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Degenerative spondylolisthesis and joint disease in adult people

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RESUMEN

Con base en los hallazgos anatómicos, hormonales y patológicos en la columna y articulaciones periféricas en pacientes con cambios degenerativos, creo que ambos son causados por isquemia progresiva debida a aterosclerosis y deficiencia de hormona de crecimiento en nuestro cuerpo. Los cambios patológicos son iniciados en los discos intervertebrales (alrededor de 30 años) y varios años después (alrededor de 50 años), en las articulaciones periféricas. Por eso, en mi opinión, el tratamiento debe estar dirigido en contra de la aterosclerosis y terapia de sustitución con hormona de crecimiento.

Palabras clave: *Aterosclerosis, articulaciones periféricas, discos intervertebrales, hormona de crecimiento.*

ABSTRACT

In base to anatomical, hormonal and pathological findings in the spine and peripheral joints in patients with degenerative changes, I believe that both of them are caused by progressive ischemia due to atherosclerosis and growth hormone deficiency in our body. The pathological changes are initiated in the intervertebral discs (about 30 years) and several years later (about 50 years), in the peripheral joints. Thereby, in my opinion, the treatment must be directed against the atherosclerosis and growth hormone replacement therapy.

Key words: *Atherosclerosis, growth hormone, intervertebral discs, peripheral joints.*

INTRODUCTION

Since 1982, some investigators[1,2] have suggested that insufficient blood supply to lumbar spine could be a significant causative factor in disc degeneration. This theory was supported later by anatomical studies[1,3] and findings of atheromatous plaques in the abdominal aorta around the aortic bifurcation.[4,5] At present there are many evidences[6-8] that the porimary cause of these degenerative changes in the spine is of microvascular origin.

Up to date, all authors support that degenerative joint disease (DJD) has no cure. However based on the anatomical and histological likeness between the intervertebral discs and peripheral joints, I postulate that the degenerative changes in both of them structures are caused by ischemia and decreasing growth hormone (GH) levels in the bloodstream. For these reasons, in this article I analyse the characteristics of these structures, as well as degenerative changes at the same joints.

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THE INTERVERTEBRAL DISCS

Normally the structural elements of the intervertebral discs have three components:

- The annulus fibrosus (constituted by fibrocartilage).
- The nucleus pulposus.
- The cartilaginous endplates (hyaline cartilage).

The greater part of the fibrocartilage in the body are found at the annulus fibrosus (constituted by a multiple concentric lamellae of collagen fibers) sites of insertion of ligaments and tendons into bone.[9,10] The nucleus pulposus consist of a small number of cells sparsely dispersed in a soft gelatinous matrix rich in hyaluronic acid. The vertebrae have a thin layer of hyaline cartilage (cartilaginous endplates) on their superior and inferior surface. The 80% of this cartilage is water and the rest, is constituted by collagen, noncollagen substance, chondrocytes and proteoglycans. The chondrocytes secrete collagen and proteoglycans in the matrix.

In children, adolescents, and individuals up to 30 years of age, the nucleus pulposus receive small blood vessels through the cartilaginous endplates.[1,3,7] Thus, the

discs and vertebral bodies receive their blood supply from branches of the vertebral arteries, aorta and middle sacral artery. After 30 years, these small vessels become gradually obliterated leaving scars in the cartilaginous endplates.[1,11,12] The consistence of the nucleus pulposus is increasing and by contrast, its size are reduced with the age. Therefore, in elderly people the nucleus pulposus and annulus fibrosus are completely without blood supply[7,11] and the chondrocytes are nourished by diffusion through its intercellular substance. The chondrocytes in the hyaline cartilage are gradually loss and the cartilage is then invaded by blood vessels, phagocytes and the matrix is resorbed and replaced by fibrous scar tissue.[9,13] Therefore, these cells have a very limited ability to regenerate, resulting in irreversible cartilage destruction.

Thus, the degeneration of the cartilaginous endplates then leads to pathological changes in the vertebral bodies such as:[7,14,15]

1. Changes of facet joints.
2. Reduced height discs.
3. Herniated discs.
4. Osteophytes.
5. Osteochondrosis.
6. Spondylolisthesis.
7. Spinal stenosis.
8. Hypertrophy of yellow ligament.

