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Volume 23 Number 5 Published by Physicians In Physical Medicine and Rehabilitation May 5, 2015

PREVENTING DELAYED ONSET MUSCLE SORENESS WITH SAFFRON

Delayed onset muscle soreness after eccentric exercise leads to muscle swelling, elevated creatinine kinase, lactate dehydrogenase and reduced strength. Saffron, a spice whose compounds have been found to have anti-inflammatory and anti-nociceptive activities, was evaluated for its effects on muscle soreness and strength following eccentric exercise.

Thirty-nine subjects were randomized to one of three groups to receive three identical capsules per day beginning one week before, and continuing three days after, an exercise protocol. These included saffron powder at 300 mg per day, indomethacin at 25 mg three times per day or a placebo capsule three times per day. All subjects underwent a muscle soreness protocol using a leg press machine with the weight loaded to 80% of their maximum isotonic force in four sessions with 20 repetitions. The groups were compared for muscle soreness at 24, 48 and 72 hours post-exercise.

In the control group, there was a significant decline in the maximum isotonic force at 24 hours (15.3%), 48 hours (23.8%), and 72 hours (24.3%) after the eccentric protocol. Creatinine kinase concentrations were increased in the placebo group, peaking at 48 hours (125.8%), while the saffron group increased by 3.7% at 24 hours and then returned to normal. In addition, LDH levels were less in the saffron group than in the placebo group ($p<0.001$). The saffron group had less pain than the placebo group at 24, 48 and 72 hours ($p<0.001$), with no pain in the saffron group at 48 and 72 hours. In the indomethacin group, pain was alleviated after 72 hours.

Conclusion: This study indicates that a 10-day supplementation with saffron has a preventative effect on delayed onset muscle soreness and loss of strength following eccentric exercise.

Meamarbashi, A., et al. Preventative Effects of 10-Day Supplementation with Saffron and Indomethacin on the Delayed Onset Muscle Soreness. **Clin J Sports Med.** 2015, March; 25 (2): 105-112.

PURPOSE IN LIFE AND CEREBRAL INFARCTION

Purpose in life is a key component of psychological well-being. Previous studies have demonstrated that older people with a greater sense of purpose are less likely to develop adverse health outcomes including mortality, decline in physical function, frailty and disability. This study examined the association of purpose in life with cerebral infarctions.

Data were derived from the Rush Memory and Aging Project, a clinical-pathological cohort study of aging and dementia. Each participant was assessed annually with a standard measure of purpose in life, and followed over time for evidence of cerebral infarction. At the time of these analyses, 719 participants had died, with the majority of these undergoing autopsy. The primary outcome measure was the association between purpose in life scores and cerebral infarctions, as detected on autopsy.

Of the 453 individuals examined by autopsy, 25.3% had sustained a clinical stroke, and 47.7% had macroscopic or microinfarcts detected on autopsy. Those with a greater purpose in life had a lower odds of having more macroscopic infarcts ($p=0.005$), although the association with microinfarcts did not reach clinical significance ($p=0.283$). These results persisted after controlling for vascular risk factors.

Conclusion: This study found that individuals with a reduced purpose in life, documented in community dwelling people without dementia, are at greater risk for cerebral infarction, particularly macroscopic lacunar infarcts.

Yu, L., et al. Purpose in Life and Cerebral Infarcts in Community-Dwelling Older People. **Stroke.** 2015, April; 46(4): 1071-1076.

OPIOIDS FOR DIABETIC PERIPHERAL NEUROPATHY

It is estimated that 20% of all diabetic patients experience chronic neuropathic pain. Only duloxetine and pregabalin are currently approved by the FDA for treating diabetic peripheral neuropathy (DPN). Tramadol or opioids are generally recommended as third line agents for moderate to severe pain. This study was designed to better understand the opioid prescription patterns for patients with DPN.

A 10% random sample of IMS-Lifelink Health Plan claims data were obtained from 1998 to 2008. Adult patients were identified with a diagnosis of DPN, with data further assessed for demographics, comorbidities and medication prescriptions. Medications considered as prescribed for DPN included opioids, antidepressants, anticonvulsants, nonsteroidal anti-inflammatory drugs, topical agents and skeletal muscle relaxers.

A total of 363,241 patients diagnosed with diabetes were identified, with 666 meeting all the inclusion criteria. Of patients with DPN, pharmacologic treatment for the DPN was observed for 43.2%. Of those who received DPN related pharmacologic treatment, 53.47% were prescribed opioids. The most common first-line agents for DPN were opioids 33%, antidepressants 26.39%, anticonvulsants 22.5%, nonsteroidal anti-inflammatory drugs 19.09% and skeletal muscle relaxants 5.21%. The FDA approved agents,

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duloxetine and pregabalin, were used in 1.04% and 5.56% of the cases, respectively. Twenty-two percent of DPN patients exclusively used opioids for DPN.

