

REHAB IN REVIEW

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Volume 23 Number 11

Published by Physicians
In Physical Medicine and Rehabilitation

November 5, 2015

EMERGENCY ROOM VISITS FOR DIETARY SUPPLEMENT REACTIONS

Approximately half of the adults in the United States have reported using at least one dietary supplement in the past month. As the regulatory framework for supplements differs from that of prescription or over-the-counter pharmaceuticals, neither safety testing nor FDA approval is required before these substances are marketed. As the safety of dietary supplements remains poorly described, this study was designed to estimate the number of emergency department (ED) visits for adverse events related to dietary supplements.

Data for this study were collected by the National Electronic Injury Surveillance System-Cooperative Adverse Drug Event Surveillance (NEISS-CADES) between January 1, 2004, and December 31, 2013. From these data, ED visits were identified for which the treating physician explicitly attributed to the use of dietary supplements. Adverse events were categorized as allergic reactions, excess doses, unsupervised ingestion by children, or other.

Extrapolating from the sample, the authors estimated an average of 23,005 annual ED visits for adverse events, with 2,154 hospitalizations. Of the total, 21.2% of the ED visits involved unsupervised ingestion by children, and 28% involved adults between the ages of 20 and 34 years. After excluding unsupervised ingestion by children, 65.9% of ED visits involved a single herbal or complementary nutritional product. Cardiac symptoms were the most common symptoms associated with weight loss products and energy products, with the most common adverse events from most micronutrients being mild to moderate allergic reactions.

Conclusion: This study estimated that dietary supplements are implicated in an average of 23,000 emergency room visits and 2,000 hospitalizations annually.

Geller, A., et al. Emergency Department Visits for Adverse Events Related to Dietary Supplements. *N Engl J Med.* 2015, October 15; 373: 1531-1540.

RILUZOLE FOR CEREBELLAR ATAXIA

Hereditary ataxias due to genetic disorders are characterized by progressive postural and gait disturbances, associated with poor coordination of limbs and eye movements and impaired speech. Treatment options for most of these ataxias are extremely limited. As small conductance potassium channel openers are implicated in the pathophysiology of ataxia, riluzole has been suggested as a possible intervention. This study explored the efficacy of riluzole as a treatment option for patients with hereditary cerebellar ataxia.

Patients with hereditary cerebellar ataxia were enrolled in this 12-month, randomized, double-blind, placebo-controlled trial of riluzole at 100 mg/day. The participants were randomized to receive either the study drug or a placebo. All patients were assessed using the Scale for the Assessment and Rating of Ataxia (SARA), with a one-point drop on this scale deemed to be clinically relevant. Quality-of-life was measured by the short form health survey questionnaire (SF-36). The Beck Depression Inventory was used to assess mood.

The final analysis included 20 patients in the treatment group and 27 patients in the placebo group. The primary endpoint, the proportion of patients with a decreased SARA score at 12 months, was significantly

higher in the treatment group than in the placebo group ($p=0.02$). In addition, the proportions of patients with improved SARA scores were 50% in the treatment group and 11% in the placebo group ($p=0.002$). Changes on the Beck Depression inventory did not differ significantly between the two groups. In addition, the mean physical and mental component scores of the SF-36 did not differ significantly between the two groups at 12 months.

Conclusion: This study of patients with hereditary cerebellar ataxia found that riluzole may be an effective treatment for this disorder.

Romano, S., et al. Riluzole in Patients with Hereditary Cerebellar Ataxia: A Randomized, Double-Blind, Placebo-Controlled Trial. *Lancet Neurol.* 2015, October; 14(10): 985-991.

STATIN TREATMENT AND POST-STROKE SEIZURES

Stroke is a common cause of seizures in the elderly, accounting for 45% of seizures after the age of 60 years. As statins have been found to have neuroprotective effects in patients with acute stroke, this study assessed the effect of statin use as a means to prevent post-stroke seizures.

Subjects included patients hospitalized with ischemic stroke and without a history of epilepsy. Statins were prescribed to patients whose stroke was presumed to be of atherosclerotic origin. Those who had used regular statins at least one month before stroke were compared to those whose statin use was initiated within three days post-stroke. The participants were followed by telephone or by face-to-face assessment at a mean of 2.5 years to determine whether they had experienced a seizure-like event. Seizure activity was identified as either early seizure (ES), occurring

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within seven days of stroke, or late seizure, occurring at least seven days after stroke (LS).

Subjects were 1,832 patients with a mean age of 64.3 years. Fourteen patients used a statin before stroke only, 1,277 patients used a statin only in the acute phase, 114 patients used a statin before stroke and in the acute phase, and 427 patients never used a statin. Of the enrolled patients, 3.4% had ES and 5% had LS. Statin use was associated with a lower risk of ES ($p<0.001$), with an odds ratio of 0.35. A significant association was found between statin use and LS ($p=0.041$), though this association was diminished after adjusting for confounding variables ($p=0.349$). Multivariate analysis revealed that statin use can reduce the risk of LS among patients with ES ($p=0.026$).