Among other degenerative changes. In this respect, clinical and radiographic evidences demonstrate that herniated or extruded discs can suffer spontaneous disappearance with conservative management. In contrast, surgical treatment must be performed only on patients with neurological deficits.[7,8]

THE PERIPHERAL JOINTS

In the manner of the structural elements of the intervertebral discs, in the peripheral joints (interphalangeal, wrist, ankle, elbow, knee, shoulder and hip joints) there are morphological similarities (Figure 1). Thus, 1) the articular capsule (marginal fibrocartilage) falls to the annulus fibrosus; 2) the synovial liquid (articular liquid) to the nucleus pulposus, and 3) the articular cartilage (hyaline cartilage) to the cartilaginous endplates. In the articular cartilage, the collagen seems to be quite enduring, but the proteoglycans are slowly turned over, being replaced by newly synthesized molecules.

In the long bones, both of them epiphysis and the articular capsule are vascularized by the nutritious arteries

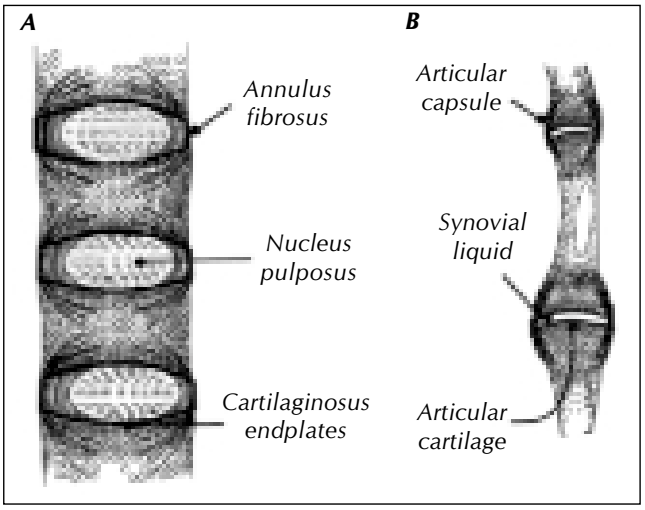

Figure 1. *Morphological likeness between intervertebral discs* ***(A)*** *and interphalangeal joints* ***(B)*** *or another peripheral joints. The cartilaginous endplates and articular cartilage, both of them are hyaline cartilages.*

from the diaphysis and in less quantity by small arteries from the articular arteries.[10] Likewise, in elderly people, the chondrocytes of the articular cartilage are nourished by diffusion from the matrix, which is constituted essentially by water.

Clinical, radiological or pathological evidences suggests that DJD in the peripheral joints, is primarily a disease of hyaline cartilage; which then leads to secondary changes of bone, such as subchondral sclerosis and osteophytes formation.[16] In other words, new bone formation is developed in subchondral bone and at the margins of the articular cartilage. The bone at joint margins responds to cartilage damage with osteophytes formation. This DJD occurs in a very high percentage in elderly persons, especially after 45 years of age and is more common in women than in men. The diagnosis of DJD (also known as primary osteoarthritis or osteoarthrosis) is based on the medical history and physical examination. Laboratory tests do not reveal signs of inflammation.

It is important to understand that until now, there is no cure for DJD and that all of the therapy is aimed at slowing the progression of the disease and alleviating the clinical signs with medical management such as:

- Nonsteroidal anti-inflammatory drugs (NSAIDs).
- Corticoids.
- Chondroprotective agents (hyaluronan, polysulphated glycosaminoglycan and oral chondroprotective agents).

