Bladder ischemia detection with infrared spectroscopy in patients with partial bladder outlet obstruction secondary to benign prostatic hyperplasia

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ORIGINAL ARTICLE

Abstract

Background: Near-infrared spectroscopy (NIRS) is a noninvasive method that determines the concentrations of deoxyhemoglobin (HHb), oxyhemoglobin (O2Hb), total hemoglobin (tHb), and cytochrome c (cytC) in real time, detecting a process of hypoxia and/or ischemia of the bladder that can be produced by a prostatic pathology.

Material and methods: Model URO-NIRS-2000 equipment was used to detect HHb, O2Hb, tHb, and cytC concentrations. Measurements were carried out during micturition in two groups: 1) healthy adult subject control (n= 4); 2) patients diagnosed with partial bladder outlet obstruction secondary to benign prostatic hyperplasia (BPH) (n= 6).

Results: In the control group, the change pattern in the concentration of the detected components coincided with the dynamic process of bladder emptying. In the patient group, there was a de-phasing in the concentration of all the metabolites, which was interpreted as a hypoxic process caused by an ischemia-reperfusion phenomenon.

Conclusions: NIRS-based technology is a tool that aids in the evaluation of bladder function by correlating metabolic processes with the dynamic processes of the bladder and establishing the opportune diagnosis of a hypoxic process produced by an ischemia-reperfusion phenomenon.
Introduction

Lower urinary tract dysfunction syndrome is a complex of symptoms that presents in both sexes in which the most affected organ is the bladder. The predominant clinical presentation of this organ is urinary urgency with or without incontinence that importantly affects patient quality of life.1 The presence of mechanical obstruction in the lower urinary tract secondary to prostate pathology (mainly hyperplasia and/or hypertrophy) can cause difficulty in emptying the bladder, that in turn produces an increase in intravesical pressure during micturition.1-2 Partial bladder outlet obstruction (PBOO) and the consequent reduction in intravesical pressure, altering the contraction pattern of the detrusor muscle contraction alterations.14,18-21 it has been demonstrated in this type of experimental model that ischemia induction (by obstructing the arterial irrigation of the bladder) produces hypoxia in the bladder tissue followed by an increase in the contractile activity of the detrusor muscle. In addition, circulation re-establishment produces a reperfusion phenomenon that is accompanied with excessive oxygen availability in the tissues that again modifies the detrusor muscle contraction pattern. In the bladder (where the bladder) produces hypoxia in the bladder tissue followed by an increase in the contractile activity of the detrusor muscle. In addition, circulation re-establishment produces a reperfusion phenomenon that is accompanied with excessive oxygen availability in the tissues that again modifies the detrusor muscle contraction pattern. Consequently, the development of hyperactive bladder syndrome is not completely understood, but much effort has been made to comprehend the participation of the detrusor muscle because the alterations in its contraction pattern play an important role in bladder physiology.12-20

Experimental studies on animals in whom PBOO was produced, have shown that ischemia and the subsequent development of hypoxia can be an important factor in detrusor muscle contraction alterations.14,18-21 It has been demonstrated in this type of experimental model that ischemia induction (by obstructing the arterial irrigation of the bladder) produces hypoxia in the bladder tissue followed by an increase in the contractile activity of the detrusor muscle. In addition, circulation re-establishment produces a reperfusion phenomenon that is accompanied with excessive oxygen availability in the tissues that again modifies the detrusor muscle contraction pattern.12-21 Therefore, the determination of tissue oxygenation combined with hemodynamic studies can be aids in detecting an ischemia-reperfusion process, which is thought to be one of the most important pathophysiologic components in the development of PBOO.
of hyperactive bladder syndrome in the obstructed patient.12,22

Urodynamic studies are the criterion standard for detecting hyperactive bladder. However, these studies produce much discomfort and risk for the patient.3,5,7 Thus, the development of noninvasive diagnostic procedures for evaluating bladder function can be valuable, especially in patients that require regular urodynamic evaluations.10,11,22-25

Doppler ultrasound studies have been very helpful in the detection of blood flow variations in the bladder wall during the emptying cycle. However, methodological problems impede its use in detecting bladder contractions.26,27

In recent years, technology that utilizes noninvasive procedures for the patient has been developed that has been shown to be a good auxiliary in the study and detection of lower urinary tract physiologic problems caused by bladder outlet obstruction.23-25