Conclusion: This study found that, of patients with diabetic peripheral neuropathy, 57% did not receive prescription pharmacologic treatment. Among those with prescriptions, opioids were the most frequently prescribed, first-line agents.

Patil, P., et al. Opioid Use in the Management of Diabetic Peripheral Neuropathy (DPN) in a Large Commercially Insured Population. **Clin J Pain.** 2015, May; 31(5): 414-424.

PRE-EXISTING SLEEP PATTERNS AND RECOVERY FROM CONCUSSION

Although the association between poor sleep hygiene and declining neurocognitive function has previously been demonstrated, it is unclear whether pre-injury sleep patterns affect recovery from sport-related injury. This study assessed neurocognitive impairment and symptoms among athletes presenting with concussion, comparing those with and those without self-reported premorbid sleep difficulties.

This prospective study included athletes, 14 to 23 years of age with a baseline neurocognitive assessment and a diagnosis of sports related concussion (SRC). Outcome measures included Immediate Post-Concussion Assessment and Cognitive Test (ImPACT) and Postconcussion Symptom Scale (PCSS) results, as well as sleep difficulties, characterized as difficulty falling asleep or sleeping less than usual. Postconcussive data were compared between the athletes with pre-existing sleep difficulties and those without.

Significantly worse performance was found in the poor sleep group for measures of verbal memory, visual memory and reaction time as compared with controls. While the differences between groups were no longer apparent after seven days for verbal memory and reaction time, visual memory was worse in the poor sleep group for up to 14 days. Patients in the poor sleep group reported higher total symptoms and sleep-related symptoms than did the control group.

Conclusion: This study of collegiate athletes with concussion found that pre-injury sleep difficulties were correlated with decreased post-concussion neurocognitive performance and increased symptoms.

Sufrinko. A., et al. Effect of Pre-Injury Sleep Difficulties on Neurocognitive Impairment and Symptoms after Sport Related Concussion. **Am J Sports Med.** 2015, April; 43(4): 830-838.

TIME TO RETURN TO TRAINING AFTER STRESS FRACTURES

The incidence of stress fractures in military recruits can be as high as 12%. In addition, those who sustain a stress fracture during basic training are at higher risk of subsequent stress fractures. As little is known about the length of time required for rehabilitation and return to pre-injury level of physical activity after these injuries, this study used longitudinal prospective data to help clarify this issue.

Subjects were 4,200 Marines undergoing commando training between April of 2004 and April of 2008. Among these, 220 stress fractures were diagnosed. When diagnosed, the patients were removed from training and placed in physiotherapy and rehabilitation. When fully recovered, they were placed in a recovery group to regain fitness and military skills. Data were reviewed for stress fracture type and course of recovery.

The most common stress fracture sites were metatarsal 65%, tibia 24%, femur 10%, and fibula 3%. The mean rehabilitation time for a single metatarsal was 12.2 weeks, multiple metatarsals 15.4 weeks, tibia 21.1 weeks, fibula 13.3 weeks and femur 21.1 weeks.

Conclusion: This four-year study of military recruits in commando training identified a stress fracture prevalence of five percent, with recovery times ranging from 12.2 weeks to 21.1 weeks, depending upon the site of the fracture.

Would, A., et al. Incidence and Time to Return to Training for Stress Fractures during Military Basic

Training. **J Sports Med**. 2014. 10.1155/2014/282980

ATHLETE RECALL VERSUS CLINICALLY DOCUMENTED CONCUSSION

Recurrent concussion is thought to be associated with adverse health effects, including cognitive, neurobehavioral and somatic conditions. A weakness in the knowledge of the long-term effects of concussion in the former athlete is the absence of information regarding the validity of athlete recall. This study estimated the agreement between athlete recall and clinically documented concussion.

Former college athletes who had played at the University of North Carolina at Chapel Hill between 1987 and 2012 were sent online Qualtrics questionnaires concerning concussion history. The participants were asked to report the number of concussions that they had sustained during participation in high school, college and professional sport. For those with concussions during college, the athletes were asked the dates of injuries. The participants were asked about impacts that they had sustained which they thought should have been, but had not been, diagnosed as concussions by team medical staff. Responses to these questionnaires were linked to clinical records collected by the University athletic department concerning concussions during participation.

