Karolinska University Hospital, Stockholm, among outpatients.

POPULATION: Thirty-six patients with obstructive pulmonary disease.

METHODS: Forty patients were randomized with 36 (24 women, median age = 64, age range: 40-84 years) participating in HY (N.=19) or CTP (N.=17). Both HY and CTP involved a 12-week program with a 6-month follow-up. Functional capacity (using the 6-Minute Walk Test), lung function (spirometry), respiratory muscle strength (respiratory pressure meter), oxygen saturation (SpO2), breathlessness (Borg), respiratory rate (f) and disease-specific quality of life (CRQ) were measured at baseline, at 12 weeks and at a 6-month follow-up.

RESULTS: Testing for interactions (group x time) with ANOVAs showed significant effects on the CRQ fatigue (P=0.04) and emotional (P=0.02) domains, with improvements in the CTP group after the 12-week intervention (P=0.02 and 0.01, respectively) but not in the HY group. No between group effects emerged, however, within each group, significant improvements emerged for the six-minute walk distance (6MWD) after 12-week intervention (HY: mean difference 32.6 m; CI: 10.1-55.1, P=0.014; CTP: mean difference 42.4 m; CI: 17.9-67.0, P=0.006).

SECONDARY OUTCOMES: within-group improvements in CRQ appeared in both groups. Within the HY group, f decreased and SpO2 increased. Improved effects after follow-up emerged only for the CTP group for diastolic blood pressure (P=0.05) and CRQ emotional and fatigue domain (P=0.01).

CONCLUSIONS: There were no between-group differences. After 12 weeks, 6MWD improved significantly within both groups. Within the HY group, improvements in the CRQ mastery domain, f and SpO2 emerged. Within the CTP group, there were improvements in lung function parameter forced vital capacity, respiratory muscle strength and all CRQ-domains. The CTP also exhibited effects on CRQ after the 6-months follow-up.

CLINICAL REHABILITATION IMPACT: Limited effects of HY and CTP emerged. HY seems feasible and safe as a form of physical exercise for pulmonary disease patients. As part of the rehabilitation, HY may constitute an alternative to other physical training activities and may be a useful addition to formal rehabilitation programs.

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