This technology uses near-infrared spectroscopy (NIRS), which, as its name indicates, utilizes a part of the electromagnetic spectrum in which the light emitted by a generator is located in the 750 to 2 600 nm range. This enables it to penetrate tissue, and depending on the selected wavelength, the emitted spectrum is absorbed, transmitted, or reflected, in accordance with the molecular characteristics of natural components called “chromophores”. They emit a response that is captured by the detector and directly correlates their structure, color, and concentration. Thus, it is possible to associate a single wavelength from the NIRS spectrum with the specific absorption of a chromophore.23-25

The most abundant chromophore of the organism is hemoglobin (Hb) and the NIRS spectrum is capable of distinguishing the different species of this molecule, depending on its chemical state with respect to oxygen. And so, the NIRS spectrum can detect the concentration of deoxyhemoglobin (HHb), oxyhemoglobin (O2Hb), total hemoglobin (tHb), and cytochrome c (cytC) in tissue in real time.23-25 Equipment based on NIRS technology has an emission spectrum in the range of 700 to 900 nm in which the different chemical species of Hb, together with cytC, present their maximum absorbance and has enabled the study and evaluation of urinary bladder activity to be carried out on experimental models and humans in real time. This has also made the detection of ischemia phenomena possible by monitoring the changes in tissue oxygenation (using the changes in HHb and O2Hb concentration), as well as the hemodynamic phenomena (using the changes in tHb and cytC concentration) that provide information on oxygen presence or intake in a specific area. NIRS technology detects the variations in concentration of HHb, O2Hb, tHb, and cytC in the detrusor muscle. The spectrophotometric signals generated by these compounds are detected during the filling and emptying process of the bladder and enable the effect of the compression on the detrusor vasculature to be evaluated and to associate them with the self-regulatory hemodynamic changes in the tissue and to detect a process of hyper or hypo activity in this muscle. In such a way, the changes in Hb oxygen saturation, together with flow changes in the bladder vasculature, are associated with changes in detrusor muscle contraction, and as a result, are an important diagnostic tool in problems of bladder function.9,14,23-25,31

The aim of the present study was to detect the dynamics of the concentration changes in HHb, O2Hb, tHb, and cytC in the detrusor muscle in patients presenting with PBOO during micturition.

Methods

Participant selection

Six male patients with a 49 to 56-year age range were selected that presented with lower urinary tract symptoms and that had been diagnosed with PBOO secondary to BPH (diagnosed through ultrasound and uroflowmetry studies). None of the patients had undergone previous lower urinary tract surgery, nor had they had any type of infection or chronic pathology (for example: diabetes mellitus, heart or vascular failure, pulmonary or muscle diseases, renal failure, local or general neurologic alterations, etc.). As part of the comprehensive study protocol, each patient had general blood and urine work-ups. The International Prostate Symptom Score (IPSS) questionnaire was also applied to the patients for quality of life evaluation. Four apparently healthy men (paired in age to the patient group) that presented with no urinary or prostate symptoms were selected to make up the control group. All the subjects were willing participants and they signed letters of informed consent.

Near-infrared-based technology use

URO-NIRS-2000 (Urodynamicx Tech, Ltd, Canada) equipment was used. It consists of three transmitters/detectors (of 785, 808, and 830 nm) integrated in a single rack that is placed on the skin approximately 5 cm above the suprapubic region. The rack is connected with an interface to a computer that integrates the information so that micromolar range concentrations of deoxyhemoglobin (HHb), oxyhemoglobin (O2Hb), total hemoglobin (tHb), and cytochrome c (cytC) can be detected simultaneously and in real time in the detrusor muscle. The relation between HHb and O2Hb concentrations reveals the presence of a hypoxic phenomenon, whereas the relation between tHb and cytC detects an ischemic process, according to previous reports.23-25,30-34

The concentrations of all the metabolites were recorded during the lapse of time that micturition took place in the two study groups: a) the control group (n = 4) of healthy adult men with no lower urinary pathology and b) adult patients (n = 6) diagnosed with PBOO secondary to BPH. At the same time the abovementioned metabolites were detected, a flowmetry study was carried out using URO-NIRS-2000 software provided by the manufacturer.
Statistical analysis
The GraphPad Prism V-4.00 (GraphPad Software, San Diego, Cal., U.S.A.) statistical program was used to analyze the study results. The qualitative results were evaluated using contingency tables and applying the corresponding chi square test or Fisher exact test and the quantitative results were analyzed with the Student’s t test. In all cases, $p < 0.05$ was considered to have statistical significance.