Conclusion: This study of patients with ischemic stroke found that statin use in the acute phase of stroke recovery can reduce the risk of early onset seizures.

Jiang, G., et al. Statin Treatment Reduces the Risk of Post-Stroke Seizures. **Neurology**. 2015, August 25; 85(8): 701-707.

ADHERENCE TO ORAL MIGRAINE-PREVENTATIVE MEDICATION

Migraine is an episodic, neurologic disorder affecting approximately 12% of Americans. Patients with chronic migraine (CM) may benefit from oral migraine preventive medications (OMPMs). This study describes adherence to OMPMs among a population of patients with CM.

Data were collected from the Truven Health MarketScan Research Databases, containing claims for patients covered by commercial, Medicare supplemental and Medicaid insurance plans in the United States. From these records, individuals selected were 18 years of age or older, diagnosed with CM and initiated on an OMPM between January 1, 2008, and September 30, 2012. Preventative medications included tricyclic antidepressants, selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, beta blockers and anticonvulsant medications. Adherence was calculated by the medication possession ratio (MPR)

and the proportion of days covered (PDC).

From the database, 74,870 patients with a diagnosis of CM were identified, of whom 49% had been prescribed an OMPM. Adherence was found among 29% of the patients at the end of six months and 20% at 12 months, when using an 80% cutoff with MRP criteria. Using an 80% cutoff with PDC criteria, the adherence rates were 26% at six and 17% at 12 months. Compared with topiramate, amitriptyline, nortriptyline, gabapentin and divalproex had significantly lower odds of adherence.

Conclusion: This review of patients with chronic migraine found that adherence to oral, migraine-preventative medications ranges from 17% to 29%. Compared with topiramate, amitriptyline, nortriptyline, gabapentin and divalproex had significantly lower odds of adherence.

Hepp, Z., et al. Adherence to Oral Migraine-Preventative Medications among Patients with Chronic Migraine. **Cephalalgia**. 2015, May; 35(6): 478-488.

OCCIPITAL NERVE BLOCK FOR MIGRAINE PREVENTION

Migraine headaches are a common neurologic disorder, with lifetime incidence of 43% in women and 18% in men. While blocks of the greater occipital nerve have been employed for the treatment of migraine, cervicogenic headache, and cluster headache for years, no placebo-controlled trials have demonstrated this efficacy. This study was designed to better understand the short-term preventative efficacy of occipital nerve blockade in patients with episodic and chronic migraine.

Subjects were patients, 18 to 75 years of age, diagnosed with episodic or chronic migraine, with at least one migraine attack per week. The subjects were randomized to receive either 2.5 mL of 0.5% bupivacaine plus 0.5 mL of 20 mg methylprednisolone at the occipital nerve, or 2.75 mL of normal saline plus 0.25 mL of 1% lidocaine, as a placebo. The primary outcome was defined as $\geq 50\%$ reduction in the frequency of moderate or severe migraine headache days in the 28 days after, compared to the 28 days before the injection. No significant difference was found

between groups in the primary outcome measure. Triptans were used by 65% of the treatment group and 80% in the placebo group, while opioids were used by 23% in the active group and 13% in the placebo group. No significant differences were found between the groups in any of the secondary outcome measures.

Conclusion: This study of patients with chronic migraines found that a greater occipital nerve block with corticosteroid and local anesthetic did not reduce the frequency of moderate to severe migraine days in patients with episodic or chronic migraine, as compared to placebo

Dilli, E., et al. Occipital Nerve Block for the Short-Term Preventative Treatment of Migraine: A Randomized, Double Blinded, Placebo-Controlled Trial. **Cephalalgia**. 2015, October; 35(11): 959-968.

EPIDEMIOLOGY AND PREDICTORS OF MORTALITY IN MULTIPLE SCLEROSIS

Multiple sclerosis (MS) is a common neurologic cause of disability in young adults. However, despite advances in treatment research, knowledge of its etiology and clinical onset remains limited. This cohort study examined the predictors of all-cause mortality in patients with MS.

The United Kingdom's Clinical Practice Research Datalink (CPRD) was used to identify 1,713 patients diagnosed with MS between 1993 and 2006. Information concerning covariates included age at first MS diagnosis, gender, lifestyle factors, acute infections, chronic comorbidities, and MS treatment.