ATHEROSCLEROSIS AND HYPOTHALAMIC ISCHEMIA

During the fetal stage, as soon as the blood begins to flow through the aorta artery and its branches, the elastic properties of the aortic arch[17] onset to present deterioration and focal accumulation of fatty streak in the intima. This predilection of the aortic arch for atherosclerotic changes is determined by the hemodynamic forces.[4] Thus, the pathological changes have a course centrifugal, ie., from the aortic arch towards the peripheral arterial system.[12,17] In the aorta of the great majority of newborns and in virtually every children there are a focal accumulation of containing and surrounded by deposit of lipids.[18]

So therefore, these hemodynamic and pathological changes indicate that in early stages of life, the atherogenesis is a biological response of the intima to stimuli of the hydraulic forces (primary factors: Bernoulli's and Poiseuille's theorem, and the ventury effect, among anothers),[4,12] and later on, in children, adolescence and mature age are incorporated secondary factors (risk factors: cigarette smoking, carbon monoxide, hydrocarbon solvent and obesity, among anothers,[12,19] that accelerates the development of atherosclerosis, especially after the sixth decade. So that, in persons about 30 years of age, we can find atherosclerotic plaques in the supraclinoid carotid arteries (about 3% of cases) and distal end of the basilar artery (about 8% of ceses), it observed during arteriographic studies[20] and in large series of autopsied cases.[21]

Within the hypothalamus, the number of capillaries is influenced by the demands which the parenchymal elements make on the bloodstream.[22-24] There are not end-arteries, because their terminal branches anastomose with branches of other arteries of the diencephalon. The capillary walls in these highly vascularized hypothalamic nuclei are fused with the membranes of neuronal perikarya and process.[22,25] In these areas of contact there are no evidence of glial interposition between the neuronal and vascular elements (neuronal-vascular relationships). Such neuronal vascular contact are characteristics in the supraoptic and paraventricular nuclei.[22,23]

However, between 25 to 30 years of age, the producing hypothalamic nuclei (lowermost portion of the ventromedial nuclei, arcuate nucleus and tuber cinereum) of growth hormone-releasing hormone (GHRH) are the first one in to suffer ischemic injury.[26-28] After 25 years, there is a direct correlation between decreasing GH levels and the effects of aging,[29,30] and on the other hand, the total number of neurons in the arcuate nucleus decrease with age.[31] These observations suggest that in the mature brain, the neurogenesis starting from undifferentiated cells (stem cells)[32-34] located in the walls of the third ventricle (subventricular zone) decline with age up to disappear. That is, about 30 years of age, the adult stem cells located in this hypothalamic region are scarse or do not exist.[28] Simultaneously or few years later, this ischemic lesion in the producing hypothalamic nuclei of GHRH may also affect to another hypothalamic nuclei and to cause disorders such as obesity,[35] type 2 diabetes mellitus,[36] neurogenic hypertension,[37] narcolepsy[38] and metabolic syndrome.[39,40] Because, in contrast to this, the revascularization of the hypothalamus can cure or improve these diseases.

GROWTH HORMONE AND ARTICULAR CARTILAGE

In Humans, about 25 to 30 years of age, there is parallelism decreasing in the daily secretion of GHRH and GH from the hypothalamic nuclei (Figure 2) and adenohypo-

