Upsala J Med Sci 87: 163–174, 1982

Oxygen Tension Alterations in the Intervertebral Disc as a Response to Changes in the Arterial Blood

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ABSTRACT

Measurements of oxygen tension in the canine lumbar intervertebral disc, by the use of a polarographic oxygen electrode, were performed. The oxygen tension in the arterial blood was changed by regulating the oxygen concentration in the inspired air. The alterations in oxygen tension in the nucleus pulposus, as a function of distance to the vertebral endplate were determined. The response times registered in the disc matrix were relatively short (within five min.), which implies an efficient solute transport from the vertebral blood pool underneath the hyaline cartilage into the avascular intervertebral disc.

INTRODUCTION

The largest avascular tissue in the body is the disc between the vertebrae. The intervertebral disc is a specialized connective structure designed to give strength and mobility. For its normal function it must possess visco-elastic properties. Metabolic and/or mechanical changes are liable to interfere with properties that are needed for equalization and absorption of the various stresses put upon the vertebral column (13, 16). As the intervertebral discs are large and avascular the question has therefore been asked whether or not diffusion alone could adequately supply nutrients to the cells in various parts of the disc (11, 12).

Solute gradients (sulphate, oxygen, and lactate) in various places in the

disc have recently been measured and shown to be steep and very sensitive to the distance from the endplates and partially, but to a lesser extent (in the central disc), dependent on the distance from the periphery of the annulus fibrosus (5, 17). Despite the relatively low partial pressures of oxygen in the central area of the disc, an aerobic metabolism was found and thus a continuous supply of oxygen is needed (4, 5). Vascular blood pools are present both underneath the cartilaginous endplate as well as in the area adjacent to the annulus fibrosus (17, 18).

Nourishing solutes can be principally supplied to the disc via two main routes, namely through the periphery of the surrounding annulus fibrosus and through the central portion of the vertebral endplate (2, 12, 16, 18). It must, however, be taken into consideration that there may be variations in the effectiveness of the important diffusion routes due to the characteristics of the solute itself, as well as the transport properties due to the degree of degeneration of the disc system (13).

In the peripheral parts of annulus fibrosus it is reasonable to believe that the disc cells are supplied with oxygen from the capillaries outside the annulus periphery with perhaps a small, additional contribution from the vertebral endplate, although the latter pathway has been shown to give almost zero diffusion in experiments performed using the sulphate ion as a tracer (17).

The nucleus pulposus as well as the inner part of the annulus are, however, supplied with solutes by transport mainly through the vertebral endplate. In an avascular structure as the disc, the distances from nourishing fluids to the central parts of the tissue are very long (5).

Theoretical calculations based upon adequate oxygen consumption rates show that the oxygen needed for cell metabolism available in the central canine nucleus pulposus was predominately diffusing through the vertebral endplates (5, 16).

These calculations also give indications that oxygen, an uncharged little molecule in contrast to large and especially negatively charged complexes, can

diffuse into the central parts of the disc within minutes.

The purpose of the experiment reported here was to study, for the first time, changes under in vivo conditions intradiscal oxygen partial pressure when the arterial oxygen partial pressure was altered.

MATERIALS AND METHODS

Measurements were taken in lumbar discs (L3 - L6) from seven adult labrador dogs (3 - 5 years old). Anaesthesia with Pentothal sodium (Abbott, Italy) was injected intravenously (30 mg/kg body weight) and maintained during the operation. All animals were intubated and ventilated with an Engstroem respirator. The ventilation rate was kept constant throughout the experiment and was 16 strokes per min. The stroke volume (ranging from 4 - 6 litres) was chosen to give normal values for the arterial oxygen tension and the partial pressure of CO_2 when the animals were ventilated with room air. The different arterial oxygen tensions were obtained by changing the partial pressure of oxygen in the inspired gas, keeping the stroke volume and the respiratory rate constant.

The femoral artery was cannulated with a PE 120 catheter, which was used for blood sampling. Blood pressure was controlled regularly, using a pressure transducer (Elema, EMT-35 Solna, Sweden). The blood samples were taken and analysed immediately in an automatic bloodgas analysator (ABL-1, Radiometer, Copenhagen).

The oxygen probe used consisted of a modified polarographic electrode protected by a stainless steel cannula (1, 4). The electrode had an overall diameter of 1.0 millimeter and a thin rubber modified polystyrene membrane was dipcoated onto it (4, 15). The electrode was bathed just prior to each run in warmed ($37^{\circ}C$) oxygen-saturated saline, as well as in solutions equilibrated with different oxygen concentrations. These solutions served as calibration tensions for the electrode (14).