Of the sample studied, 74% were female, with a mean age at diagnosis of 42 years and a mean age at death of 56.9 years. A history of smoking was common with 31.4% current and 11.7% former smokers. The most common acute comorbidity was infection in 80%, while the most common, chronic comorbidity was depression, present in 46%. Among infections, urinary tract infections were the most significant predictor of death, with a hazard ratio of 4.1. Of note, those treated for MS with an immunosuppressant drug had a reduced risk of death, with a hazard

ratio of 0.6. Several comorbidities were found to be significant predictors of death, including pneumonia and influenza, urinary tract infections, heart disease and cancer.

Conclusion: This population-based study found that patients with multiple sclerosis have multiple comorbidities, with infection and depression being the most common.

Jick, S., et al. Epidemiology of Multiple Sclerosis: Results from a Large Observational Study in the United Kingdom. **J Neurol**. 2015, September; 262(9): 2033-2041.

FRACTURE PREVALENCE AMONG WOMEN UNDERGOING CHRONIC GLUCOCORTICOID THERAPY

Glucocorticoid (GC) medications are widely used to treat various inflammatory and autoimmune disorders. As GC therapy is associated with an increased risk of fractures, this study reviewed the prevalence of fractures in patients using GC therapy for autoimmune disorders.

This population-based, cross-sectional, outpatient study was conducted in 28 centers in Spain including adult, female outpatients, diagnosed with rheumatoid arthritis and/or systemic lupus erythematosus, all of whom were prescribed GC treatment at 2.5 mg or more on a daily basis for at least three months. At visits to their rheumatologists, the participants were assessed for vertebral and non-vertebral fractures, as well as for health-related quality-of-life. Vertebral fractures were assessed using x-rays, with non-vertebral fractures assessed by questionnaire. The primary outcome measure was the percentage of women with morphometric vertebral fractures.

Of the 576 included in the study, morphometric vertebral fractures were found in 18.9% overall, with only 6.4% aware of the vertebral fractures before x-ray. In the radiographic assessments, 235 vertebral fractures were detected in 109 patients. Non-vertebral fractures were reported by 9.8% of patients with RA and by 5.3% of those with SLE. The cumulative dose of GC and the time from the start of GC use were not significantly different between those with and those without morphometric vertebral

fractures. The cumulative GC dose was 40% higher for patients with, as compared to those without, self-reported vertebral fractures (p=0.026).

Conclusion: This study found a higher rate of vertebral fractures in women with rheumatoid arthritis and/or systemic lupus erythematosus who were chronically treated with glucocorticoid steroids, with negative impacts on quality-of-life, particularly physical functioning.

Rentero, M., et al. Prevalence of Fractures in Women with Rheumatoid Arthritis and/or Systemic Lupus Erythematosus on Chronic Glucocorticoid Therapy. **BMC Musculoskel Dis**. 2015, October; 16: 300.

MEDITERRANEAN DIET AND BRAIN STRUCTURE

The Mediterranean diet has been recognized as one of the healthiest diets, with adherence shown to reduce the risk of Alzheimer's disease. This study evaluated the relationship between the Mediterranean diet and structural neuroimaging markers.

This study included participants of an ongoing, prospective study of aging and dementia, identified from a probability sample of elderly Medicare beneficiaries. At baseline, a medical and neurologic history was obtained, with cognitive status determined using a neuropsychological battery. Participants were followed every 18 months, repeating baseline examinations. An imaging sub-study was begun in 2004 among active, dementia free participants. Information regarding diet, averaged over the prior year, was collected, with these data used to calculate Mediterranean diet scores (MeDi). Magnetic resonance imaging was completed to determine total brain volume (TBV), total gray matter volume (TGMV), total white matter volume (TWMV), mean cortical thickness (mCT) and regional volume (RV). The MRI findings were compared between groups with different MeDi adherence scores.

Relative to those with low MeDi adherence, those with high adherence were found to have significantly larger TBV, TGMV and TWMV. Among the food components of the Mediterranean diet, higher fish

intake, lower red meat intake and moderate alcohol intake were associated with larger brain volumes after adjusting for age. The association remained significant for fish and meat according to a multivariable adjusted model. The difference between brain volumes of those with high MeDi scores and in those with low scores was equivalent to a five-year difference in age.

Conclusion: This study found that close adherence to the Mediterranean diet may be associated with larger brain volume, with these findings driven by higher fish and lower red meat intake.

Gu, Y., et al. Mediterranean Diet and Brain Structure in a Multiethnic, Elderly Cohort. **Neurol.** 2015 (published ahead of print) DOI: 10.1212/WNL.0000000000002121

FROG LEG TEST MANEUVER TO DIAGNOSE KNEE INJURIES

To diagnose posteriolateral knee instability, varus stress testing is the preferred examination technique. Other tests include the external rotation recurvatum test, the reverse pivot shift test and the dial test. These authors offer the frog leg test maneuver as an alternative means to diagnose posteriolateral knee instability.

