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PST (Pulsed SIgnal Therapy): a proposal for chondroprotection with physical methods

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Summary: PST (Pulsed SIgnal Therapy) is suggested as a method of long-term physical chondroprotection by means of the administration of very low frequency magnetic fields, ranging between 3 and 30 Hz.
The results provided by an open study still in progress are reported. The pathologies examined are knee arthritis and non-disc low back pain.
The results achieved are satisfactory but further confirmation (both histological and instrumental) is required in support of the effectiveness of the chondroprotective mechanism as claimed.

Key words: Electromagnetic fields, proteoglycans, osteoarthritis, articular cartilage

Introduction

Osteoarthritis is a disease which affects about 1.8% of the population in developed countries and its incidence is rising continuously in parallel with the increase in average life expectancy. The current approach to it consists of a therapeutic programme based:
- on application of behavioural standards directed towards bringing about articular economy;
- on the use of symptomatic drugs such as the non-steroidal anti-inflammatories (NSAIs) to control painful symptoms and signs of inflammations;
- on the use of chondroprotective drugs capable of intervening in the process of degradation of the cartilage and at the same time of stimulating repair mechanisms.

Osteoarthritis is a pathological condition of articular cartilage which commences earlier than was once thought, probably as early as the age of 20-25 years, but which has a fairly slow course.
Articular cartilage consists histologically of cells, the chondrocytes, and intercellular substance or matrix, consisting in turn of collagen fibres and an amorphous component. The chondrocytes are provided with a complete set of enzymes, both synthetic and degradative; they are thus responsible for both the synthesis and degradation of proteoglycans and collagen although they are not able to ensure its metabolism in adults. Current knowledge attributes the origin of the progressive alteration of the cartilage to damage to the chondrocytes, even if the causes of the initial disorder of the chondrocyte are not yet known.
The basic elements of the amorphous component are the proteoglycans (PG) which are arranged in high molecular weight aggregates (aggrecans). The proteoglycans consist of a central protein chain (core protein), to which are bound polysaccharide compounds called glycosaminoglycans (GAG), the main ones of which are chondroitin-4 sulphate, chondroitin-6-sulphate, keratan sulphate and, to a lesser extent, hyaluronic acid; the chondroitin sulphates are present in a greater proportion than the keratan sulphates, though the latter increase physiologically in old age.

Various studies indicate that the capacity of the cartilaginous tissue to withstand compressive stresses is linked to the level of proteoglycans in the intercellular substance; the sulphated glycosaminoglycan chains have an increased concentration of negative electrical charges which give considerable rigidity to the system by their reciprocal repulsion and hold bound a large part of the cartilaginous water in states of rest. Once the destructive process has begun, similarly to the operation of factors which stimulate the chondrocytes to produce harmful substance in pathological quantities, the same cells initiate an attempt at regeneration of the cartilage by increasing the synthesis of glycosaminoglycans. However, they are not capable of supporting such hyperactivity for long so the glycosaminoglycan content is reduced with a more marked reduction in the chondroitin sulphates and an increase in the keratan sulphate/chondroitin sulphate ratio.
The reduction int the proteoglycans, the breaking up of the proteoglycan aggregates, their increased extractibility and the change in tissue hydration cause a reduction of the resistance of the amorphous substance and the collagen fibrils are subjected to intolerable mechanical pressure. There have been numerous studies showing that the process is reversible initially; if maintenance of an adequate concentration of GAG is successful, the cartilage damage can be hindered or slowed and use of chondroprotective drugs and also of PST is based on this assumption.
Pulsed Signal Therapy (PST) is based on a patent developed by the American doctor and biophysicist of German origin, Richard Markoll. This is a therapeutic method which differs from the so-called magnetic field therapy used for many years for slowly consolidating fractures. PST, while it can be used in bone tissue also, finds its main indication in the treatment of cartilage and of soft and connective tissues.
To understand the effect of PST, it must be remembered that when a joint is subjected to compressive stress, there is a displacement of the water present in the matrix accompanied by sodium ions, leaving the negative charges of the proteoglycan molecules unneutralised. By a mechanism of mechanical-electrical transduction, the mechanical stimulus is transformed into a weak electric current (potential streaming) which is thought to represent the main signal for the cartilage cells to increase the synthesis of proteoglycans and collagen.
If the potential streaming is the signal for chondrocytes to produce new matrix, the same effect can be obtained by exposing the joint to an electromagnetic field, producing currents which simulate those of the organism. Administration in this way of low strength pulsed signals at a frequency similar to the biological one is capable of creating an electrical field in the joint, promoting the regeneration of the cartilaginous tissue, and thus conferring physical chondroprotection.
Controlled double-blind studies in the United States at Yale University documented positive results for PST in osteoarthritis, but satisfactory results have also been achieved in open studies conducted in France and Germany.
When we were invited to be the first in Italy to use this therapy, we began a study in May 1997 of patients with arthro-rheumatic disorders with the aim of assessing the efficacy in the short and medium term of PST. We report the results obtained in two distinct conditions, one with precise characteristics of a degenerative articular disorder (arthritis of the knee) , the other with a pathogenesis which is less easily individualisable and often multifactorial, selected because of its wide incidence (low back pain).

