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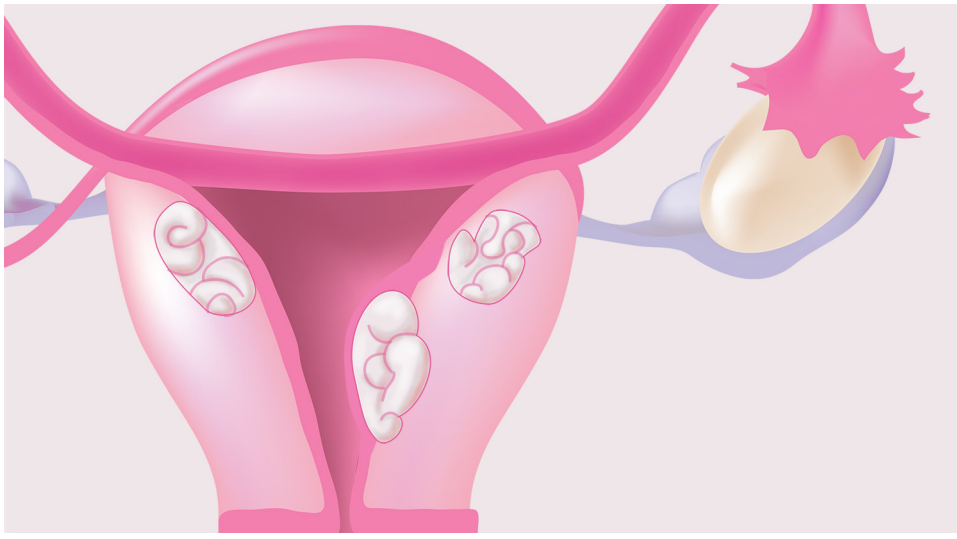
Advances made in uterine fibroid therapy

Uterine fibroids affect 20–40% of women who are of reproductive age. Gonadotrophin-releasing hormone agonists are approved as a preoperative therapy for the fibroids; however, they are associated with a number of side effects that limit their use. Esmya® (ulipristal acetate; Gedeon Richter Plc., Budapest, Hungary) is a preoperative therapy that quickly controls uterine bleeding and reduces anemia and fibroid size. Furthermore, this treatment is said to have fewer side effects than others.

Esmya is a once-daily tablet and, until now, could only be prescribed for up to 3 months to women of reproductive age with moderate-to-severe uterine fibroid symptoms who require a procedure. However, recently the European Commission has approved its use to retreat patients for an additional 3 months. This approval was obtained following clinical studies demonstrating that a repeated course of Esmya provides continued efficacy and a positive opinion from the Committee for Medicinal Products for Human Use.

A total of 209 patients were recruited in the PEARL III study, which examined the safety and efficacy of a single 3-month open-label treatment with ulipristal acetate 10 mg. When the PEARL III study ended, 132 patients continued to take ulipristal acetate 10 mg in the extension study, which investigated the safety and efficacy of repeated ulipristal acetate 10-mg courses on uterine bleeding, pain, quality of life and myoma size. It is expected that, like the 10-mg dose, the 5-mg dose efficacy in the first therapy course will be maintained in the second therapy course.

In the Gideon Richter press release, Martin Powell, a consultant gynecologist in Nottingham (UK) comments: "Esmya has made a significant impact on patients, as it shrinks the fibroids so they are easier to remove, with less blood being lost, making it a safer and shorter operation. Whilst waiting for surgery, women also have the added benefit of not having heavy bleeding, which can be very debilitating and have a serious impact on quality of life." Furthermore, one individual who was affected by uterine fibroids stated: "I took Esmya for 3 months and felt great – no pain and the heavy bleeding stopped. I had the operation in August 2013 and it went well – I've been absolutely fine since then."



Managing Director of Gedeon Richter Plc., Erik Bogsch, explains: "We will now be working with local regulatory agencies to communicate the implications of this label variation to physicians in Europe." Furthermore, additional clinical trials are now in process to determine the sustained safety and efficacy of long-term on/off therapy of uterine fibroids with Esmya.

– Written by Hannah Branch

Source: Gedeon Richter press release: New development in the treatment of uterine fibroids: www.esmya.co.uk/

Improving activity by improving sleep: study suggests sleep is key for chronic pain

New research from the University of Warwick's Department of Psychology (Warwick, UK) suggests that chronic pain sufferers could be kept physically active by improving the quality of their sleep. The authors reported that sleep was a worthy target for treating chronic pain and not only as an answer to pain-related insomnia.