Subjects were adult patients, 60 years of age or under, with varus instability during normal gait, and posteriolateral corner injury confirmed by MRI. A control group was age matched to the case group, with no knee injury. The frog leg maneuver was performed with patients supine, with the soles of the feet touching, with knees flexed to 90°. While varus stress was applied simultaneously to the posterior corner of both knees, the index finger of each hand palpated the respective lateral joint line to assess for gapping. The results were compared between the frog leg maneuver test and the varus stress test.

In the case group, both examiners had 91.6% positive findings on the frog leg test and 83.3% positive findings on the varus stress test. In the control group, examiner one had 88.8% negative findings on the frog leg test, and 100% negative findings on the varus stress test. Examiner two had 100% negative findings on both tests.

Conclusion: This pilot study of a new test for injuries to the posteriolateral corner of the knee suggests that the frog leg maneuver may be useful as an ancillary tool to the varus stress test for diagnosing these injuries.

Gomes, J., et al. Frog Leg Test Maneuver for the Diagnosis of Injuries to the Posteriolateral Corner of the Knee: A Diagnostic Accuracy Study. **Clin J Sport Med.** DOI: 10.1097/JSM.0000000000000237

NAPROXEN WITH CYCLOBENZAPRINE VERSUS OPIOIDS FOR ACUTE LOW BACK PAIN

Low back pain (LBP) is responsible for 2.4% of visits to the emergency department (ED) in the United States, with ED physicians often prescribing nonsteroidal anti-inflammatory drugs, skeletal muscle relaxants and opioids in combination. This study was designed to better understand the efficacy of muscle relaxers or opioids, as compared to nonsteroidal anti-inflammatory drugs, for the treatment of nontraumatic non-radicular back pain.

Subjects were patients 21 to 64 years of age, presenting to the ED primarily for the management of acute LBP. Patients excluded had radicular pain, back pain from direct trauma to the back within the previous month, pain of more than two weeks' duration or a recent history of LBP of more than one episode per year. All patients received naproxen 500 mg, q 12 hours. In addition subjects were randomized to receive, every eight hours, placebo, cyclobenzaprine 5 mg, or oxycodone 5 mg/acetaminophen 325. The primary outcome variable was improvement on the Roland-Morris Disability Questionnaire (RMDQ).

At week one, improvement on the RMDQ for those in the placebo group was 9.8, for those in the cyclobenzaprine was 10.1 and for those in the oxycodone/acetaminophen group was 11.1. There were no significant differences between groups. Three months after the emergency department visit, one fourth of each study group reported moderate or severe LBP and use of medication for that pain.

Conclusion: This study of patients with acute low back pain, seen in the emergency department, found that adding cyclobenzaprine or oxycodone/acetaminophen to naproxen did not improve functional outcome or pain at one week follow-up.

Friedman, B., et al. Naproxen, Cyclobenzaprine, Oxycodone/Acetaminophen or Placebo for Treating Acute Low Back Pain. A Randomized, Clinical Trial. **JAMA.** 2015, October 20; 314(15): 1572-1580.

SEXUAL FUNCTION BEFORE AND AFTER FEMOROACETABULAR IMPINGEMENT SURGERY

Chronic pain has been shown to significantly affect a patient's ability to perform activities of daily living, including sexual function. As femoroacetabular impingement (FAI) is a common cause of symptoms that may lead to chronic hip pain, this study was designed to determine the presence and significance of sexual difficulties in patients with chronic hip pain due to symptomatic FAI, before and after hip surgery.

This retrospective review included 305 patients who underwent hip arthroscopic surgery for FAI between 2011 and 2013. All patients underwent unilateral hip arthroscopic surgery with labral repair or debridement and capsular repair. An anonymous, 23-item, Likert-style questionnaire assessed preoperative and postoperative sexual function. A comparative analysis was performed between gender and age groups.

A total of 131 patients returned the questionnaire, resulting in a response rate of 43%. Of these, 66% strongly agreed or agreed that they experienced preoperative sexual difficulties. The most commonly reported contributors to altered sexual function were hip pain in 77.9%, stiffness in 47.1% and loss of interest in 21.4%. Resumption of sexual activity occurred at a mean of 29.2 days post-surgery, while sexual activity with minimum pain occurred at a mean of 40.8 days. Female patients resumed sexual activity later than did males. Postoperatively, only 10.8% strongly agreed or agreed that they experienced current sexual difficulties. The frequency of sexual activity increased in 32% of the

patients and was unchanged in 40.5%.

Conclusion: This study of patients undergoing hip arthroscopic surgery for symptomatic femoroacetabular impingement found that hip arthroscopic surgery may improve sexual function postoperatively.

Lee, S., et al. Evaluation of Sexual Function Before and After Hip Arthroscopic Surgery for Symptomatic Femoroacetabular Impingement. *Am J Sports Med.* 2015, August; 43(8): 1850-1856.