The arterial oxygen tension was also checked with the electrode used for intradiscal measurements (8). For zero oxygen tension calibration, pure

nitrogen in saline, contained in specially designed test-tubes to prevent oxygen interface, was used. Calibration checks were immediately done preceeding and following each introduction into either the blood or the intervertebral disc.

An abdominal midline incision was made and by carefully performed surgery, in order to prevent bleeding, the lumbar region of the spine was approached. The ventral aspects of the lumbar (L3 - L6) discs were freed by blunt dissection and under careful haemostasis. The probe attached to the specially designed electrode holder of the manipulator was introduced into the nucleus pulposus of the disc. After allowing a few minutes for equilibration to steady state, oxygen tensions were registered. Only one introduction per disc was made in order not to change the matrix properties and disturb the cells. By means of a modified Horsley-Clark micromanipulator, which was attached to a mechanical support, it was possible to reach any position with the probe in the disc via the exposed annulus periphery of the vertebral column. The position and angle of the electrode could, at any time, be registered on the scales of the instrument. Verification of the measuring point was also made by means of X-ray pictures. The position of the electrode could with these methods be determined with an accuracy of $\pm$ 0.4 millimeters.

RESULTS

The effect of changes in the arterial oxygen tension of the disc tissue is shown in Fig. 1. Changes in the arterial oxygen tension, after each change of oxygen concentration in the inspired gas, were noted almost immediately (within 10 seconds). As can be seen from this figure, changes in the arterial oxygen tension caused changes in the intradiscal oxygen tension. These changes occurred within minutes (response time) (Fig. 2). In order to compare the different experiments, the first oxygen tension response - "the response time" - is defined as the time when the first significant increase in intradiscal oxygen tension was noted. The time for reaching equilibrium - "equilibrium time" - was determined when no changes in oxygen tension were

noticed over a period of at least 5 minutes.

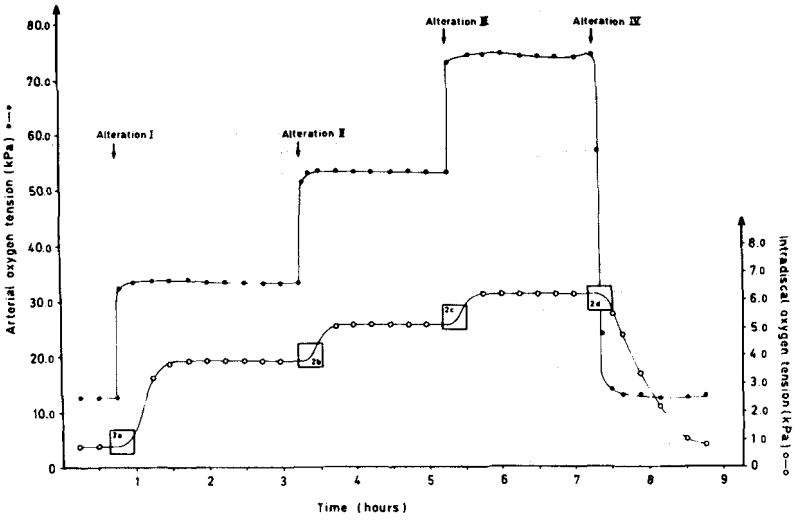

Fig. 1. Schematic presentation of results from a typical experiment showing oxygen tension changes in the arterial blood and in the intervertebral disc (nucleus pulposus).

Seven experiments, where the distance from the electrode to the vertebral endplate was varied, but otherwise carried out in an identical fashion, are summarized in Table 1. The distance to the vertebral endplate from the measuring point ranged from 0.4 to 2.1 millimeters.

The response time never exceeded 5 min. The response time, plotted as a function of the distance from the hyaline cartilage to the tip of the electrode is shown in Fig. 3. The response times were longer the longer the distance from the endplate.

The time for reaching oxygen equilibrium varied from approximately 15 to 145 min. (Table 1). There were longer equilibrium times when the electrode was situated further away from the endplate. The longest equilibrium times were seen when maximal alterations were performed, i.e. when altering ventilation from the highest oxygen concentration level to a normal state (air).

Table 1. Oxygen tension measured in the arterial blood and in the intervertebral disc both initially and after alterations of the oxygen tension in the respirating air. Response time and approximate equilibrium time at various distances from the endplate are also included.