The recall data indicated that 43.8% had sustained one or more concussions during college, with 40.8% occurring during collegiate sports. The clinically documented concussion data indicated that 22.3% had sustained one or more concussions during college. The athletes failed to recall 31.6% of the clinically documented concussions, with no clinical documentation associated with 79.6% of the athlete-recalled concussions. Of those who did not disclose their concussions, 90.9% did not think that the event was serious enough to report.

Conclusion: This study of former collegiate athletes found a low agreement between athlete recalled and clinically documented concussion history.

Kerr, Z., et al. Agreement between Athlete – Recalled and Clinically Documented Concussion Histories in Former Collegiate Athletes. **Am J Sport Med.** 2015, March; 43: 606-612.

ANTIPLATELET THERAPY FOLLOWING LACUNAR STROKE

Lacunar stroke, or small vessel ischemic stroke, represents approximately 25% of all ischemic strokes. As the optimal antiplatelet treatment for the secondary prevention of stroke remains unclear, this literature review and meta-analysis was designed to better understand the efficacy of antiplatelet agents in the setting of lacunar stroke.

A literature search was conducted for randomized, controlled trials evaluating the use of antiplatelet therapy as a secondary prevention after acute lacunar stroke. The primary outcome of interest was any stroke recurrence.

This literature review included 17, randomized trials with 42,234 participants with lacunar stroke who were treated with antiplatelet therapy or placebo. Those treated with antiplatelet monotherapy had significantly lower rates of any stroke than those administered a placebo (a relative risk of 0.77). The meta-analysis revealed no significant advantage of any single antiplatelet agent above aspirin alone. However, dual anti-platelet therapy was found to have a modest advantage over aspirin alone.

Conclusion: This literature review and meta-analysis suggests that any single antiplatelet agent, including aspirin, clopidogrel or ticlopidine, can be effective in secondary stroke prevention after lacunar infarct.

Kwok, C., et al. Efficacy of Antiplatelet Therapy in Secondary Prevention following Lacunar Stroke. Pooled Analysis of Randomized Trials. **Stroke**. 2015, April; 46(4): 1014-1023.

CREATINE AND CO-ENZYME Q 10 FOR MILD COGNITIVE IMPAIRMENT IN PARKINSON'S DISEASE

Creatine and coenzyme Q 10 are important, active components of energy metabolism in mitochondria with known protective effects against neurodegenerative diseases. This study was designed to determine the effects of combining creatine and coenzyme Q 10 on the cognitive function of patients with Parkinson's disease (PD) related cognitive impairment.

This study included 75 patients diagnosed with PD, each with confirmed, gradually declining cognitive function. All were assessed with the Unified Parkinson's Disease Rating Scale (UPDRS) at baseline and again at 12 and 18 months. The subjects were initially assessed with the Montréal Cognitive Assessment (MoCA) and for plasma phospholipid levels. The participants were randomized to a treatment group receiving creatine monohydrate at 5 g BID and oral Coenzyme Q 10 at 100 mg three times per day, or a control group receiving placebo capsules.

After 12 and 18 months, MoCA scale scores of the treatment group were significantly higher than those of the control group ($p<0.05$, and $p<0.01$, respectively). In addition, at 12 and 18 months follow-up, the treatment group's phospholipid levels were significantly lower than those of the controls ($p<0.01$ and $p<0.01$, respectively). After 12 and 18 months, no significant differences were found between the two groups in UPDRS scores.

Conclusion: This study of patients with Parkinson's disease and mild cognitive impairment found a positive effect in delaying the decline in cognitive function of these patients with the daily use of Coenzyme Q10 and creatine.

Wanag, L., et al. The Effect of Creatine and Coenzyme Q 10 Combination Therapy on Mild Cognitive Impairment in Parkinson's Disease. **Euro Neurol**. 2015, April; 75(3-4): 205-211.

EARLY STATIN USE IN ACUTE INTRACEREBRAL HEMORRHAGE

Hemorrhagic stroke accounts for 10 to 15% of all strokes, and carries a high, early mortality rate. In patients with intracerebral hemorrhage (ICH) who have been discharged from the hospital, recurrent ischemic cardiovascular events, including stroke and myocardial infarction, are common. While statins have been shown to reduce the risk of such

ischemic events, previous studies have suggested that statins may also increase the risk of hemorrhagic stroke. This study was designed to better understand whether early statin therapy in patients with ICH affects the risk of recurrent ICH and mortality.

A total of 8,332 adult patients, admitted for ICH, and with no recent history of statin use, were included in this study. Subjects who were prescribed at least one statin during hospitalization or within three months of discharge were assigned to the early statin group, while the remaining patients were assigned to the control group. The participants were followed for recurrent ICH with the secondary outcome being all-cause mortality.