EFFICACY OF TOTAL KNEE REPLACEMENT

In 2012, 670,000 total knee replacements (TKRs) were performed in the United States. As the population ages, the number of TKRs is expected to increase, adding future economic burden. Despite these increases, there is no randomized, controlled trial illustrating the effectiveness of TKR compared with nonsurgical alternatives. This study investigated whether TKR, followed by a 12-week, nonsurgical treatment program, can produce greater pain relief and improvement in function than nonsurgical treatment alone.

One hundred patients with radiographically confirmed knee osteoarthritis were recruited. The participants were randomly assigned to undergo TKR followed by 12 weeks of rehabilitation or to a control group, who received only the 12 weeks of rehabilitation. The rehabilitation involved exercise training, education, dietary advice, and pain medications. The subjects were followed up at three, six and 12 months, with the primary outcome being the mean scores on the Knee Injury and Osteoarthritis Outcome Score (KOO) subscales covering pain, symptoms, activities of daily living and quality-of-life.

The TKR group demonstrated significantly greater improvements in KOO scores than did the nonsurgical treatment group, with an adjusted mean difference of 15.8. Compared to the nonsurgical group, the surgical group had significantly greater improvements on all five KOO subscales, as well as scores on the Timed Up And Go Test, the 20 m Walk Test and the EQ-5D descriptive index general health assessment.

Serious adverse events occurred in 24 of those in the surgical, and six in the nonsurgical treatment groups.

Conclusion: This randomized, prospective study of patients with severe degenerative joint disease of the knee found that total knee replacement, followed by nonsurgical treatment, is superior to nonsurgical treatment alone for providing pain relief and improved function.

Skou, S., et al. A Randomized, Controlled Trial of Total Knee Replacement. *N Engl J Med.* 2015, October 22; 373(17): 1597-1606.

LOWER EXTREMITY SURGERY FOR SPASTIC PARAPLEGIA

During the past two decades, the use of three-dimensional gait analysis has permitted multiple deformities to be corrected during one surgery. This study of patients with cerebral palsy (CP) was designed to determine whether such surgeries improve gait parameters and gait function over time.

Subjects included 34 children with an average age 11.6 years, all diagnosed with CP with spastic diplegia. Among the patients, 195 lower extremity surgical procedures were performed. Preoperatively, as well as one and five years postoperatively, the children underwent physical examination and instrumented, three-dimensional gait analysis. Gait function was compared between baseline and five-year follow-up.

Gait function, as evaluated by the Functional Mobility Scale, improved from baseline to the one-year follow-up for the 5 m and 50 m distances ($p=0.04$ and $p=0.01$, respectively), without significant change in the 500 m distance ($p=0.07$). At five years, improvement in all three distances was significant, as compared with baseline. Measures of gait quality, using the gait profile score, improved from baseline to five-year follow-up, although no significant difference was noted between one year and five years. The mean parental satisfaction score was 7.7 on a 10 point scale.

Conclusion: This five-year follow-up of children with CP and spastic diplegia found that surgery to correct gait abnormalities resulted in improved gait at five-year follow-up, based upon findings of gait analysis.

Terjesen, T., et al. Gait Improvement Surgery in Ambulatory Children with Diplegic Cerebral Palsy. A Five-Year, Follow-Up Study of 34 Children. *Acta Orthopædica.* 2015, August; 86(4): 511-517.

ONE-YEAR FOLLOW-UP OF BANKART REPAIRS

Anterior shoulder instability can be managed surgically by an anterior capsulolabral repair (Bankart repair). The recurrent dislocation rate after Bankart repair is high, with estimates ranging from nine to 58%. This study reports on recurrence rates of anterior shoulder instability without osseous lesions 20 years after Bankart repair.

This retrospective cohort analysis reported on the shoulder dislocation recurrence rates of 47 patients who underwent a Bankart procedure between 1989 and 1994 for recurrent anterior shoulder instability. Preoperative imaging excluded patients with significant glenoid bone loss or a large Hill-Sacks lesion. Of the 47 patients, 40 underwent clinical follow-up 20 years after surgery.

At 20-year follow-up, 40 of the 47 patients were contacted and agreed to be evaluated. Of those, 27 were examined clinically with the Western Ontario Shoulder Instability Index, the Rowe score, the Subjective Shoulder Value, a visual analogue scale for pain and range of motion.

Recurrent instability during the follow-up period occurred in seven (17.5%) of the patients. Of those, five sustained a complete dislocation requiring reduction by a physician. Six of the seven experienced the first postoperative instability episode after more than eight years without symptoms. Three late failures were the result of a high-energy sports injury while two occurred due to a minor trauma.

Conclusion: This study of patients undergoing open Bankart repair found that, even after excluding osseous glenoid defects, the recurrence of instability was 17.5%, with most episodes of failure associated with shoulder specific activity.