Results
Six patients diagnosed with PBOO secondary to BPH with a range of eight to 15 months of progression and four apparently healthy subjects that did not present with any type of urologic pathology were enrolled in the study.

Table 1 shows the general somatometric and biochemical characteristics of the patients and the control group. The patients presented with a mean age < 60 years and overweight, but with no apparent alterations in the remaining somatometric or biochemical variables, compared with those of the control group. In addition, urinalyses were negative for any type of additional infection or pathology, but their scores on the IPSS questionnaire ranged from 24 to 35 points. None of the patients presented with an added general or local pathology.

BPH is known to produce bladder alterations that turn into lower urinary tract symptomatology. It is also a known fact that the main active action factor of the bladder is the detrusor muscle.

We analyzed the behavior of the detrusor muscle using NIRS technology with equipment whose principal element was a transmitter/detector that was placed at the suprapubic region as shown in Figs. 1A and 1B. Once the transmitter/detector was in place, and during micturition, the HHb, $O_2$Hb, tHb, and cytC concentration detection was carried out. Fig. 1C shows an experimental graph of the concentration changes in these metabolites in the microcirculation of the muscle that underwent arterial occlusion. Hypoxia is indicated by a reduction in $O_2$Hb concentration together with an increase in HHb concentration, while ischemia is characterized by an increase in tHb concentration (Fig. 1C).

We used URO-NIR-2000 equipment to determine these metabolites and Figs. 2A and 2B show representative graphs of the changes in the detrusor muscle micromolar concentrations of the HHb, $O_2$Hb, tHb, and cytC metabolites (using the scale to the left). These metabolites are detected in real time during micturition, which is represented by the flow changes that are measured by the scale on the right. Fig. 2A represents the temporal course of the concentration changes of the abovementioned metabolites during micturition in a control subject. At the time of micturition, the metabolite concentrations did not present with important changes during that length of time. In this case, all the metabolite concentrations remained within the positive quadrant of the scale and only the variation in the behavior of the tHb concentration can be observed, a moment before and during the micturition process.

On the other hand, Fig. 2B shows an example of the temporal course of the metabolite concentrations of the detrusor muscle in a patient presenting with PBOO. The urine flow curve during micturition is less sharp and has a longer duration when compared with that obtained in the control (Fig. 2A). In addition, there are important variations in the concentration of all the metabolites during the entire length of time of the micturition process. Most striking is

<table>
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<tr>
<th>Table 1</th>
<th>General somatometric and biochemical characteristics of patients and control subjects included in the study</th>
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<tbody>
<tr>
<td>Variable</td>
<td>Patients (n=6)</td>
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<tr>
<td>Age (years)</td>
<td>52.33 ± 3.51 (49-56)</td>
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<tr>
<td>Weight (Kg)</td>
<td>76.73 ± 12.55 (63-88)</td>
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<tr>
<td>Size (m)</td>
<td>1.71 ± 0.14 (1.55-1.83)</td>
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<tr>
<td>BMI (Kg/m2)</td>
<td>26.3 ± 2.7 (23.6-29.07)</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>76 ± 5.29 (70-80)</td>
</tr>
<tr>
<td>RR (breaths/min)</td>
<td>17.02 ± 17 (0.5-16)</td>
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<tr>
<td>Temp. (ºC)</td>
<td>36.02 ± 36.3 (0.15-36)</td>
</tr>
<tr>
<td>Hb (g/ml)</td>
<td>16.53 ± 0.21 (16.3-16.7)</td>
</tr>
<tr>
<td>Ht (%)</td>
<td>49.33 ± 2.02 (47.7-51.6)</td>
</tr>
<tr>
<td>Platelets (1x106/mL)</td>
<td>267 ± 64.21 (198-325)</td>
</tr>
<tr>
<td>Erythrocytes</td>
<td>6 ± 0.18 (5.42-5.79)</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>31.4 ± 5.35 (26.2-36.9)</td>
</tr>
<tr>
<td>Monocytes</td>
<td>8.9 ± 1.56 (8-10.7)</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>51.9 ± 7.8 (44.1-59.7)</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>2.13 ± 1.4 (1-3.8)</td>
</tr>
<tr>
<td>Basophils</td>
<td>0.4 ± 0.17 (0.2-0.5)</td>
</tr>
</tbody>
</table>