Materials and methods
Our study comprises 58 ambulant patients, 24 suffering from back pain and 34 from knee pain. All of the subjects admitted to the study had to have painful symptoms persisting for at least three months, incompletely relieved by common treatments, based on the use of NSAIs,

analgesics and forms of physical therapy. Patients who did not complain of pain at the time of recruitment were excluded even if they reported recurrent episodes in the preceding three months; similarly, patients who had undergone pharmacological and/or physiotherapy in the preceding 30 days were also excluded. Other reasons for exclusion were: the presence of a neoplastic illness, previous surgical procedure to remove a neoplastic growth, presence of an unstable medical condition (hepatic cirrhosis, decompensated diabetes etc.), presence of a pacemaker.
The patients with low back pain, 24 in total, 7 males and 17 females, with an average age of 65.43 years had to have characteristics as similar as possible. Accordingly, we considered only low back pain associated with a minor intervertebral disorder of L4-L% or L5-S1, excluding patients with back pain of low dorsal origin. Patients therefore underwent a regional and segmental clinical examination according to the schema descirbed by Maigne. Inclusion criteria were the presence of painful back movement, presence of DIM (?), and absence of signs suggestive of a radicular cause. For instrumental examination, we were limited to radiographic study to exclude tumours, inflammatory and infectious conditions; patients with spondylolisthesis and vertebral malformations were also not admitted to the study. We did not have an opportunity of requesting a CT scan, but those patients who had had one in the preceding months which showed herniation, even if slight, were also not enrolled in the study.
The sample of patinets with knee pain consisted of 34 subjects, 8 males and 26 females with an average age of 67.85 years with degenerative disease diagnosed clinically and radiologically. The pain had to have a score of at least 5 on the visual analogue scale and have mechanical characteristics. As radiological criteria for inclusion, we adopted reduction of the joint line and the presence of at least one of the following: subchondral osteosclerosis, sharpening of the intercondylar tibial spines, marginal osteophytes, lateral subluxation of the patella, subchondral cysts, remodelling of the bone structure.
For our study we used PST (Pulsed Signal Therapy) equipment duly obtained from Germany. The electromagnetic field generated is low strength, about 12.5 Gauss, of extremely low frequency. This emits trains of unidirectional pulses of an almost rectangular shape with modulations in both amplitude and duration and with a "biological" frequency between 1 and 30 Hz (Figure 1); the frequency is not constant throughout the duration but has six variations in the course of the entire session. The physical parameters used are the result of work carried out for some years aimed at finding the parameters which most "simulate" those obtained from calculation of the potential streaming.
The protocol was standard: a cycle of nine sessions of one hour each on successive days; any interruptions should not exceed 48 hours. The relaxed patient is placed seated or lying on a suitably designed chair or couch while the joint to be treated is positioned eccentrically in an air-filled sleeve (Figure 2, 3).

Fig. 1: Trains of unidirectional pulses between 1 and 3 Hz

Fig. 2: Positioning of knee

Fig. 3: Positioning of lumbar region

Table 2: Low back pain

Tests of function		
Have you pain turning in bed?	yes	no
Have you pain coughing or sneezing?	yes	no
Have you tingling in a leg (or both legs)?	yes	no
Have you pain going up or down stairs?	yes	no
Have you pain when you wash at the wash-basin?	yes	no
Have you difficulty getting in or out of a car?	yes	no
Have you difficulty putting on socks/stockings?	yes	no
Have you difficulty walking on your toes?	yes	no
Have you difficulty walking on your heels?	yes	no
Finger-ground distance in flexion?	+ 10 cm	- 10 cm

Table 2: Arthritis of knee

Tests of function		
Do you complain of pain at rest	yes	no
Have you pain after standing for long periods?	yes	no
Have you pain squatting?	yes	no
Have you pain after sitting for short periods?	yes	no
Have you pain after sitting for long periods?	yes	no
Have you difficulty getting in or out of a car?	yes	no
Have you difficulty putting on socks/stockings?	yes	no
Have you difficulty walking normally?	yes	no
Have you difficulty walking quickly?	yes	no
Have you difficulty doing housework?	yes	no