Moroder, P., et al. Open Bankart Repair for the Treatment of Anterior Shoulder Instability without Substantial Osseous Glenoid Defects: Results after a Minimum

Follow-Up of 20 Years. **J Bone Joint Surg (Am)**. 2015, September 2; 97 (17): 1398-1405.

NECROTIZING AUTOIMMUNE MYOPATHY

Necrotizing autoimmune myopathy (NAM) is characterized by necrotic muscle fibers with absent/minimal inflammation, proximal muscle weakness and high creatinine kinase levels. This retrospective study reviewed the clinical, serologic and electrophysiological characteristics of patients with NAM, as well as relevant treatment strategies and outcomes.

Cases reviewed included 63 adult patients at the Mayo Clinic, identified with NAM between January of 2004 and December of 2013. The charts were reviewed for history and neurologic findings, laboratory data, drug therapy, clinical response, and muscle histopathologic findings. All patients received immunotherapy. Outcome measures included weakness severity based on the Medical Research Council (MRC) grade of the weakest muscle. In addition, response to treatment, and autoimmune serologic testing results were reviewed.

Muscle weakness was severe in 32 (51%) patients and generally worse in the lower limbs. Twenty-three patients had dyspnea with five requiring intubation. The mean age of onset was 62 years, with 32 idiopathic, 22 statin associated, six neoplastic associated and three with connective tissue disease associated etiologies. Electrodiagnostic testing revealed fibrillation potentials in all patients, with 14% demonstrating electrophysiologic evidence of coexisting chronic axonal peripheral neuropathy. Of the 53 patients tested, SRP-IgG was detected in 13 (24%). Associated with favorable outcome were the use of two or more immunosuppressant drugs, initiated within three months of symptom onset.

Conclusion: This retrospective study of patients diagnosed with necrotizing autoimmune myopathy found that statin medications are the most commonly identified risk factor, with early recognition and aggressive management likely to result in a favorable outcome.

Kassardjian, C., et al. Clinical Features and Treatment Outcomes of Necrotizing Autoimmune Myopathy.

JAMA Neurol. 2015, September 1; 72(9): 996-1003.

PREVENTION OF KNEE OSTEOARTHRITIS IN OVERWEIGHT FEMALES

Previous studies have suggested that, among overweight individuals, weight loss can prevent the occurrence of knee osteoarthritis (OA). Other studies have suggested the use of glucosamine as a treatment for OA. This study evaluated the effects of oral glucosamine sulfate and a tailored diet and exercise weight reduction program on the incidence of knee OA in a high-risk group of overweight women.

Subjects were women, 50 to 60 years of age, with no history of OA and with a body mass index of 27 kg/m² or greater. The participants were randomized to a treatment group, to receive a tailored diet and exercise program (DEP), with or without 1,500 mg glucosamine, or to a control group who were not offered an intervention. The predefined, primary outcome measure was the difference between groups in the incidence of knee OA or joint space narrowing. The subjects were followed for a mean of 2.5 years.

A total of 407 women were studied, with a mean age of 55.7 years and a mean body mass index of 32.4 kg/m². Of these, 17% showed incident knee OA, including 19% in the DEP control/placebo group, 13% in the DEP control/ glucosamine group, 9% in the DEP /placebo group and 23% in the DEP /glucosamine group. No significant differences were seen between the groups.

Conclusion: This study of overweight women failed to demonstrate a protective effect of weight reduction or oral glucosamine for the prevention of knee osteoarthritis.

Runhaar, J., et al. Prevention of Knee Osteoarthritis in Overweight Females: The First Preventative, Randomized, Controlled Trial in Osteoarthritis. **Am J Med**. 2015, August; 128(8): 888-895.

EFFECTIVENESS OF ANTI-OSTEOPOROTIC THERAPY AFTER FRAGILITY FRACTURE

Previous studies have indicated that the lifetime risk of osteoporotic

fragility fractures is between 40 and 50% in women and 13 to 22% in men. Studies have shown that biphosphonate treatment in patients with osteoporosis can achieve a 40 to 70% reduction in the risk of initial fragility fracture, though no studies have examined the effectiveness of initiating anti-osteoporotic therapies for preventing subsequent fragility fractures.

This retrospective study used the Truven Health MarketScan databases, which provided person specific claim data for 17 to 51 million individuals per year between 2003 and 2012. Data were reviewed for individuals 50 years of age or older who had sustained a fragility fracture and had prescription medication coverage as part of the insurance. Patients were compared between those who had sustained a fragility fracture and then were treated with anti-osteoporotic therapy, and those who had received no such prescription. Patients were followed for three years. The primary outcome measure was subsequent fracture, defined as a fragility fracture occurring more than 90 days following the index fracture.

