

Explanation to the article

"Effects of Zeel comp. on experimental osteoarthritis in rabbit knee" (Stancikova M. et al.)

Background

The effects of medicines on complex pathological processes (such as rheumatic disease) are generally difficult to demonstrate. One reason for this is that their course often differs widely from one patient to another, thus presenting a considerable obstacle to a precise and complete evaluation of the process at the time of investigation. A further problem in investigating the action mechanisms of medicines is finding sufficient numbers of patients for clinical trials who show as similar a pathogenesis as possible and are e.g. at the same stage of the disease. However, an objective demonstration of the way in which drugs exert their effects is particularly desirable when it is a matter of finding medicines with the fewest possible side effects whose intended effects are sufficiently strong.

Options

One way of standardizing the test conditions is to switch to cell cultures. These only allow certain aspects of diseases to be investigated, however, if the systemic influence of the medicine on the totality of processes in the organism is to be investigated, a study in an animal model is generally the only option. But animal studies cannot be considered relevant unless the causes and pathogenetic mechanisms are sufficiently similar to those of the human disease. A considerable advantage of the animal study is the absence of a placebo effect. This aspect is particularly important for medicines whose effects are often dismissed as imaginary, as frequently happens with homeopathics.

The model

A recognized animal model of osteoarthritis with high transferability of the results to humans is the induction of an analogous disease picture in rabbits via experimental destabilization of the knee joint (surgical division of the cruciate ligament). This model was adopted by an international working group (German-Slovak-Hungarian) to permit a more precise evaluation of the effects of a homeopathic combination product on the development and progression of osteoarthritis.

Study design

The rabbits were divided into two groups, of which the first received only the solvent while the second received the test product (Zeel comp., manufactured by Biologische Heilmittel Heel GmbH, Baden-Baden). Both the control solution and the test product were injected intraarticularly (twice weekly) in accordance with the instructions for administration of Zeel comp. Each group was treated for 9 weeks. The treatment was followed by macroscopic examination of the joint surface and microscopic (histochemical) evaluation of the tissue structure of the cartilage layer.

Results

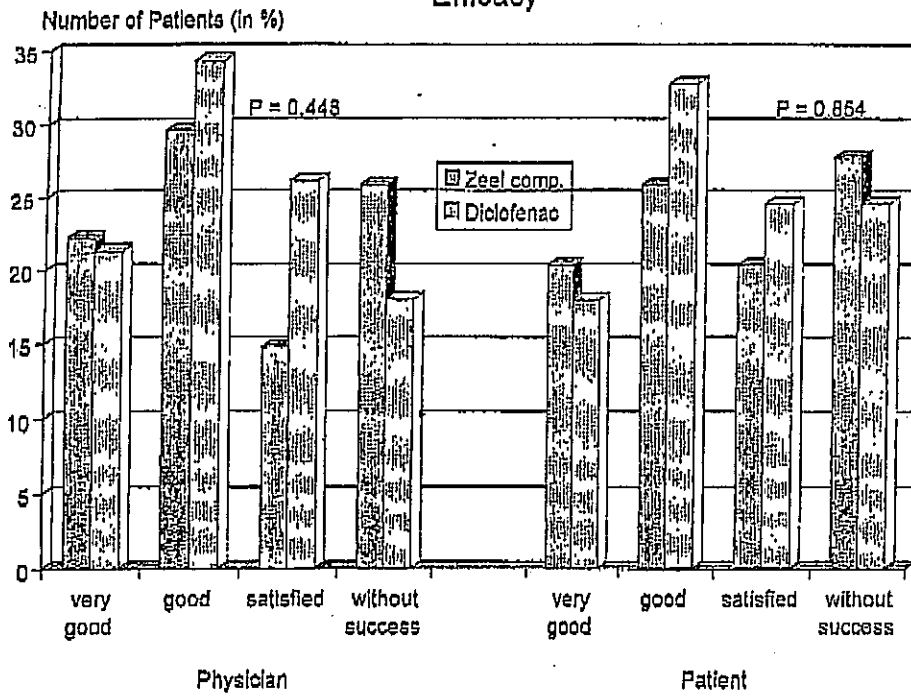
While the control group showed macroscopically evident erosions and the picture of a hypertrophic cartilage surface, the group treated with Zeel comp. showed much less noticeable changes in surface structure. The histochemical investigations confirmed these initial findings: the deeper cartilage layers in the control group treated only with solvent were strongly vascularized. This parameter too showed clear superiority of the Zeel treatment, only a few blood capillaries being detectable in the Zeel group. Finally, whereas the control animals showed largely unstructured tissue, the group treated with the test product showed not only a virtually normal arrangement of the chondrocytes but also an only slightly altered cartilage border.

Conclusions

By administering the homeopathic injection solution Zeel comp. in accordance with the instructions in an animal model broadly corresponding to human osteoarthritis, the damage to the articular cartilage can be almost entirely prevented. Since a placebo effect can be excluded in this model and the pathophysiological mechanisms correspond to those of the human disease, it may be inferred that the existing good empirical experience with the clinical use of Zeel comp. is due to genuine effects of the medication and not to imaginary effects.