Method of assessment
The patients were assessed at three points in the course of the study: at the start of treatment (time 0), at the end of the treatment (time 1) and six weeks after the end of the treatment (time 2). The subjective report of pain and certain functional parameters were taken into account. To measure the former, we used a Scott-Huskisson Visual Analogue

Scale (VAS). We recall that the presence of pain constituted the essential condition for admission to the study. Apart from the VAS, we made use of a personal questionnaire of 10 questions asking the patient about the functional consequences produced by the pain (table 1, 2); this questionnaire was compiled by a doctor at each of the three survey times.
Analysis of variation by repeated measurements was employed; however, analysis of descriptive type was used for detailed examination of the cases and the tests of function, bearing in mind the frequency distribution of the different items.

Results
A significant improvement was found, already present at the end of the therapeutic cycle, which continued to increase in the following weeks.

Patients with knee pain
Considering pain, the VAS score changed from an initial 7.12 to 5.41 and finally to 3.09, with an improvement of 24% and 43.4% respectively (Table 3). With regard to the score in the tests of function, this changed from an average figure of 7.15 to 5.88 and finally to 2.26 , with an improvement of 17.8% and 68.4% respectively. However, analysis of the results obtained in the individual tests is more interesting (Table 4). Comparing the data at time 0 with that at time 2, pain at rest was no longer present in the 11 initial subjects; pain occurring after prolonged sitting was reported by 25 subjects and this fell to only 7; the pain on squatting present in all 34 subjects enrolled in the study persisted in 22 (improvement in 35.3%). Of the 26 women in the group, 21 initially reported difficulty in doing housework; this number fell to 16 at time 1 and 0 at time 2. It can be seen that the results confirm that this treatment has a beneficial effect at the end of the therapy but reaches its maximum effect later. This fact appears to justify the proposal of PST not only as an analgesic treatment but as a treatment aimed at intervening in the pathogenesis of the painful symptoms.

Table 3: Subjective assessment of pain using VAS

	Osteoarthritis of knee				
	N	Average +/- SD	Minimum	Maximum	P
Time 0	34	7.12 +/- 1.01	6	8	
Time 1	34	5.41 +/- 1.44	2	8	**
Time 2	34	3.09 +/- 1.88	1	6	**

** $p < 0.01$ vs baseline (analysis of variance by repeated measurements)

	Low back pain				
	N	Average +/- SD	Minimum	Maximum	P
Time 0	24	7.92 +/- 1.10	6	10	
Time 1	24	6.25 +/- 1.36	4	8	**
Time 2	24	3.92 +/- 2.10	1	8	**

** $p < 0.01$ vs baseline (analysis of variance by repeated measurements)

Table 4: Tests of function, arthritis of knee

		TIME 0		TIME 1		TIME 2	
		N.	%	N.	%	N.	%
Have you pain	NO	23	67,5	28	82,4	34	100,0
at rest?	YES	11	32,4	6	17,6	0	0,0
Have you pain after	NO	5	14,7	8	23,5	18	52,9
standing for long period	YES	29	85,3	26	76,5	16	47,1
Have you pain	NO	0	0,0	0	0,0	12	35,3
squatting?	YES	34	100,0	34	100,0	22	64,7
Have you pain after	NO	32	94,1	34	100,0	34	100,0
sitting for short periods?	YES	2	5,9	0	0,0	0	0,0
Have you pain after	NO	9	26,5	13	38,2	27	79,4
sitting for long periods?	YES	25	73,5	21	61,8	7	20,6
Have you difficulty	NO	2	5,9	14	41,2	30	88,2
getting in / out of a car?	YES	32	94,1	20	58,8	4	11,8
Have you diffic. Putting	NO	5	14,7	8	23,5	28	82,4
on socks/stockings?	YES	29	85,3	26	76,5	6	17,6
Have you difficulty	NO	7	20,6	16	47,1	33	97,1
walking normally?	YES	27	79,4	18	52,9	1	2,9
Have you difficulty	NO	1	2,9	1	2,9	13	38,2
walking quickly	YES	33	97,1	33	97,1	21	61,8
Have you difficulty	NO	13	38,2	18	52,9	34	100,0
Doing houswork?	YES	21	61,8	16	47,1	0	0,0

Patients with low back pain
The pain according to the VAS fell from 7.92 (time 0) to 6.25 (time 1) amd 3.92 (time 2) with an improvement of 21.1% and 50.5% respectively (Table 3). Considering the individual tests of function (Table 5), we would like to observe that the result with regard to ability to put on socks or stockings, a fairly indicative test, which was initially quite difficult in 23 of the 24 subjects, persisted in only 13 at time 2. Likewise, the result of the question about the difficulty in washing at a wash-basin is also interesting: all of the subjects complained of it prior to undertaking the treatment but none reported it at time 2.

