Degenerative Joint Diseases

Enzyme therapy as effective as an NSAID

Treating activated arthrosis or a traumatized joint without non-steroidal analgesics— is that possible? Yes, as a recent meta-analysis shows. In patients with knee arthrosis, an enzyme combination preparation had similar efficacy but was superior in terms of tolerability and safety.

Arthrosis is the most common joint disease worldwide. In Germany every third woman and every fourth man in the age group between 46 to 64 years is affected, and beyond the age of 65 years every second woman and every the third man. With the increase in the average age of the population in Germany, the number of people suffering from arthrosis therefore also increases. Overload, misalignment or injuries are the triggers that accelerate the wear of the joint cartilage. In principle, any joint can become diseased with arthrosis. It is most commonly observed in the high weight bearing knee and hip joints. These joints are subjected to a load of 3.5 times the body weight during walking. The small vertebral joints and the finger joints are further predisposed regions.

The onset of osteoarthritis is gradual. The predominant symptom, joint pain, is initially only felt under exertion, or in the morning as start up pain. In the further course, it becomes permanent and is increasingly accompanied by loss of function. In phases of activated arthrosis, the lining membrane of the joints become inflamed; the joint capsule and therefore the joint become overall swollen. Inflammation and swelling irritate the nerve endings of the joint capsule, which explains the strong pain during an acute arthrosis episode. The pain reaches a higher and higher level during the active phases.

Inhibiting inflammation is a central goal of therapy

Cartilage damage does not heal. Reduction of the pain-triggering inflammation and a slowdown of the degenerative process are important therapy objectives for arthrosis. An optimal therapy should combine physiotherapy and medication approaches. Medicines such as paracetamol, non-steroidal anti-inflammatory analgesics/anti-inflammatory drugs (NSAID), opioids, glucocorticoids and Externa are drugs used to treat the symptoms of arthrosis. The side effects of NSAID and glucocorticoids are especially problematic in the target group of elderly patients, particularly in the case of prolonged use and at higher doses. In the foreground are gastrointestinal complications and disturbances of renal function. Ulcers or a history of gastrointestinal bleeding prohibit the use of NSAIDs. To limit damage, the recommendation is made to use NSAIDs only in the short term and to prescribe them at the lowest effective dose with concomitant use of proton pump inhibitors.

Enzyme therapy as an alternative

Cytokines, which control the course of an inflammatory reaction, include pro- and anti-inflammatory cytokines. In contrast to the suppression of the pro-inflammatory prostaglandin formation by NSAIDs, certain proteolytic enzymes and flavonoids can help re-establish the balance between pro- and anti-inflammatory messenger molecules. This allows for the actually healing inflammatory process to occur faster and more effectively.

A corresponding active substance combination can be found in the oral medicine Wobenzym® plus, which is approved for the supportive treatment of swelling, inflammation and pain as a result of injuries, for activated arthrosis and soft tissue rheumatism, amongst others. Bromelain, trypsin and rutoside are included in tablets with a gastric-resistant coating, which release the enzymes for resorption only once they are in the intestine. Bromelain contains cysteine proteases from the pineapple plant, adjusted to an enzyme activity of 450 F.I.P units, and has an anti-inflammatory and swelling reducing effect. Trypsin is a proteolytic pancreatic enzyme that has minor anti-coagulation and also anti-inflammatory effects. The antioxidant rutoside from the Japanese pagoda shrub helps normalize the abnormal permeability of vascular walls in inflamed regions.

A&W COMPACT

Profile Wobenzym® plus

- Proteolytic enzymes plus rutoside: regulate inflammation, reduce swelling, thereby alleviate pain
- Approved for swelling, inflammation or pain as a consequence of trauma, activated arthrosis and soft tissue rheumatism
- Long-term therapy possible, also in combination with other medicines
- Frequently, the dose can be increased when used as acute medication
- Intake recommended 30 to 60 minutes before or 90 minutes after a meal
- Contraindications: for example, hypersensitivity to pineapple
- Side effects: only occasionally gastrointestinal disorders
- Interactions: enhancement of anticoagulant effects, platelet aggregation inhibitor; increased plasma and urine levels of tetracyclines
The overall effect of inhibiting inflammation and reducing swelling also leads to pain alleviation. The advantages of the special enzyme combination of Wobenzym® plus are good tolerability and safety, in particular in comparison to the gastrointestinal and cardiovascular effects of NSAIDs.