Of the 8,332 patients, 749 had early statin therapy. At two-year follow-up, an adjusted multivariate analysis determined that early statin use did not increase the risk of recurrent ICH. Overall, those in the statin group had a lower, all-cause mortality than did the control group (adjusted hazard ratio: 0.742).

Conclusion: This study of patients with acute intracerebral hemorrhage found that statin use, initiated during or shortly after hospitalization, does not significantly increase the risk of recurrent hemorrhage, but does decrease the risk of all-cause mortality.

Chen, P., et al. Early Statin Therapy in Patients with Acute Intracerebral Hemorrhage without Prior Statin Use. **Euro J Neurol**. 2015, May; 22(5): 773-780.

COMPARISON BETWEEN TIBIAL NERVE BLOCK AND NEUROTOMY FOR SPASTIC EQUINOVARUS FOOT

Spastic equinovarus foot is a common deformity among patients with hemiplegia. Treatment for this condition includes physical therapy, stretching, orthoses, functional electrical stimulation, chemical neurolysis with phenol, alcohol, botulinum toxin, tendon transfers and selective tibial neurotomy. This study compared the effect of a diagnostic motor nerve block with anesthetics, with that of a selective tibial neurotomy.

Patients were consecutively recruited by an interdisciplinary spasticity group at a university hospital. All participants underwent a diagnostic nerve block with a one mL dose of lidocaine 2% at the different motor branches of the tibial nerve until the triceps spasticity had disappeared. The patients then underwent a neurotomy of the same branches of the tibial nerve. Before and after diagnostic nerve block, and two months and two years after selective tibial neurotomy, spasticity, muscle strength, passive range of ankle motion, gait parameters and gait kinematics were assessed.

Of the 144 consecutive patients who benefited from a diagnostic nerve block, 49 met the inclusion and exclusion criteria, and underwent surgery. Thirty of the 49 patients completed the study. At two-year follow-up the decrease in spasticity and improvement in gait kinematics were similar after the diagnostic nerve block and two years after neurotomy.

Conclusion: This study of patients with spastic equinovarus foot secondary to hemiplegia found that a diagnostic nerve block with anesthetics is an effective tool in predicting the result of a tibial neurotomy.

Deltombe, T., et al. Comparison between Tibial Nerve Block with Anesthetics and Neurotomy in Hemiplegic Adults with Spastic Equinovarus Foot. **Ann Phys Rehab Med**. 2015, April; 58(2): 54-59.

ROTATOR CUFF RECONSTRUCTION IN WHEELCHAIR BOUND PATIENTS

Of patients with paraplegia, 32 to 67% have complaints of pain and limitation of movement, with rotator cuff tears common in this population. This study assessed the effect of rotator cuff repair in patients with paraplegia.

This retrospective study included patients with paraplegia who underwent rotator cuff repair between October of 1995 and October of 2011. All patients had full thickness rotator cuff tears with surgical repair and postoperative rehabilitation. After surgery, a shoulder abduction brace was applied for eight weeks. The functional evaluation included pre- and postoperative pain scores, range of motion, muscle power, American Shoulder and Elbow Surgeons (ASES) scores, and Constant scores. Tendon integrity was evaluated by MRI at an average of 31.2 months post-surgery.

At follow-up, ASES scores had improved from 53 to 85 points ($p<0.001$). Constant scores had improved from 48 to 75 points ($p<0.001$). The ASES scores were above 80 points in 87.5% of the patients, indicating satisfactory results. Structural integrity of the repair was maintained in 88% of the patients, while recurrent tears were observed in 12%.

Conclusion: This study of patients with paraplegia who were wheelchair ambulators with rotator cuff tears found that rotator cuff repair surgery can provide satisfactory functional outcomes.

Jung, H., et al. Reconstruction of Rotator Cuff Tears in Wheelchair Bound Paraplegic Patients. **J Should Elbow Surg.** 2015, April; 24(4): 601-605.

SHORT-TERM USE OF NONSTEROIDAL ANTI-INFLAMMATORY DRUGS AND STROKE RISK AMONG HYPERTENSIVE PATIENTS

Previous studies have suggested an association between selective and nonselective nonsteroidal anti-inflammatory drugs (NSAIDs) and the risk of cardiovascular and cerebrovascular events. Limited data exist, concerning patients taking these medications who are at an increased risk of vascular disease. This study examined the short-term effect of selective and nonselective NSAIDs on the risk of ischemic or hemorrhagic stroke among patients with hypertension.

