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Oxygen-Ozone Autohaemotherapy and Intravescical Oxygen-Ozone Insufflations in Treatment of Recurrent and Interstitial Cystitis: Preliminary Results

Muzi, F., and Tati, G.

Department of Urology, S. Eugenio Hospital, Rome 00144, Italy

Abstract: Introduction: Cystitis has high incidence in female population. Inflammation is responsible of irritative symptoms; it is supposed the existence of an arterial obstructive disease connected with bladder ischaemia. Direct bacterial damage and/or inflammation are responsible of the activation of ROS (radicals of oxygen) and consequent cell damage. NF-kB protein is protagonist in ROS synthesis. High levels of O_2 in periphereal tissues reduce ischaemia, responsible of recurrent inflammation and increase antioxidant effects in presence of controlled oxidation. The aim of this study is the essay of anti-inflammatory effects of OOT (oxygen-ozone therapy) in chronic cystitis, employed in combined subministration. OOT properties could decrease bacterial concentration and eliminate dysuriac disturbances, reducing ischaemic effects. Methods: This study proposes a combined treatment for cystitis with oxygen-ozone AHTM (autohaemotherapy) and intravescical insufflations. It has been selected 8 Women aged 40-55 years with recurrent cystitis, associated with pain and urge incontinence. We have used certified medical OOT generator. Results: After therapies, all patients showed sterile urine and progressive reduction of symptoms with a sensible improvement of quality of life. Conclusions: Nevertheless, in a little group of patients, preliminary results could suggest the use of OOT for recurrent cystitis after failure of conventional therapies.

Key words: Recurrent cystitis, interstitial cystitis, ozonetherapy.

1. Introduction

UTIs (urinary tract infections) are common in female population. Cystitis is the most representative in clinic [1, 2].

General symptoms of cystitis include urgency, frequency, and dysuria. Less common symptoms are hematuria, dyspareunia and/or bladder pain and spasms. For specific diagnosis, sometimes it is necessary to repeat cultures or urologic procedures, including cystoscopy [2].

Bacterial cystitis is more frequent, especially induced by *E. coli*.

Nonbacterial cystitis is attributed to various medical disorders including PBS/IC (painful bladder syndrome/interstitial cystitis).

Corresponding author: Fabrizio Muzi, M.D, research fields: gas-therapy, prolotherapy and integration techniques in urology and andrology.

PBS/IC describes a syndrome of pain and genitourinary symptoms (eg. frequency, urgency, pain) for which there is not a clear etiology [2, 3].

IC is a chronic condition characterized by cycles of exacerbations and remissions; inflammation induces chronic progression to small-capacity bladder.

Severe lower urinary tract symptoms begin with a highest risk of upper tract involvement [3].

It is supposed the existence of particular pathological pattern: an arterial obstructive disease connected with bladder ischaemia responsible of bladder dysfunction. Direct bacterial damage and/or inflammation are responsible of the activation of several proteins involved in the production of ROS (radicals of oxygen) [2, 3].

2. Materials and Methods

For this study we selected a group of 8 women, aged

40-55, two of them affected by recurrent abacterial cystitis, 4 patients affected by bacterial cystitis (*E. coli*) and 2 patients affected by interstitial cystitis. All patients showed recurrent pain and episodical urge incontinence as collateral symptoms.

All patients affected by abacterial and interstitial cystitis have been submitted to cystoscopy, (as bacterial infection is a contraindication for cystoscopy) with evidence of diffuse hyperhaemia of urothelium.

All patients have been submitted to a weekly application of sistemic ozone therapy: the AHTM (autohaemotherapy). It has been taken to the patient a blood sampling of 150 cc and enriched by a combination of oxygen and ozone (total concentration of ozone: 30-40 mcg/mL) once a week and two weekly ozone bladder insufflations of 30mcg/mL for 100 Ml through a 8 Fr Nelaton catheter. All the ozone volumes are obtained by using an oxygen-ozone certified medical generator.

