Intervertebral Disk Nutrients and Transport Mechanisms in Relation to Disk Degeneration: A Narrative Literature Review

Christopher M. De Geer, DC, MSc

Abstract

Objective: The purpose of this paper was to review the literature regarding the mechanisms leading to degeneration in intervertebral disks and to discuss contributing mechanical and biological factors.

Methods: The inclusion criteria for the literature review were research studies conducted in the last 3 decades with free full-text available in English. Review articles and articles pertaining to temporomandibular joints and joints of the body other than the intervertebral disk were excluded. The following databases were searched: PubMed, EBSCOhost, and Google Scholar through September 9, 2016.

Results: A total of 57 articles were used in this review. Intervertebral disk cells require glucose for sustainability and oxygen to synthesize matrix components. Nutrients enter the disk via 2 vascular supply routes: capillary beds of end plates and the peripheral annulus fibrosus. Solute size, shape and charge, compression, and metabolic demand all influence the efficiency of nutrient transport, and alterations of any of these factors may have effects on nutrient transport and, potentially, disk degeneration.

Conclusions: Progressive nutrient transport disruptions may actively contribute in advancing the phases of degenerative disk disease. Such disruptions include dysfunctional loading and spinal position, lack of motion, high frequency loading, disk injury, aging, smoking, an acidic environment, and a lack of nutrient bioavailability. (J Chiropr Med 2018;17:97-105)

Key Indexing Terms: *Intervertebral Disk Disease; Diet, Food, and Nutrition; Intervertebral Disk Degeneration*

Introduction

Mechanisms behind nutrient delivery that may lead to intervertebral disk (IVD) degeneration are complex.[1-5] Understanding how nutrients play a role in degeneration may help in treatment and prevention of spinal disease. This study reviews the literature on biomechanical and biological factors in nutrient transport mechanisms and the role these processes have in IVD degeneration.

Methods

PubMed, Google Scholar, and EBSCOhost were searched from January 1977 to September 9, 2016. The search included the following terms: intervertebral disk, disk nutrition, and degeneration. Inclusion criteria were use of human participants or animal subjects and English language. Studies pertaining to temporomandibular joints and joints of the body other than the IVD and any articles that were not available in full text were excluded. Fifty-seven articles were included in this review.

Results

Overview

The IVD cells require energy supplied through vital nutrients. Glucose is a major nutrient necessary for cell survival in the disk. Glycolysis is the energy pathway of choice and consists of breaking down glucose to produce adenosine triphosphate (ATP), with lactate as a byproduct. Oxygen is needed to produce glycosaminoglycans (GAGs),[1] which provide mechanical strength and integrity for the disk's extracellular matrix (ECM).[2] There are 2 blood delivery routes to supply nutrients to the avascular disk. The predominant route is via the capillary beds of the cartilaginous end plate, and the other is via the peripheral annulus. Impeding any of these paths deprives the disk of

Department of Research, Logan University, Chesterfield, Missouri.

Corresponding author: Christopher M. De Geer, DC, MSc, Department of Research, Logan University, 777 South New Ballas Road, Suite 218 E, Creve Coeur, MO 63141. Tel.: +1 314 541 8188. (e-mail: *christopherdegeer@gmail.com*).

Paper submitted August 20, 2017; in revised form November 18, 2017; accepted November 20, 2017.

1556-3707

https://doi.org/10.1016/j.jcm.2017.11.006

vital nutrients. Transport of these nutrients mainly depend on the size of nutrient solutes; the larger solutes (ie, GAGs, growth factors, proteins, enzymes, and hormones)[2-5] rely on convection as a transport mechanism whereas smaller ones (ie, glucose, oxygen, and lactate) rely on diffusion. Convection is powered by hydraulic pressure gradients influenced by mechanical loading, and diffusion is mainly influenced by solute concentration gradients.

Disk Nutrients

Glucose. Glucose may serve as the disk's main energy supply.[3,6,7] It is essential for cell survival.[6,8,9] If its concentration falls below 0.5 mmol/L for more than a few days, cell death may result.[3] A combination of low pH and no glucose causes greater cell death than either variable acting alone.[8] Cell death may begin as glucose concentration reaches 0.5 mM and as pH reaches 6.8.[10] As these numbers progressively diminish to 0.2 mM and pH 6.4, all cells are likely considered dead.