Data for this study were obtained from the National Health Insurance Research Database in Taiwan. Patients were identified with an incident stroke in 2010, each of whom was diagnosed with hypertension. Each was matched with a control. Data were also reviewed to identify prescriptions of NSAIDs, including selective COX-2 inhibitors and nonselective NSAIDs, within 30 days of stroke (study period), and at 91 to 120 days before the stroke (control period). Data were analyzed to determine the effect of recent prescriptions for NSAIDs and the subsequent risk of stroke.

Of the 1,653 patients with hypertension who were hospitalized for stroke in 2010, 84% were admitted for ischemic, and 16% for hemorrhagic, stroke. The use of NSAIDs during the 30 days before stroke was associated with a 1.51 fold increased risk of stroke and a 1.57 fold increased risk of ischemic stroke. Nonselective NSAIDs significantly increased the risk of stroke, with an adjusted odds ratio (AOR) of 1.54, ischemic stroke AOR of 1.55 and hemorrhagic stroke AOR of 1.56.

Conclusion: This study of hypertensive patients found that the recent use of nonsteroidal anti-inflammatory drugs increases the risk of ischemic stroke.

Chuang, S., et al. Association of Short-Term Use of Nonsteroidal Anti-Inflammatory Drugs with Stroke in Patients with Hypertension. **Stroke**. 2015, April; 46(4): 996-1003.

CAROTID INTIMA-MEDIA THICKNESS AND COGNITION IN THE ELDERLY

Previous studies have demonstrated that increased carotid intima-media thickness (CIMT) is a surrogate marker of atherosclerosis and a strong predictor of future vascular events. This study assessed the association between cardiovascular risk factors, including CIMT, and the risk of clinically diagnosed mild cognitive impairment (MCI) or dementia.

This study was conducted as part of the Korean Longitudinal Study on Health and Aging, a prospective, cohort study of Korean elders, ages 65 years or older. Patients underwent assessment of cardiovascular disease risk factors and surrogate markers, including anthropometric and biochemical parameters, ultrasound measurement of the CIMT and assessment of plaque formation of the carotid artery. Patients were also assessed at baseline and follow-up for cognitive impairment.

At baseline, 278 subjects were cognitively normal and 70 had MCI. After five years, 261 subjects were cognitively normal, 81 had MCI and six had dementia. Patients whose cognitive impairment progressed had a higher prevalence of hypertension and a greater CIMT compared to those who did not progress. The cutoff value of baseline CIMT which predicted the development of MCI was 0.805 mm, with MCI developing in 12.7% of those with a CIMT of less than and 27.5% of those with a CIMT greater than 0.805 mm.

Conclusion: This longitudinal study of Korean subjects found that carotid intima media thickness is associated with the progression of cognitive impairment among elderly individuals.

Moon, J., et al. Carotid Intima Media Thickness Is Associated with the Progression of Cognitive Impairment in Older Adults. **Stroke.** 2015, April; 46(4): 1024-1030.

ELEVATED CALCIUM AFTER ACUTE ISCHEMIC STROKE

Previous studies have demonstrated that calcium can influence the cascade of events leading to neuronal injury. This study further assessed the association between serum calcium levels and outcome after stroke.

Subjects were patients with acute ischemic stroke, admitted to a university hospital between 2002 and 2008, within seven days of symptom onset. Data were gathered concerning patients' stroke subtype, National Institutes of Health Stroke Scale (NIHSS) score at the time of admission, thrombolytic treatment and modified Rankin scale (mRS) score at discharge. Baseline demographics and clinical characteristics were obtained, with the latter including serum levels of glucose, hemoglobin A-1 C, lipids and albumin corrected calcium levels. These levels were compared to mortality.

Patients enrolled in this study included 1,915 patients with stroke, with a mean age of 65.7 years. The mean follow-up period was 917 days, with a mortality rate of 1.6% at one month post-admission, and an overall mortality rate of 17.3%. The second ($p<0.01$) and third ($p<0.04$) tertile of serum calcium level, and the third tertile ($p<0.04$) of albumin corrected calcium level, were all found to be independent risk factors for poor outcome (mRS) at discharge. The third tertile of serum calcium level was found to be an independent risk factor for long-term mortality ($p=0.02$). The albumin corrected calcium was associated with long-term mortality. In addition, male gender, age, serum glucose level, serum triglyceride level, serum albumin level, stroke subtype and NIHSS scores on admission were significantly associated with long-term mortality.

Conclusion: This study found that high levels of albumin corrected calcium are associated with a worse discharge outcome and increased incidence of mortality after acute ischemic stroke.

Chung, J., et al. Elevated Calcium after Acute Ischemic Stroke: Association with Poor Short-Term Outcome and Long-Term Mortality. **J Stroke.** 2015, January; 17(1): 54-59.