Distance to Endplate (mm)	Oxygen Tension Changes in Respirating Air (kPa)	Oxygen Tension (kPa) Blood	Disc	Response Time in Disc (min)	Approx. EQ Time in Disc (min)
	Basal Levels	12.7	1.9		
	Alteration I	30.0	3.9	1.6	15
0.4	- " - II	51.7	5.8	2.0	20
	- " - III	70.3	7.3	2.4	15
	- " - IV	13.1	2.0	3.1	70
	Basal Levels	13.9	1.5		
	Alteration I	35.0	3.6	2.1	30
0.8	- " - II	55.4	5.8	2.3	30
	- " - III	75.6	7.8	2.8	40
	- " - IV	14.1	1.6	3.6	100
	Basal Levels	12.9	1.0		
	Alteration I	28.7	3.5	2.3	40
1.1	- " - II	50.1	4.8	2.7	35
	- " - III	68.9	6.2	3.1	35
	- " - IV	13.0	1.0	4.1	95
	Basal Levels	11.9	0.9		
	Alteration I	32.7	3.3	2.6	50
1.3	- " - II	50.9	5.2	3.0	45
	- " - III	72.4	6.8	3.3	45
	- " - IV	12.1	0.9	4.3	90
	Basal Levels	12.8	0.8		
	Alteration I	32.3	3.7	3.1	85
1.5	- " - II	52.8	4.9	3.4	60
	- " - III	72.1	6.3	3.6	65
	- " - IV	13.2	0.9	4.3	110
	Basal Levels	12.4	0.9		
	Alteration I	33.4	3.1	3.3	95
1.6	- " - II	53.1	4.9	3.4	105
	- " - III	74.8	6.4	3.8	95
	- " - IV	12.6	1.0	4.5	100
	Basal Levels	13.6	0.6		
	Alteration I	30.9	3.1	3.8	135
2.1	- " - II	51.2	4.4	3.7	85
	- " - III	72.0	5.9	4.1	105
	- " - IV	13.7	0.7	4.7	145

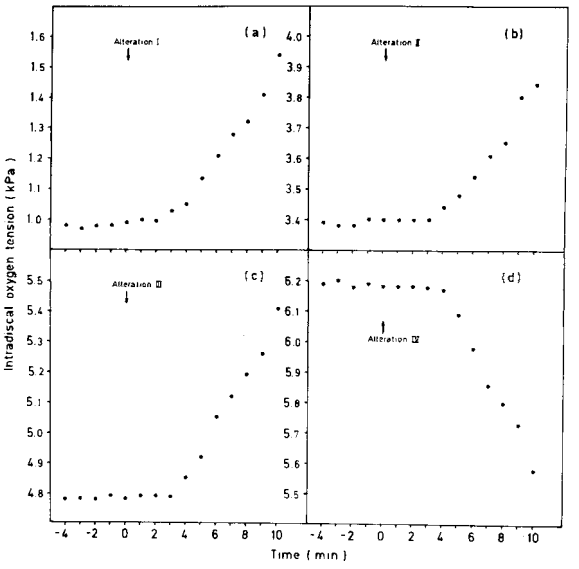

Fig. 2. Enlarged views of areas marked in Fig. 1., showing intradiscal oxygen tension before and after the alterations of the oxygen tension in the respiring air. From this and similar plotted graphs the corresponding response times have been obtained.

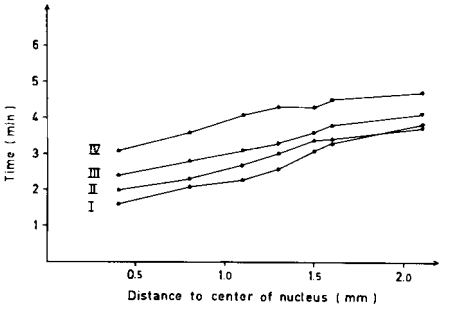

Fig. 3. Response time as a function of distance from the hyaline cartilage of the vertebral endplate in the region of the nucleus pulposus. The roman numerals correspond to the alterations in the respirating air.

DISCUSSION

The results clearly indicated that within minutes there was an obvious change in the intradiscal oxygen tension. The response time (2 - 4 min.) must be considered to be short in this avascular system, taking into account the distance from the nearest blood pool to be between 0.5 and 2.2 millimeters.

An explanation for this very quick response could be that oxygen transport

is more efficient through a cartilaginous tissue such as the intervertebral disc, under in vivo conditions, than when incubating excised specimens in vitro. A very important factor in the present situation is that there will be no blockage of blood capillaries underneath the hyaline cartilage, and therefore, the exchange of solutes between tissue and body fluids will not, from this point of view, be specially restricted.

Other factors, which may affect the oxygen response (and probably the solute gradients) in an avascular structure could be cell distribution (disturbed cell function i.e. shock effects) and derangements of the tissue constituents when introducing the electrode. Previous studies indicate, however, that the latter factor is not of significant importance (5).