BMI: Body mass index; HR: heart rate; RR: Respiratory rate; Temp.: body temperature; Hb: hemoglobin; Ht: hematocrit.
the fact that the HHb, O2Hb, and tHb concentrations start from the negative quadrant of the scale, in addition to the fact that there are changes in their profiles characterized by a greater drop in concentration during the most acute micturition phase that occurs from approximately 20 to 50 seconds of the study; at the same time, an increase is produced in the cytC concentration (Fig. 2B).

Discussion

The use of NIRs is a noninvasive technique recognized for its technical advantages and great sensitivity that enables real time monitoring of the concentration of chromophores that are vitally important for the organism as a whole, the tissues, and the cells. 2,9,23-25

In the field of urology NIRs technology is used for monitoring changes in HHb and O2Hb concentration to detect the presence of hypoxia in the detrusor muscle and to determine whether there are changes in the hemodynamics of that organ that give rise to an ischemic process. This is achieved by monitoring tHb and cytC concentrations.2,9,23-25,28-33

And at the same time these processes are being evaluated, a NIRs study simultaneously adjusts to a uroflowmetric study, with which it has an added study element that can detect alterations in the micturition process and establish the presence of bladder emptying dysfunction.28-34

In regard to BPH, it is well known that an important part of the symptomatology of the patient is caused by the active factor of the bladder, which is the detrusor muscle.1,2,8,12 When there is a BPH process, the urine exit becomes obstructed and the detrusor muscle presents with alterations in its physiology that can be acute or chronic, depending on the duration of the obstruction.12-20

Urodynamic studies are among the diagnostic procedures for bladder pathology, however, as stated before, they produce important discomfort and risk for the patient.2,6-8

In contrast, non-invasive procedures such as those using NIRs technology are currently a very good option for studying physiologic and functional phenomena, because, in addition to not requiring invasive procedures, they have a high degree of accuracy, detecting changes in metabolite concentrations that reveal physiologic alterations in the smooth muscle that can be associated with hypoxia caused by an event of ischemia and reperfusion.23-33

Using experimental models with laboratory animals and NIRs technology, it has been demonstrated that the detrusor muscle presents a transitory ischemic process during micturition, caused by contraction of that muscle. This transitory ischemic process produces hypoxia in the bladder tissue, mainly in the detrusor muscle. Once the muscle contraction diminishes, blood flows normally, which is why the ischemia and hypoxia end when reperfusion is established in the microcirculation. Moreover, detrusor muscle distension when the bladder is filled with urine also contributes to the ischemia phenomenon (and thus, hypoxia), because the blood vessels of the detrusor microcirculation collapse due to the effect of the pressure. This ends when the bladder is emptied and the muscle

Figure 1  Schematic representation of the main components and demonstration of the use of the URO-NIRs-2000 apparatus.  
A) Diagram of the NIRs transmitter/sensor and how it acts on the surface of the skin.  
B) Photograph showing how and where to place the NIRs transmitter/sensor on the patient for detecting different metabolic chromophores.  
C) Graph showing the variation through time in the concentrations of HHb, O2Hb, and tHb when there is a vascular obstruction process that is indicative of hypoxia caused by an ischemic process.
Conclusions

Based on the above, we can state that in our patients, technology based on NirS was capable of detecting an ischemia-reperfusion phenomenon that we could observe in real time in the detrusor muscle, caused by obstruction secondary to BPH. This ischemia-reperfusion phenomenon can create reactive species that are highly damaging for the cell, tissue, and the bladder in general. As a direct cause of this damage to the detrusor muscle created by the free radicals, this organ presents with transitory or permanent alterations that cause clinical presentations characteristic of detrusor muscle hyperactivity. Therefore it is of great importance to better understand these types of phenomena in order to have tools that enable us to act adequately and opportunely to improve patient quality of life. By understanding the pathophysiologic mechanisms of damage and their temporality, we can improve our diagnostic and management algorithms for PBOO caused by BPH.

Conflict of Interest

The authors declare that there is no conflict of interest

Financial disclosure

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