OBESITY PARADOX IN STROKE

Obesity is related to an increased risk of cardiovascular disease, and is recognized as an important risk factor for primary stroke. Studies of patients with established cardiovascular disease have, however, found that overweight/obese patients tend to have a more favorable prognosis, referred to as the obesity paradox. This study investigated the association between obesity and mortality, as well as hospital readmission.

Subjects were identified from discharges from the hospitals of the Spanish Public Health Service between 2005 and 2011. Cases were selected if they were discharged with a diagnosis of cerebrovascular disease. Outcomes were compared between patients with a diagnosis of obesity and those with a lower body mass index.

A total of 201,272 patients were discharged with acute stroke, with a median age of 70 years. Of those, 14,047 were obese. Using a multivariable logistic regression analysis, it was determined that obese patients had a 29% lower risk of mortality than did those who were not obese. After adjusting for potential confounding factors, patients with obesity were less likely to be readmitted for stroke, with an odds ratio of 0.89.

Conclusion: This Spanish study found that, among patients hospitalized with stroke, those with obesity had less in-hospital mortality, and a reduced risk of readmission for stroke.

Barba, R., et al. The Obesity Paradox in Stroke: Impact on Mortality and Short-Term Readmission. **J Stroke Cerebrovasc Dis.** 2015, April; 24(4): 766-770.

EFFECT OF EXERCISE ON ABDOMINAL OBESITY AND GLUCOSE TOLERANCE

Exercise is thought to be important for individuals who wish to reduce obesity and related glucose tolerance. This randomized, clinical trial investigated the separate effects of habitual exercise, differing in amount and intensity, on abdominal obesity and glucose tolerance.

This randomized, controlled trial included 300 sedentary, obese adults. The subjects were randomized to a control group receiving no exercise (C), a low amount/low intensity group (LALI), a high amount/low intensity (HALI) group and a high amount high-intensity group (HAHI). Target heart rates were adjusted to maintain VO_2 peak at 50% for the low intensity and 75% for the high-intensity groups, respectively. At these exercise intensities, the target amounts of exercise for women and men, respectively, were 180 and 300 kcal for the low amount group, and 360 and 600 kcal for the high amount groups. The primary outcome measures were waist circumference and two-hour glucose tolerance, measured at baseline, 16 weeks and 24 weeks. Secondary measures included measures of cardiovascular fitness.

Reductions in the waist circumference at 24 weeks were greater in all exercise groups ($p<0.001$ for all) than the control group, but did not differ between the exercise groups. Reductions in the two-hour glucose levels at 24 weeks were greater in the HAHI group than in the control ($p=0.027$) and LALI ($p=0.03$) groups. No significant changes were noted for the LALI or HALI groups. Compared with the control group, body weight and cardiorespiratory fitness levels were significantly improved in all exercise groups, although cardiorespiratory fitness improved with increased volume and intensity of exercise.

Conclusion: This study of patients with abdominal obesity found that obesity decreases with exercise, regardless of intensity, although only high-intensity exercise can reduce two-hour glucose levels.

Ross, R., et al. Effects of Exercise Amount and Intensity on Abdominal Obesity and Glucose Tolerance in Obese Adults. **Ann Intern Med**. 2015, March 3; 162(5): 325-334.

EXERCISE THERAPY AND INFLAMMATORY MARKERS FOR KNEE OSTEOARTHRITIS

The knee is the joint most commonly affected by osteoarthritis (OA). Although initially considered a non-inflammatory disease, recent studies have demonstrated the role of cytokines and prostaglandins in cartilage destruction. This study assessed the effects of an exercise therapy protocol on physical performance, pain and inflammatory markers.

Subjects included ambulatory patients with radiographically demonstrated OA of the knee. Excluded were those with a history of ligament or meniscus injury at the knee, or other medical issues that might reduce their ability to participate. All participants underwent 12 weeks of training involving three, weekly, 80-minute sessions, including strength and flexibility exercises. Three sets were performed for each muscle group. Before and after the exercise intervention, blood was collected for measures of inflammatory markers, including IL-6, TNF-alpha and soluble TNF-alpha receptors. Pain perception was measured using the visual analogue scale (VAS), as well as the WOMAC.

The average VAS score was decreased from 6.6 at baseline to 2.5 after training ($p<0.001$). The stiffness subscale, the physical functional subscale, as well as the global scale of the WOMAC were all significantly improved after training ($p<0.004$, $p<0.001$ and $p<0.001$, respectively). After the exercise protocol, a reduction was seen in serum IL-6, with the other markers failing to show a statistically significant change.

Conclusion: This study of patients with osteoarthritis of the knee found that strengthening exercise could reduce some markers of inflammation, while decreasing pain and increasing function.