Oxygen. Although disk cells may remain alive for several days without oxygen supply,[6,7] this nutrient is required for proper cell function. It plays a vital role in the rate of sulfated GAG and protein synthesis.[1,7] At 5% oxygen content, matrix synthesis rates are maximized.[7] Levels dropping below 5% limit matrix production drastically.[3] Complete oxygen deprivation, as well as acidic pH, decrease proteoglycan production, which is a property seen in disk degeneration.[6]

Oxygen levels do not seem likely to affect mitochondrial function until they fall to extreme levels (0.1-0.3 kPa).[8] In the disk's nucleus, the central area has the lowest level of oxygen concentration and, in turn, produces more lactic acid via glycolysis. Hypoxia often coincides with low pH and low glucose concentrations.[8,11] Such oxygen-deprived conditions predictably shift the main energy source from glucose to amino acids.[8]

Lactate. In anaerobic glycolytic metabolism, cells consume glucose to create ATP and produce lactic acid as a metabolite at fairly high rates.[3,10,11] Any buildup of lactic acid and carbon dioxide can lower the disk's pH and activate certain pH-dependent proteolytic enzymes that degrade the matrix.[1,3]

Nutrient Transport Mechanisms

There are 2 mechanisms for solute transport into disk tissue: passive molecular diffusion and convection (or fluid flow).[1] Figure 1 provides an overview. Overall, diffusion is more effective than fluid flow in supplying nutrients to the disk.[12] Diffusion efficiency depends highly on concentration gradients, the absolute concentration, solute properties, and tissue integrity.[1,13,14] Conversely, fluid convection is dependent upon hydraulic (or osmotic) pressure gradients and mechanical loading of the matrix to deliver nutrients.[1,14] Small

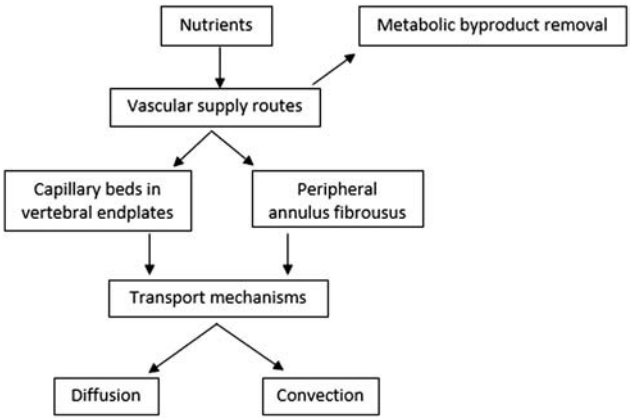

Fig 1. *Nutrient delivery mechanisms to the intervertebral disk.*

solutes, such as glucose, oxygen, sulfate, and lactate, almost exclusively rely on diffusion for transport.[1,3,15-17] In contrast, the pumping action of convection (mechanical loading) plays a greater role with large-solute transport.[3-5,15-18]

Nutrient Delivery Routes/Channels. The disk is largely avascular, but there are many arterioles and capillaries in the outer annulus, limited to the marrow space of vertebrae on the end plate side.[19] The cartilaginous end plate absorbs nutrients rapidly and delivers them into the disk.[20] A greater amount reaches this destination via the annulus, with a greater nutrient concentration found toward the periphery of the disk and decreasing amounts toward the nucleus pulposus (NP). The dorsal aspect is also more saturated with nutrients.

Nearly the entire disk receives its nutrients from its end plate's blood supply.[3,4,8,11,12,21-24] From there, it diffuses across 7 to 8 mm of end plate and matrix into the cells of the disk. Metabolic waste is removed via this system in a reverse route.[3] Only the outer annulus depends on peripheral vasculature, whereas the inner annulus receives its nutrients from the end plates.[3,4,12]

Uncharged solutes, such as oxygen and glucose, enter the disk via the end plate and annulus; anions such as sulfate ions diffuse mostly via the annulus and cations such as Ca^{2+} via the end plate.[1,16,22]

Potential Factors Responsible for Disk Degeneration From a Disk Nutrition Perspective

Disk degeneration has 2 main contributing pathways: decreased nutrition and structural failure (by its subsequent damage to the NP framework).[24] Macro damage can lead to such structural failure, whereas minor ones are able to heal.

Acidic Environment. In the glycolytic pathway, glucose is broken down to lactate, accounting for the acidic pH in the center of the disk.[11] Oxygen concentration is inversely related to pH and oxygen consumption.[25] Oxygen