Conclusions
The results obtained from this group of patients are definitely positive and better than those which could be attributed to a simple placebo effect. The mechanism of action by which PST exerts its beneficial effect remains to be clarified. It is known that osteoarthritis is slowly progressive and this allows a reactive

response to slow its development; experimental observations show that there is an increase in the synthesis of ptoteoglycans in the initial phase of the arthritic process so that the process is still reversible. In time, this response becomes inadequate to compensate the increasingly severe lesions which become apparent in the articular cartilage; this loses elasticity and becomes insufficient for withstanding the stresses to which it is subjected. The reduction in GAG synthesis combined with increased activity of the metalloproteases which degrade the proteoglycan molecules (fragments of proteoglycans have been found in the synovial fluid of patients affected by arthritis) cause greater pressure to be transmitted to the bone beneath, causing pain since the periosteal covering is highly innervated.

Table 5: Tests of function, low back pain

		TIME 0		TIME 1		TIME 2	
		N.	%	N.	%	N.	%
Have you pain	NO	2	8,3	9	37,5	24	100,0
turning in bed?	YES	22	91,7	15	62,5	0	0,0
Have you pain	NO	24	100,0	24	100,0	24	100,0
coughing or sneezing?	YES	0	0,0	0	0,0	0	0,0
Have you tingling in	NO	20	83,3	21	87,5	24	100,0
a leg (or both legs)?	YES	4	16,7	3	12,5	0	0,0
Have you pain going	NO	0	0,0	0	0,0	13	54,2
up or down stairs?	YES	24	100,0	24	100,0	11	45,8
Have you pain when you	NO	0	0,0	9	37,5	24	100,0
wash at a wash-basin?	YES	24	100,0	15	62,5	0	0,0
Have you difficulty	NO	0	0,0	1	4,2	17	70,8
getting in / out of a car?	YES	24	100,0	23	95,8	7	29,2
Have you difficulty	NO	1	4,2	1	4,2	11	45,8
putting on socks/stock.?	YES	23	95,8	23	95,8	13	54,2
Have you difficulty	NO	16	66,7	17	70,8	22	91,7
walkin gon your toes?	YES	8	33,3	7	29,2	2	8,3
Have you difficulty	NO	17	70,8	17	70,8	20	83,3
walking on your heels?	YES	7	29,2	7	29,2	4	16,7
Fingerground distance	-10 cm	1	4,2	2	8,3	9	37,5
with trunk flexed?	+20 cm	23	95,8	22	91,7	15	62,5

According to Markoll, and also according to other authors who have used PST, it acts by reproducing the mechanisms of autostimulation present in cartilage, thus restoring a sufficient concentration of proteoglycans. There are various experimental studies in the literature which report the effects of pulsed magnetic fields on cartilage and in the majority of them, an increased proteoglycan content was found in response to the treatment. Grodzinski subjected a sample of cartilage to intermittent pressure and observed that an electrical current was generated and there was an increase in the synthesis of the consitutents of the matrix which was greater as the frequency of the compression exerted on the cartilage increased.
However, studies carried out in vitro on cultures of chondrocytes or cartilage are limited in some ways and must be confirmed in vivo. The possibility of assessing the state of the joint surface with a non-invasive method such as echography offers interesting prospects which would permit demonstration of early lesions not yet detectable by radiographic imaging and at the same time monitoring the efficacy of the PST.

While these results are awaited, it should be stressed that the mechanism of action claimed can be acceptable for some but not all forms of arthritis; furthermore, it is right to wait for better results in those forms in which the cartilage is not yet very worn and where the number of residual chondrocytes is still high. This could be the situation in those patients who complain of symptoms which are not accompanied by radiographic evidence of joint abnormality. Another critical consideration concerns the treatment protocols used which are the same for all sites, for both primary and secondary forms of arthritis and for both moderate and advanced joint disease.
Finally, in the light of the results obtained in patients affected by low back pain, where the joint origin of the complaint is somewhat debatable, it can be hypothesised that PST also acts by means of other mechanisms, as yet unknown.
It can be seen that much remains to be elucidated about the possibilities of PST. In undertaking our study, we had two aims: to assess the efficacy of the therapy, to understand and, if possible, document its mechanism of action. The first aim was achieved even if it remains to be clarified which disorders are more sensitive and which are less so. The second aim has not yet been achieved and we await the results of a study currently in progress in Germany.