Of the 31,069 patients studied, 3278 patients were treated with anti-osteoporotic therapy. The three-year subsequent fracture rates were 9.7% in the no treatment group, and 7.5% in the treatment group ($p<0.001$). The lower fracture rates in the treatment group were significant for the wrist ($p<0.02$), the proximal humerus ($p<0.002$), the hip ($p<0.006$), but not the vertebrae ($p<0.06$).

Conclusion: This large study of commercial insurance and Medicare claims data found that after fragility fractures, treatment with anti-osteoporotic medications can result in a significant risk reduction in such fractures.

Bawa, H et al. Anti— Osteoporotic Therapy after Fragility Fracture Lowers Rate of Subsequent Fracture. **J Bone Joint Surg (Am)**. 2015, October 7; 97(19):1555 – 1562.

PHYSICAL PERFORMANCE, ADIPOSITY AND COGNITION IN CHILDREN

Childhood obesity has been increasing worldwide, with associated increased cardiometabolic risks. In a recent systematic review, Reinhard found that being overweight is associated with low executive

function in children. However, the evidence regarding the independent and combined relationships between adiposity and cognition in children remains unclear. This study was designed to better understand the effects of cardiorespiratory performance, neuromuscular performance and body fat percentage on cognition.

Subjects were 202 boys and 201 girls between the ages of six and eight years. Cardiorespiratory performance was assessed using a maximal cycle ergometer test and was expressed as maximal workload per lean body mass. Neuromuscular performance included subgroups of muscle strength, speed, agility, balance, manual dexterity and flexibility. Body fat percentage was assessed using dual energy X-Ray absorptiometry. Cognition was assessed using Raven's Coloured Progressive Matrices (Raven's CPM).

Among all children, better overall neuromuscular performance, better overall motor performance, shorter 50-m shuttle run time and fewer errors on the Modified Flamingo Balance Test were associated with higher Raven's CPM scores. Children in the lowest third of overall motor performance had lower Raven's CPM scores than did those in the middle ($p=0.036$) and highest thirds ($p=0.011$). Children in the lowest and highest thirds of body fat percentage had lower Raven scores than did those in the middle third.

Conclusion: This study found that poor neuromuscular and motor performances are associated with poorer cognition in children. Cognition was worse among those with the lowest and highest adiposity.

Haapala, E., et al. Associations of Physical Performance and Adiposity with Cognition in Children. *Med Sci Sports Exer.* 2015, October; 47(10): 2166-2174.

PLATELET RICH PLASMA FOR LONG BONE NON-UNION

Nonunion remains a significant source of morbidity, with a negative impact on quality-of-life. While autologous cancellous bone is considered to be the gold standard for the treatment of nonunions, the limited supply and donor site morbidity have led researchers to explore alternatives. As previous studies have demonstrated that platelet rich plasma (PRP) has the

ability to accelerate bone and soft tissue healing, this study reviewed the efficacy of PRP in the treatment of established fracture nonunion of long bones.

Subjects were 94 patients with established nonunion of long bone fractures, with stable internal fixation/stable reduction plaster immobilization, acceptable alignment fracture fragments and more than 90% contact between the fragments. The average time between injury and platelet injection was 9.1 months. The participants underwent autologous PRP preparation, with injection of 15 to 20 ML of PRP under image intensified guidance. All subjects were assessed clinically and radiologically for the healing of the fracture at monthly intervals until three months. The absence of localized tenderness, abnormal mobility and pain were considered the clinical criteria for union.

Of the 94 patients, 82 had fracture healing at four months. In the patients with early fracture healing, the PRP injection had been given within two to four months of the diagnosis of nonunion. Of the 12 patients with failed union, the PRP had been injected 12 months or later from the diagnosis of nonunion.

Conclusion: This study of patients with nonunion of long bone fractures found that the administration of platelet rich plasma could assist with healing.

Malhotra, R., et al. Role of Autologous Platelet Rich Plasma in Treatment of Long-Bone Nonunions: A Prospective Study. *Musculoskel Surg.* 2015 DOI 10.1007/s12306-015-0378-8

REPEAT TPA IN PATIENTS WITH ACUTE ISCHEMIC STROKE

Improvements in the diagnosis and treatment of acute ischemic stroke have created a large and growing population of stroke survivors. Many achieve a good clinical outcome, in part, through the use of recombinant tissue-type plasminogen activator (rt-PA). Some of these patients go on to infarct. This study evaluated the safety and efficacy of administering rt-PA to patients who had received this medication for a previous stroke.

This observational, exploratory, single center study examined the clinical outcomes and complication rates of patients receiving repeat rt-

PA injections. Subjects were 24 patients with a median age of 74.5 years at initial stroke. This group suffered a second ischemic stroke, treated with tPA at a median inter-infarct time of 346 days. A good clinical outcome was defined as a modified Rankin scale (mRS) score of zero to two, or recovery to pre-stroke status, measured at three months post-stroke.