For what concerns AHTM, the blood sampling is aspired in a close sterile circuit where it is possible to introduce the mixture of oxygen and ozone according to a pressure gradient, without any mechanical processing, keeping the circuit directly connected with the peripheral vein access. At the end of the introduction of the mixture of oxygen and ozone in the blood sampling, it is also possible to reinfuse it directly in vein.

3. Results

Already after the first application, all patients refer a decrease of dysuriac disturbances, of pain sensations with a sensible improvement of quality of life and workability. After the treatment cycle the urine samples of all 4 patients affected by bacterial cystitis have resulted sterile, considering that there is not a bacterial resistance for ozone.

After 2 months, all patients have done a cystoscopy without evidence of trigonitis.

During and after the administration of AHTM and bladder insufflations, there were no side effects. The only contraindications for this protocol are: hyperthyroidism, pregnancy, G6PD deficiency.

4. Discussion

The symptoms of cystitis in the adult are dysuria, urinary urgency, frequency [2].

Nonbacterial cystitis is sometimes associated with PBS/IC, which describes a syndrome of pain and genitourinary symptoms for which there is not a clear etiology. There are many controversies regarding nonbacterial cystitis [3].

Trigonitis is often diagnosed in cystoscopy in patients with a bacterial cystitis and refers to the nonkeratinizing squamous metaplastic lesions. Squamous metaplasia in the bladder usually occurs in response to irritating processes and seems to be hormonal influenced.

However, whether hormonal influences lead to squamous metaplasia is unclear.

It is observed in squamous metaplastic cells the lack of tight junctions that eases the inflammation of the interstitial layer [2, 3].

The pathophysiology of IC is not clearly understood. Various etiologies have been proposed, including hypoxia-related, in fact where is a muscular contraction, sometimes connected with pelvic floor diseases, there is a local ischaemia in the interstitial layer of bladder [3].

IC may lead to bladder wall scarring, also progressively reducing compliance and capacity of bladder [4].

The main protein involved in bladder inflammation and in the genesis of ROS is NF-kB. The nuclear transcription factor NF-kB is a heterodimeric, sequence-specific transcription factor found in many cells. In unstimulated cells, NF-kB is found in the cytoplasm and is bound to its inhibitor kB, which prevents it from entering nuclei [5]. The stimulated cells lead to rapid degradation by proteasomes and subsequent nuclear translocation and binding of NF-kB

to specific sequences in the promoter regions of target genes. A number of stimuli have been shown to activate NF-kB, including cytokines, activators of protein kinase C, viruses, and oxidants [6].

Ozone can contrast the effects of NF-kB. It has unique biological properties which are being investigated for applications in various medical fields. Ozone best known properties play a protective role in the earth's ecological harmony interaction at ground level. It has unique biological properties which are being investigated for applications in various medical disciplines. Immunomodulating effect of OOT (oxygen-ozone therapy), sub ministered in AHTM, is based on its ability to activate the phagocytosis through the formation of peroxides and stimulation of the production of cytokines by lymphocytes and monocyte. OOT can provoke a modification of blood cell membranes and a decrease in the viscosity properties of blood. Antimicrobic and detoxication properties of OOT are successfully used in the treatment of acute and chronic cystitis. According to pathology, OOT can be realized through rectal insufflation, parenteral injection or through intravescical instillation/insufflation, suitable for urologic pathologies (cystitis, urethritis).

The intravesical use of OOT produces an anti-inflammatory effect by suppressing the growth of enterococcus, Proteus, colibacillus and completely eliminating dysuriac disturbances. Bladder irrigations with ozonated saline solutions seem less effective than insufflations oxygen-ozone gas mixture, probably according to ozone lower stability in water solutions. Saline species seems to cause OOT more rapid inactivation. Ozone is metastable in nature, so it is very reactive with saline ions [7].

5. Conclusions

Preliminary qualitative results could encourage wider studies to evaluate the application of combined use of bladder ozone insufflations and AHTM in treatment of bacterial, abacterial and interstitial cystitis, which could be considered as second line treatment in recurrent cystitis or as association with other therapies.

Considering that it does not exist a bacterial resistance for ozone, OOT could be also employed in case of multi drug resistant cystitis.

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