Aguiar, G., et al. Effects of Exercise Therapy Protocol on Inflammatory Markers, Perception of Pain and Physical Performance in Individuals with Knee Osteoarthritis. **Rheumat Intern.** 2015, March; 35(3): 525-531

NEUROENDOCRINE DYSFUNCTION IN ACUTE BRAIN INJURY

Hypopituitarism due to traumatic brain injury (TBI) can occur in up to 50% of patients. While the typical consequences of TBI include disorders of consciousness, attention, impulsive behavior, depression and sleep, some of these symptoms might be a consequence of anterior pituitary insufficiency. This study was designed to determine the prevalence of anterior pituitary hormone deficiencies in the acute phase of moderate to severe TBI.

One hundred, consecutive patients with moderate to severe TBI were studied. The participants underwent clinical assessment, with severity of injury assessed by initial Glasgow Coma Scale (GCS) results. The patients were further assessed with the Glasgow Outcome Scale (GOS). Subjects with scores of four or five were placed in a good outcome group, and those with scores of one, two or three were placed in a bad outcome group.

Of the hundred subjects, 52% had moderate, and 40% had severe, TBIs. The percentage of patients with low fT3 was 26%, fT4 12%, TSH 4%, growth hormone 28%, cortisol 2% and prolactin 6%. Thirty percent had an increased cortisol level. On day seven, the percentage of patients with a low hormone profile of fT3 was 14.89%, fT4 46.8%, TSH 44.68%, growth hormone 48.93%, cortisol 2.12% and prolactin 4.25% while 21. 27% had increased cortisol levels. The patients with severe TBI, with pressure effects and a poor GOS scores, had more abnormal hormone profiles than did patients with moderate TBI, without pressure effects and a good GOS.

Conclusion: This prospective study found that neuroendocrine dysfunction is common in the acute phase of moderate to severe traumatic brain injury, and that there is a correlation with severity of injury, Glasgow Outcome Scale and radiological findings.

Prasanna, K., et al. Neuroendocrine Dysfunction in the Acute Phase of Moderate to Severe Traumatic Brain

Injury: A Prospective Study. **Brain Inj.** 2015, March; 29(3): 336-342.

VISUAL EVOKED POTENTIALS TO ASSESS VISUAL ATTENTION IN MILD TRAUMATIC BRAIN INJURY

Due to its global nature, mild traumatic brain injury (mTBI) often results in a constellation of deficits, including sensory, motor, perceptual, linguistic, cognitive and behavioral. This study investigated the use of visual evoked potentials (VEPs) as a means to quantify visual attention among patients with mTBI.

Subjects were 16 individuals with mTBI, of whom 11 had self-reported visual/general attention deficits, and five who did not. All patients were assessed with a VEP test, with five trials for each of three test conditions, including conventional VEP, Eyes Closed (EC), and Eyes Closed Number Counting (ECNC). Patients were also assessed with the Visual Search and Attention Test (VSAT). The adult ADHD Self-Report Scale (ASRS) was used as a screening tool for general attention deficit. The different VEP tests were quantified using the VEP alpha attenuation ratio (AR).

The AR at each Alpha frequency differentiated between those with and without attention deficit. The AR for individual as well as for combined frequencies was abnormal among those with mTBI and an attention deficit. The AR was normal for those without an attention deficit. Similar results were obtained when the AR was combined across the alpha frequency band.

Conclusion: This study of patients with mild traumatic brain injury suggests that visual evoked potentials may be useful to differentiate objectively between those with and without an attentional deficit.

Yadav, N., et al. Objective Assessment of Visual Attention in Mild Traumatic Brain Injury (mTBI) Using Visual- Evoked Potentials (VEPs). **Brain Inj.** 2015, March; 29 (3): 352-365.

NATALIZUMAB IMPROVES AMBULATION IN MULTIPLE SCLEROSIS

Issues with mobility present a significant challenge for patients with multiple sclerosis (MS), and can lead to reduced quality-of-life. Natalizumab, an alpha 4-integrin antagonist, has been found to affect disease activity and reduce relapse rates among those with relapsing remitting multiple sclerosis (RRMS). This study examined the effect of natalizumab on ambulation in patients with RRMS.

This study included data from two, large, prospective studies of natalizumab for patients with RRMS. The TIMER was an international, multicenter, open label, prospective study of 215 subjects who received natalizumab, 300 mg IV, every four weeks for 48 weeks. The patients were assessed with a timed, 25-foot walk (T25FW) test and a timed, 100-m walk (T100MW) test at baseline, 24 and 48 weeks. AFFIRM was a randomized, placebo-controlled, double-blind, phase 3 study, including 942 patients with RRMS. Eligible subjects received natalizumab, 300mg or placebo, every four weeks for up to 116 weeks. Those patients were assessed using a T25FW every 12 weeks for 30 months.