Of the 24 patients, 75% achieved a good clinical outcome after the initial stroke. After the second stroke, only 41.7% achieved a good clinical outcome. No incidents of symptomatic intracranial hemorrhage occurred after the first or repeat administration. One asymptomatic intracranial hemorrhage was discovered after both the initial and repeat treatments.

Conclusion: This study of patients with acute ischemic stroke treated with recombinant tissue-type plasminogen activator found no increased risk of intracranial hemorrhage, although the clinical outcomes after the second stroke were less satisfactory than had been the first.

Laible, M., et al. Repeated Intravenous Treatment with Recombinant Tissue-Type Plasminogen Activator in Patients with Acute Ischemic Stroke. *Euro Neurol.* 2015; 74(3-4): 127-134.

THE FIFA 11+ SOCCER INJURY PREVENTION PROGRAM

Soccer (football) is the most widely played sport worldwide, with approximately 300,000,000 registered players globally. The Federation Internationale de Football Association (FIFA) and its medical assessment and research center have developed an injury prevention program, the FIFA 11+ program, in an effort to reduce the incidence of all injuries sustained during participation. This study evaluated the efficacy of the FIFA 11+ in preventing injuries in collegiate male soccer players.

All NCAA Division I and II men's collegiate soccer programs were contacted to participate in this prospective, cluster randomized, controlled trial. Sixty-one teams completed the study, with 34 control (C) and 27 intervention groups (I). The FIFA 11+ program was delivered to each athletic trainer in I group. Data concerning athletic exposure, injury, utilization of the program and

(Continued from page 2)

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compliance were compiled into an injury surveillance system. Injuries were calculated as the number of injuries per 1,000 athletic exposures (AEs).

The athletes in C group were found to have 15.04 injuries per 1,000 AEs, as compared with 8.09 injuries per 1,000 AE in group I ($p < 0.001$). The intervention group also had fewer missed days due to injury and fewer game injuries than did the control group. Three anterior cruciate ligament injuries were noted in the intervention group and 16 in the control group ($p < 0.001$).

Conclusion: This randomized, controlled trial, reviewing the efficacy of FIFA 11+ in reducing injuries in men's collegiate soccer players, found a 46.1% reduction in injuries as compared to a control group.

Silvers-Granelli, H., et al. Efficacy of the FIFA 11+ Injury Prevention Program in the Collegiate Male Soccer Player. *Am J Sports Med.* 2015, Nov; 43(11):2628-2657.

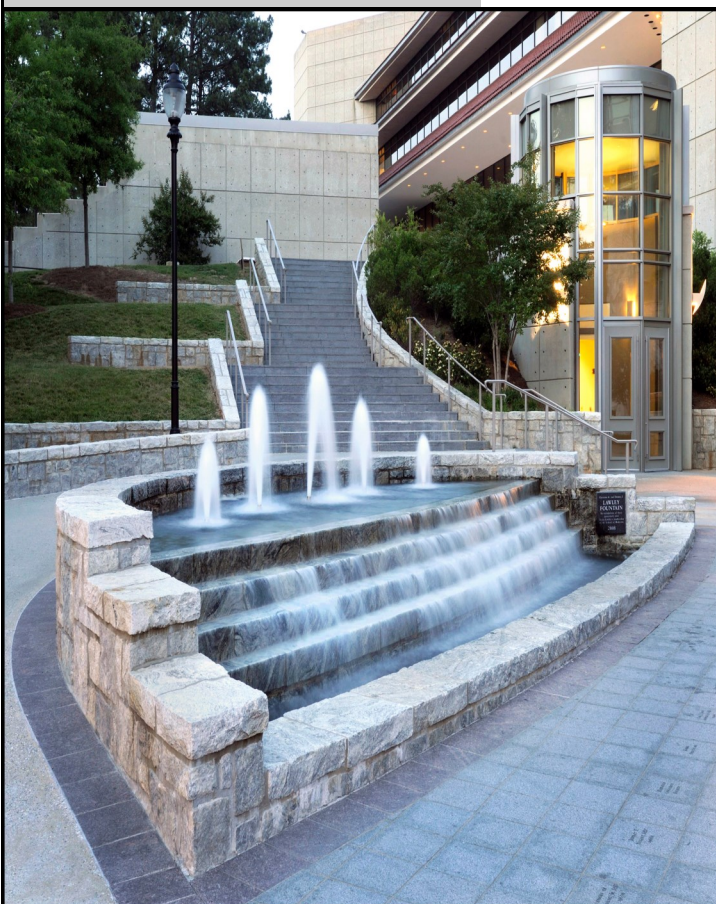
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ISSN # 1081-1303
www.rehabinreview.com



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



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