The results of the intradiscal oxygen tension measurements obtained in this investigation show low values from the start at a normal resting respiration rate, thus increasing when the arterial oxygen tension was increased. That the changes in intradiscal oxygen tensions were due to a leakage of oxygen along the electrode needle is most unlikely, since very small arterial oxygen tension increases immediately gave intradiscal responses. It cannot be fully excluded that such a leakage could, however, cause a constant but very small error when measuring during resting conditions for longer periods of time.

The equilibrium times found in this investigation are in agreement with those found for cartilage, considering diffusion from one side (one endplate in the disc system) (11).

For the disc we find that the longer the distance to the endplate or the greater the change in arterial oxygen tension, the longer the equilibrium time. There is, however, a possible source of error in assessment on the recorder chart, when equilibrium is obtained. We standardized this procedure by taking the reading when an absolute constant value (as could be seen) was obtained for at least 5 min. But of course it is not possible to detect extremely small variations in the oxygen tension when gradually approaching the equilibrium value in our experimental set-up. Thus, it is possible, from

this point of view, that our values represent a slight underestimation of the real equilibrium time in the disc tissue. The oxygen equilibrium obtained is, however, affected by several other factors such as: variations in the diffusion constant, diffusion capacity of the system, blood capacity, and variations in cell respiration. It is reasonable to believe that these factors act together and perhaps it is impossible to distinguish between them. While some factors probably remain constant, variations in cell respiration could be very important in this avascular system, at least at low oxygen concentrations where steep solute gradients exist (5, 17).

Other factors, which might affect the oxygen situation and create differences in the intradiscal oxygen tension level when comparing different discs, are the size and thus the dimensions of the system. Theoretically performed calculations and in vivo studies of ^{35}S labelled sulphate transport show that small variations, for example in the diffusion area of the endplate, will greatly affect the situation for the centrally located nucleus tissue (16).

Transport of oxygen through the tissue, predominantely by diffusion, seems to be sufficient for cell metabolism since the oxygen tension in the tissue ranges from 0.6 to 1.9 kPa when the arterial oxygen tension is 11.9 to 13.9 kPa. Since response time is a few min., the transport of oxygen may be even sufficient to meet a slightly increased demand. It should, however, be pointed out that the measurements of oxygen tension and oxygen consumption are done in vivo under resting conditions. Whether metabolic processes such as oxygen consumption change with dynamic movements of the spine or with increased vertical pressure is, at present, not fully known, although experiments in progress indicate an increased solute transport and metabolic rate with increasing spinal movements.

The first increase of arterial oxygen tension always caused a greater increase in intradiscal oxygen tension than the later alterations II and III. This is probably due to the fact that before alteration I, when the arterial oxygen tensions were in the range of 11.9 to 13.9 kPa, the haemoglobin is only partially saturated. After alteration I, much more oxygen is transported

per unit time. After alterations II and III, only the amount of physically dissolved oxygen could be increased, which still constitutes the smaller portion of the total oxygen content and this amount is directly proportional to the oxygen tension. The possibility that high oxygen concentration in the arterial blood reduces the blood flow by vasoconstriction (3, 6, 7) must also be taken into consideration when dealing with diffusion from small vessels both outside the periphery of the annulus fibrosus and in the vertebral endplate. On the other hand, low oxygen concentrations have been reported to affect cell metabolism in several ways (9, 10).

There are obvious difficulties in measuring oxygen tension in the superficial layer of the vertebral body. It is at present impossible to measure oxygen tension in the capillaries close to the hyaline cartilage and how much lower the tension is in relation to the capillary network, which is present 1 - 2 millimeters underneath the cartilaginous vertebral endplate.

Intradiscal measurements very close to the endplate show oxygen tensions of about 8 kPa (5). The hyaline cartilage of the endplate therefore seems to be a relatively small barrier. Furthermore, the capillary network just below the cartilage under the nucleus seems to be adequately supplied with vessels (18).

According to earlier studies, the central parts of the disc are very close to being deprived of solutes and, due to the long distances to the nearest blood supply, an anaerobic metabolism is predominant, with high lactic acid production on low oxygen tensions (5, 18). Small reductions in the arterial oxygen tension close to the vertebral endplate, or a decreasing diffusion capacity, can, from a theoretical point of view, easily affect the nutritional situation. How physiological changes such as aging or pathological conditions may affect the supply of nutritional solutes, including oxygen, and the disposal of waste products for the cells in the disc is an area where we have only scattered data but which, nevertheless, may prove important for the understanding of many abnormal stages of the back.

ACKNOWLEDGEMENTS

This study was supported by grants from the Swedish Work Environment Fund, Carin Trygger´s Foundation, Greta and Einar Asker´s Foundation, Riksförbundet mot Reumatism, and Göteborgs Läkaresällskap.

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Received October 1, 1981.

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