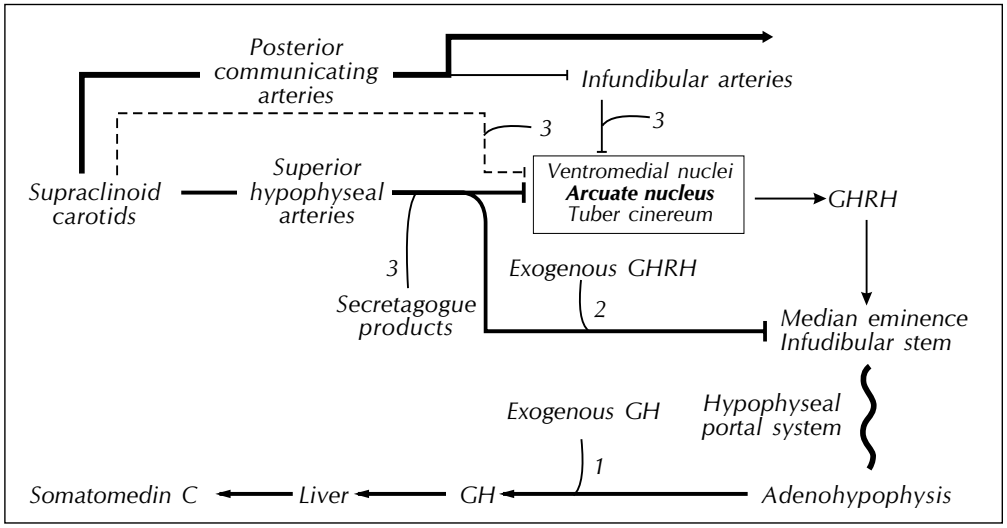

Figure 2. *The drawing shows the normal vascu larization of the produ cing hypothalamic nuclei of growth hormone relea sing hormone (GHRH) from the supraclinoid ca rotids. Growth hormone (GH) secreted by the ade nohypophysis. Therapeu tic methods used up to date against aging:* ***1.*** *exo genous GH;* ***2.*** *exogenous GHRH, and* ***3.*** *secretago gue products. Reprodu ced from references 27 and 50.*

physis, respectively.[27,31,40,41] Subsequently, on practically every persons after 30 years, there is a direct relation between the serum GH concentration and the effects of aging.[42,43] For example a 20-year-old man may secrete 4 to 5 times more of the GH than a 60-year old. For these reasons, GH deficiency in adults is called somatopause.[40]

GH acts on the liver and another tissues to stimulate the production of somatomedins (sulphating factors), especially of somatomedin C;[44] which serve as an indicator of overall growth hormone secretion. Thereby, there is a direct correlation between the serum GH concentration and the plasma concentration of somatomedins. So then, GH through the somatomedins exert many biological effects such as these:[45-48]

1. Transformation of aminoacids in proteins, especially in the synthesis of deoxyribonucleic acid (DNA) and ribonucleic acid (RNA).
2. Favours the conversion of prolin in hydroxiprolin for the collagen synthetized by fibroblasts and chondrocytes.
3. The incorporation of sulfates in the cartilage in form of chondroitin-4-sulfate and chondroitin-6-sulfate.

Among another mucopolysaccharides. In other words, GH favours the regeneration of the hyaline cartilage, especially associated with the use of NSAIDs. Because both aspirin and nonaspirin NSAIDs exert their anti-inflammatory effect for the prevention and reduction of atherothrombosis.[18,19,37] Likewise, GH associated with insulin and thyroxin are necessary requirements for the growth and proliferation of cells in the entire body and in the encephalon.

Therefore, there is no doubt that GH injections as an anti-aging therapy can play important role throughout normal adult life. Long-term follow-up data demonstrate that the GH replacement therapy is safe,[49] and to date, there is no evidence that GH replacement therapy increases de novo malignancies or tumor regrowth in patients.[43,49] But the rejuvenation can also be observed following to revascularize the producing hypothalamic nuclei of GHRH by means of omental transplantation on the optic chiasma, carotid bifurcation and the anterior perforated space.[27,50] That is, revascularization of the hypothalamus or the GH replacement therapy can reverse the effects of aging and improve health and fitness. For these reasons and based on the above-mentioned factors, I believe that the GH deficiency in adults (after 30 years of age) is cause of degenerative changes in the spine[7,15,47] and several years later (about 50 years),in the peripheral joints.

CONCLUSIONS

These anatomical, hormonal and pathological observations in the intervertebral discs, peripheral joints, genesis of atherosclerosis and GH deficiency in adults, all of them suggest that the degenerative changes in the spine and peripheral joints have the same pathophysiological mechanism. Initially the atherosclerosis affect to the producing hypothalamic nuclei of GHRH, and later on; the atherosclerosis associated with a decline of GH levels in our body, both of them are responsible of the degenerative changes. Thereby, in my opinion, the use of anti-inflammatory agents associated with GH replacement therapy or the transplants of omentum on the optic chiasma and carotid bifurcation may be used against these diseases. Because through the omentum, the hypothalamic nuclei receive an increase in blood flow, oxygen, neurotransmitters, neurotrophic factors, cytokines and omental stem cells.

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