**Gonarthritis: enzymes as effective as the NSAID Gold Standard**

The fact that Wobenzym® plus allows effective and tolerable treatment of inflammatory joint disorders is apparent from previous studies. Currently, the efficacy, tolerability and safety of the preparation in comparison to diclofenac in patients with knee arthrosis was investigated in a meta-analysis. This is an analysis of patient reports with data from six prospective randomized, double-blind parallel group studies in adults with moderate to severe gonarthritis. The average age of the study participants was 61 years and 70% were women. They received either two tablets of Wobenzym® plus three times a day or 100 to 150 mg diclofenac daily. The treatment was carried out for a period of three to twelve weeks. The change in the Lequesne index was used as the primary endpoint, a validated and reliable self-assessment questionnaire to register pain, walking performance and coping with everyday life with knee or hip arthrosis. Secondary endpoints related to responder rates, pain relief, side effects and laboratory parameters. Of the 697 patients randomized for treatment (ITT-population), 524 were available for the efficacy analysis (per protocol). The Lequesne index as a measure for joint function and pain dropped significantly and comparably strong in both treatment arms; with baseline values of 12.6 (enzyme preparation) or 12.7 (diclofenac) both groups reached a value of 9.1 at the study end.

- Movement-related pain on a numeric 11-point scale improved from 6.4 to 3.8 in the enzyme-treated group, or from 6.6 to 3.9 in the NSAID arm, respectively.
- Side effects over the course of treatment occurred in 14.7 per cent of the Wobenzym® plus-treated patients, compared to 21.1 percent in those under diclofenac. This was reflected in an almost twice as high study discontinuation rate under the NSAID (5.9% versus 10.2%).

Laboratory values were analyzed in 500 patients.

**A&W GRAPH**

**Anti-inflammatory osteoarthritis therapy—alternative to NSAID?**

Change of safety-relevant laboratory parameters under therapy with Wobenzym® plus (blue bar, n=247) vs. diclofenac (red, n=253) vs. placebo (gray, n=86). Source: Dr. Michael Überall, Road Show Italy, Turin/Milan/Bologna 2016.

**Sources:**

1. Empfehlungen zur Therapie von degenerativen Gelenkerkrankungen [Recommendations for therapy of degenerative joint diseases]. Arzneimittelkommission der deutschen Ärzteschaft [Drug Commission of German Medical Doctors] November 2008
2. Informationen von Mucos pharma/www.wobenzym.de
• Decrease in hemoglobin, hematocrit or erythrocyte count was recorded in around 19 percent of the enzyme-treated participants, but in more than 86 percent of the patients under diclofenac. A similarly large discrepancy was seen in the change of the liver values (AST, ALT, GGT) with 28.2 percent versus 72.6 percent.

Conclusion by the Authors
The efficacy of the enzyme preparation Wobenzym® plus in the treatment of gonarthrosis is comparable to that of diclofenac. However, the product has a superior safety and tolerability profile with fewer side effects, less study discontinuations and barely changed laboratory parameters.

Not a question of age
Even if the “wear and tear” disease arthrosis occurs more frequently with increasing age, it is no longer considered only a pure old-age disease today: the increasing prevalence of obesity in all age groups causes a shift of degenerative diseases into the phase of working life. Heightened strain during recreational and also professional sports, especially in sports with rapid changes of direction (squash, handball), as well as wearing unfavorable footwear (high heels) cause the appearance of painful wear and tear even in people of very young age. The use of enzyme preparations has also been beneficial for sports injuries, such as strains, contusions or compressions: under the inflammation regulating and also swelling reducing effects, the pain decreases quickly and the injury heals faster.

Effective treatment alternative to anti-rheumatic drugs

PD Dr. Michael Überall is the director of the Regional Pain Center DGS in Nuremberg and Chairman of the German Pain League e.V.

Pain-afflicted osteoarthritis patients’ only choices are the current pain killers – does it have to be that way? Are there more tolerable alternatives?
A recent meta-analysis showed that under the oral enzyme combination product Wobenzym®, plus a significant improvement of pain, walking performance and management of everyday living was achievable to the same extent as with the “gold standard” diclofenac, although the maximum dose of 12 tablets/day had not been used. In particular, patients with more pain and an initially more severe impairment of their everyday life profited very well from the treatment. Wobenzym® plus provides a safe and effective treatment alternative to antirheumatics for joint pain, which is, moreover, better tolerated by the patients. Many doctors are of the opinion that concomitant administration of proton pump inhibitors eliminates the side effects of analgesic therapy in arthrosis patients; however, the problem is merely shifted to the small intestine.

The study situation on the enzyme preparation
Numerous studies, the latest from 2015, are available on the efficacy of Wobenzym® plus in comparison to diclofenac, which is still considered the standard treatment for arthrosis. However, these studies comprise only a few case numbers and use different analysis methods, so that the chairman of the German Society for Pain Medicine and the German Pain League commissioned a meta-analysis in the interest of patients.

The meta-analysis for comparison of Wobenzym® plus with diclofenac could be performed on the individual patient data level, thanks to the raw data made available by the company Mucos, and is therefore statistically more significant than analyses based purely on publications.

Conclusion
In the majority of patients the meta-analysis within 3 to 12 weeks under standard therapy with diclofenac, a worsening of the blood and liver values was already demonstrable by laboratory chemistry. Even if not clinically relevant in each case, this must nevertheless be objectively evaluated as an alarm sign of the serious undesirable effects of NSAIDs. These complications can be avoided, because there is an equally effective, but significantly less risky, alternative: Wobenzym® plus.

Expert statement

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