One of the study's authors study Nicole Tang (Warwick University) commented: "Engaging in physical activity is a key treatment process in pain management. Very often, clinicians would prescribe exercise classes, physiotherapy, walking and cycling programs as part of the treatment, but who would like to engage in these activities when they feel like a zombie?"

> "...a comparison between multilevel models demonstrated that sleep was a better predictor of physical activity than morning ratings of pain intensity or mood."

In the study the authors examined the day-to-day association between night-time sleep and daytime physical activity in chronic pain patients, Tang commented that "Many of the patients struggled to stay physically active after the onset of pain and we found that chronic pain patients spontaneously engaged in more physical activity following a better night of sleep," adding that "The research points to sleep as not only an answer to pain-related insomnia but also as a novel method to keep sufferers physically active, opening a new avenue for improving the quality of life of chronic pain sufferers."

In the study chronic pain patients wore an accelerometer that measured motor activity to monitor their physical activity round the clock for a week in their usual sleeping and living environment. The patients also they gave ratings of their sleep quality, pain intensity and mood using a mobile electronic diary.

The researchers then used the time-specific data to determine, whether the quality of their sleep had an impact on their levels of physical activity the following day. Multilevel models for each of the predictors were fit, and the only reliable predictor of physical activity was sleep quality.

The authors reported that a comparison between multilevel models demonstrated that sleep was a better predictor of physical activity than morning ratings of pain intensity or mood.

Discussing the study Tang said that, "the prospect of promoting physical activity by regulating sleep may offer a novel solution to an old problem ... The current study identified sleep quality, rather than pain and low mood, as a key driver of physical activity the next day. The finding challenges the conventional target of treatment being primarily focused on changing what patients do during the day. Sleep has a naturally recuperative power that is often overlooked in pain management. A greater treatment emphasis on sleep may help patients improve their daytime functioning and hence their quality of life."

– Written by Dominic Chamberlain

Source: University of Warwick press release: www2.warwick.ac.uk/newsandevents/pressreleases/sleep_may_stop/

Predicting response: new study offers insight into which osteoarthritis patients will respond to NSAIDs

Results reported in a scientific poster today at the 30th Annual Meeting of the American Academy of Pain Medicine suggest that scientists can predict which osteoarthritis (OA) patients with neuropathic pain symptoms will respond to treatment with NSAIDs by assessing the nervous system's own capacity to regulate pain. In the study, patients whose tests had indicated superior conditioned pain modulation (CPM) had less pain and fewer neuropathic symptoms at study's end.

One of the investigators Ajay D. Wasan (University of Pittsburgh, PA, USA) noted: "Clinically, these results indicate that neuropathic symptoms are very common in knee OA and that neuropathic processes – such as changes in conditioned modulation – predict who will respond to a common treatment for knee OA. Patients with neuropathic pain symptoms in OA respond equally as well to topical NSAIDS as those who do not have neuropathic pain symptoms."

The results come from a 5-week effectiveness study of diclofenac topical gel in 44 patients with knee OA. Patients were extensively tested as to genetically and environmentally influenced physical characteristics.

The authors also used the Neuropathic Pain Questionnaire, the Knee Injury and Osteoarthritis Outcome Score, an exercise performance task and quantitative sensory testing (QST).

"Patients with neuropathic pain symptoms in osteoarthritis respond equally as well to topical NSAIDS as those who do not have neuropathic pain symptoms."

Of the 38 subjects who completed the study, 40% had significant neuropathic symptoms, that included burning or shooting sensations and sensitivity to touch. Pain sensitivity at baseline, as measured by QST, had modest correlation to symptoms.

After 4 weeks of treatment with diclofenac gel, there was 30% improvement in pain on average and significant response for neuropathic symptoms and improved function.

Using CPM, an index of endogenous pain-inhibitory capacity, calculated from QST measurements, investigators correctly predicted changes in pain intensity and in neuropathic symptoms. Subjects with higher CPM at baseline, representing better functioning endogenous pain-inhibitory systems, reported lower pain intensity and neuropathic pain symptoms at the study's end.

The variability of the pain experience along with observations that pain can change in the presence of other factors, including past memories, stress, anxiety, distraction or attention, further suggests the presence of endogenous pain modulatory systems.