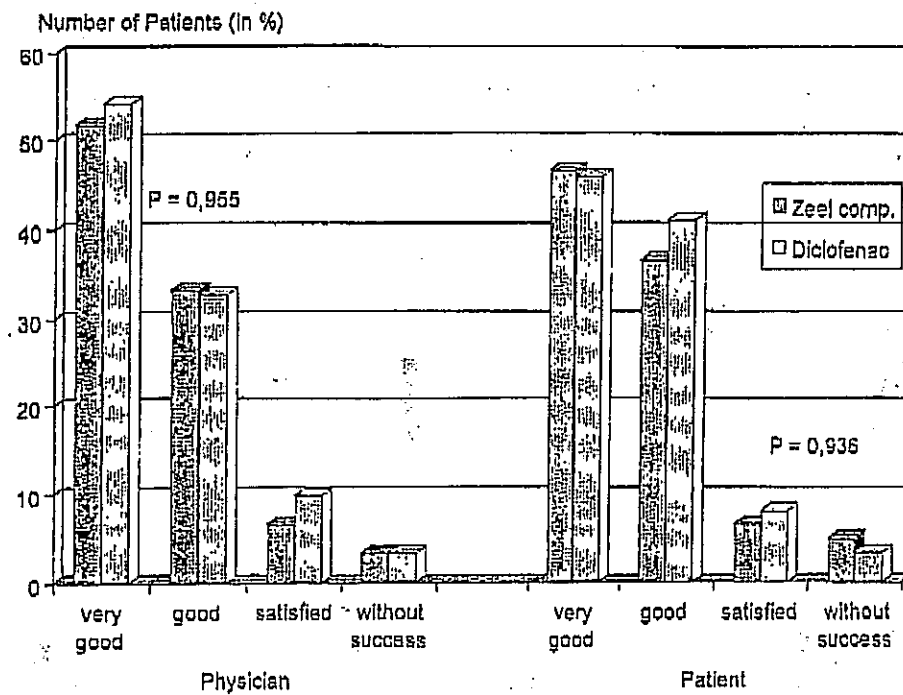
These graphs are for your information – I would not recommend to use them for marketing as they might be easily misinterpreted.

Zeel comp. vs. Diclofenac Global Assessment Efficacy



Study: HE6708

Zeel comp. vs. Diclofenac Global Assessment Tolerance



Study: HE9706

Zeel comp. vs. Diclofenac - Points which might be criticized together with suitable replies

Critical fact	Additional information	Possible reply
Dosage of Diclofenac low (75 mg/ day)	The dosage of Diclofenac depends on the severity of the symptoms. The study was conducted in Germany where the recommended dosage lies between 50 - 150 mg/ day	Zeel is as effective as Diclofenac in the treatment of <u>mild to moderate forms</u> of gonarthrosis – in severe cases Zeel might help reduce the dosage of Diclofenac. 3 x 25 mg Diclofenac is appropriate for chronic arthritis – which is the major indication for Zeel
All graphs show Zeel comp. to be slightly inferior to Diclofenac	See graphs	1) Nevertheless Zeel is equivalent to Diclofenac as calculated objectively by statistical analysis (see text to first graph) 2) The values for Zeel are still within the 95% confidence interval (CI) – (see graph) 3) The efficacy of Zeel comp. (a homeopathic medication) has been proven to be within the same dimension as Diclofenac.
The study is not placebo-controlled	Diclofenac is an established medication (NSAID) against arthrosis	1) It is very difficult to find >100 patients suffering from osteoarthritis who are willing to take the 50:50 risk of getting no treatment (placebo) for 10 weeks. Especially as Zeel is not a new medication which can only be tried by participating in a study. 2) Whether or not placebo-controlled is really the best type of study is discussed very controversially.
There were more adverse events (AE) reported in the Zeel comp. group than in the Diclofenac group	44 patients (81 AE) in total, 24 in Zeel and 20 in Diclofenac group It is an accepted fact that NSAIDs do cause severe adverse events (see first Infoletter of 16 th of July 1999 for figures and facts)	1) More important is the following: only for 21 out of the 44 patients, it was estimated as possible that the adverse event was <u>caused</u> by the medication. And here only 9 were of the Zeel but 12 of the Diclofenac group. 2) Side effects of NSAIDs usually occur at a higher dose than 75mg/ day. Therefore, ulcers, bleedings, an important side effect of NSAIDs, were not especially investigated.

The last point is the most important one – do not use this study to demonstrate the tolerance of Zeel. As NSAIDs have such a bad reputation regarding tolerance, it is not a positive result that the tolerance of Zeel is equivalent to the tolerance of Diclofenac. Nevertheless, there is no doubt that Zeel is far better tolerated (we never had any serious side effects like those associated with NSAIDs reported in our history) – only this study does not show it.