In TIMER, there was an increase in the T100MW speed at weeks 24 and 48, as compared with baseline ($p \leq 0.0001$ for both). In addition, the T25FW speed increased at week 24 ($p=0.0074$), although not at week 48 ($p=0.16$). In AFFIRM, at two years, 78% more of those in the treatment arm showed a 20% or greater improvement in the T25FW, as compared to placebo.

Conclusion: This study of patients with relapsing remitting multiple sclerosis found that natalizumab can improve ambulation.

Voloshyna, N., et al. Natalizumab Improves Ambulation in Relapsing-Remitting Multiple Sclerosis: Results from the Prospective TIMER Study and a Retrospective Analysis of AFFIRM. **European J Neurol.** 2015, March; 22(3): 570-577.

INTRA-ARTICULAR INJECTIONS IN THUMB OSTEOARTHRITIS

Osteoarthritis (OA) of the carpometacarpal joint of the thumb is thought to affect at least 30% of women over the age of 65. While intra-articular corticosteroid use is often studied in patients with hip and knee OA, studies of intra-articular therapy for thumb OA are scarce. This systematic literature review was designed to better assess the effects of intra-articular injections for OA of the thumb.

A systematic literature review was performed of studies of OA of the thumb, which included treatment with intra-articular injections of corticosteroids and/or hyaluronic acid. Outcome measures included pain and/or functional capacity and/or pinch force.

The meta-analysis included 428 patients, with 168 treated with hyaluronic acid, 166 with corticosteroid and 94 with placebo injections. Among studies of hyaluronic acid versus placebo, hyaluronic acid was superior for functional improvement, but not for pain. Among those comparing hyaluronic acid and steroid injections, no difference was noted between the groups at short-term follow-up, although hyaluronic acid seemed superior on pulp pinch force status, while steroids were superior for pain relief at week 24.

Conclusion: This literature review of patients with osteoarthritis of the thumb found corticosteroids to be useful for decreasing pain, while hyaluronic acid may be useful to increase function at 24 weeks after injection. The authors note that the great heterogeneity of the results limits a clear understanding of the efficacy of each.

Him, S., et al. Intra-Articular Injections in Thumb Osteoarthritis: A Systematic Review and Meta-Analysis of Randomized, Controlled Trials. **Joint, Bone, Spine.** DOI:10.1016/ j.jbspin.2015.02.002

EXERCISE PRESCRIPTION AFTER OSTEOPOROTIC VERTEBRAL FRACTURE

Osteoporotic vertebral fracture is common among people with osteoporosis, and is linked with a reduced quality of life. Although exercise is recommended as a component of the management of osteoporosis, it is unclear whether exercise intervention has benefits among those with osteoporotic vertebral fractures. This literature review evaluated the benefits and harms of exercise among adults with a history of osteoporotic vertebral fracture.

A literature review was completed of men and women over the age of 40, with a history of nontraumatic or

(Continued from page 2)

minimal trauma osteoporotic fracture of the vertebrae, treated with exercise. The primary outcome variable was the incidence of future fractures and adverse events.

The literature review identified seven studies, including 480 participants. Four adverse events were reported, including three fractures (fracture of the costal cartilage, rib fracture and metatarsal fracture), that were directly attributable to exercise. For secondary outcomes, the data demonstrated that exercise improves pain, performance on the timed get up and go test, walking speed, back extensor strength, trunk muscle endurance and quality-of-life.

Conclusion: This literature review revealed an absence of large, randomized trials of the effects of exercise on patients with osteoporotic vertebral fractures. The data do, however, suggest that exercise can improve pain, performance and quality of life.

Kasch, R., et al. Exercise Prescription for People with Osteoporotic Vertebral Fracture. **Br J Sport Med.** 2015, April; 49(7): 489-490.

Parisa Salehi, M.D.
U. of Minnesota, Minneapolis, MN

*Thiru Annaswamy, M.D.
Kimberly Davis, M.D.
UTSW Medical Center, Dallas TX

*Ryan Solinsky, M.D.
Erica Bechtel, M.D.
Jaclyn Russell, M.D.
Jen Soo Hoo, M.D.
Sarah Wittry, D.O.
University of Washington, Seattle, WA

*Sean Stockhausen, D.O.
Wiaam Ahmed, M.D.
Greg Condie, D.O.
VCU, Richmond, VA

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ISSN # 1081-1303

www.rehabinreview.com

REHAB IN REVIEW

Produced by the Department of Rehabilitation Medicine, Emory University School of Medicine

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