– Written by Dominic Chamberlain

Source: Newswise press release: www.newswise.com/articles/higher-functioning-endogenous-opioid-system-predicts-better-treatment-response-for-neuropathic-pain-treated-with-topical-nsaids-study

Intradiscal biacuplasty could offer better outcomes for select few

A recent study from researchers at Carolinas Pain Institute and Center for Clinical Research (NC, USA) suggests that patients who benefited from intradiscal biacuplasty (IDB) to treat discogenic low-back pain maintained initial gains in pain relief and physical function at a 1-year follow-up. Additionally, the paper appears to demonstrate that patients who were in the sham treatment group and were later offered IDB achieved the same positive results as patients in the original treatment arm.

"The treatment involves placing two cooled radiofrequency electrodes in affected discs to ablate the nerve fibers of the intervertebral disc cover, thus interrupting the generation of pain sensations."

With the need for less invasive treatment options to treat discogenic low-back pain, interest in the use of IDB is growing. The treatment involves placing two cooled radiofrequency electrodes in affected discs to ablate the nerve fibers of the intervertebral disc cover, thus interrupting the generation of pain sensations.

Discussing the study Leonardo Kapural (Carolinas Pain Institute and Center for Clinical Research) highlighted the importance of candidate selection: "This minimally invasive procedure should be limited to younger patients with discogenic pain arising only from one or two lumbar discs and without other sources of lower back pain."

The study is a follow-up to a 6-month, double-blind, sham, randomized study. After unblinding, the investigators continued to follow 22 out of 27 subjects in the original active treatment group for 12 months. Patients reported outcomes on physical function, pain and disability via the SF-36 health survey, the 11-point pain numerical rating scale and the Oswestry low-back pain disability questionnaire.

Clinically significant improvements reported at 6 months in the original treatment arm were maintained at 9 and 12 months for physical function.

Additionally, crossover patients who had been randomized to sham therapy during the initial study reported improvements after IDB that did not differ statistically from those of patients originally randomized to IDB treatment.

Discogenic pain is the most common cause of chronic low-back pain and although the findings appear exciting, Kapural emphasizes that the majority of sufferers have multilevel disease and would not be candidates for IDB, adding that current surgical treatment options are limited to fusion and disc arthroplasty and have been suggested to yield very low success rates.

– Written by Dominic Chamberlain

Source: Newswise press release: www.newswise.com/articles/study-shows-long-lasting-improvements-for-discogenic-low-back-pain-treated-with-minimally-invasive-intradiscal-biacuplasty

Mood-stabilizing drug linked to reduced risk of head and neck cancer

Johann Christoph Brandes of Emory University (GA, USA) recently led an investigation into the anticancer potential of the mood-stabilizing drug valproic acid. Valproic acid is able to inhibit the action of histone acetyl transferase enzymes, which assist in the regulation of gene expression by orchestrating epigenetic changes to DNA. Such changes are known to play a major part in the carcinogenesis of tobacco-related cancers. The results of the study, published online ahead of print in *Cancer*, indicate that use of valproic acid is associated with a lower risk of developing head and neck cancers.

> "...those who took valproic acid for at least 1 year were associated with a 34% decreased risk of head and neck cancer, compared with those who did not receive the treatment."

Utilizing a data set linked to the Veterans Affairs Central Cancer Registry, the authors conducted a retrospective cohort study to evaluate the effect of valproic acid treatment on the risk of developing cancers of the head and neck, prostate, bladder, colon and lung. Overall, they evaluated this potential anticancer effect in 439,628 veterans aged >40 years, 26,911 of whom were receiving valproic acid for the treatment of bipolar disorder, post-traumatic stress disorder, migraines and seizures.

Hazard models indicated that those who took valproic acid for at least 1 year were associated with a 34% decreased risk of head and neck cancer, compared with those who did not receive the treatment. Additional benefit was noted with higher doses and longer duration of treatment. However, no differences in incidence were observed in the other malignancies investigated.

"A 34% risk reduction for the development of head and neck cancer with valproic acid use could result in the prevention of up to approximately 16,000 new cases and 3000 to 4000 annual deaths in the USA alone," commented Brandes. "Head and neck cancer is an important global health crisis, and low cost and low toxicity prevention strategies like valproic acid use have a high potential impact on pain, suffering, costs, and mortality associated with this disease."

– Written by Emily Brown

Sources: Kang H, Gillespie TW, Goodman M *et al*. Long-term use of valproic acid in US veterans is associated with a reduced risk of smoking-related cases of head and neck cancer. *Cancer* 120(9), 1394–400 (2014); Wiley press release: http://eu.wiley.com/WileyCDA/PressRelease/pressReleaseId-110490.html