Original Article

Chronic prostatitis and small intestinal bacterial overgrowth: is there a correlation?

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Background: Clinical management of chronic inflammation of prostate and seminal vesicles is very complex. Among the causes of recurrent chronic prostatitis (CP), a possible malabsorption, such as lactose intolerance, in turn related to small intestinal bacterial overgrowth (SIBO), should be considered.

Methods: We have performed lactose and lactulose breath test (BT) in 42 patients with CP, in order to evaluate the prevalence of SIBO in this kind of patients and the concordance of the two tests.

Results: A positive lactulose BT was present in 33/42 patients and in 73% (24/33) was associated to lactose malabsorption. Five patients had positive response after lactulose, while only 4 had both negative tests.

Conclusions: Our data showed an association between lactose and lactulose BT positivity. They also indicated high prevalence of bacterial colonization of small bowel in patients with CP, possibly related to recurrence or chronicity of genitourinary tract inflammation. The research for these phenomena could be relevant in diagnostic route of infertile patients in whom slight gastro-enteric symptoms can be underestimated.

Keywords: Chronic prostatitis (CP); malabsorption; small intestinal bacterial overgrowth (SIBO)

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Introduction

Clinical management of chronic inflammation of prostate and seminal vesicles is very complex. When on infectious bases, cultural semen analysis can be useful in determining etiological agents even if, also in presence of leukocytospermia, a clear responsible microorganism is not easy to identify. In presence of bacterial growth in semen, the eradication is not always easy to attempt.

Infections can be cause of infertility but also the presence of leukocytes can have negative effect on seminal parameters and the spermatozoa function. Chronic prostatitis (CP) is often associated with granulocytes in prostatic fluid with a generation of radical species of oxygen (ROS) with a vicious circle on fertility.

It has been shown that ROS levels are significantly higher in patients with leukocytospermia then in normal subjects; moreover, total antioxidant capacity (TAC) in seminal plasma, index of non-enzymatic antioxidant defenses is lower also in patients without leukocytospermia. Therefore, oxidative stress can be present in CP independently from leukocytospermia (1).

Among the causes of recurrent CP, a possible malabsorption, such as lactose intolerance, in turn related to small intestinal bacterial overgrowth (SIBO), should be considered; bacterial population moves toward small bowel for better disposable of sugar, even if digestive capacity for

sugar is preserved (2,3).

In order to evaluate the prevalence of positive breath tests (BTs) in patients affected by CP, we have evaluated a group of patients, consulting our center for infertility, with recurrent positive cultural tests, performing lactose and lactulose BT.

Methods

We have studied 42 patients aged 25–40 years. Subjects involved in this study were admitted to the University Hospital "Policlinico Gemelli" Department of Internal Medicine and were enrolled after being given an explanation of purposes and nature of the study, conducted in accordance with the Declaration of Helsinki, as revised in 2013. The study protocol was approved by our Institutional Board and written informed consent was obtained from all patients. They underwent H_2 BT using lactose and lactulose and microbiologic semen analysis for aerobic and anaerobic bacteria, mycetes and mycoplasms by cultural and molecular methods.

Biochemical analysis

Standard semen analysis was performed according to WHO criteria (4). In both BT, H_2 respiratory air samples has been assayed by gascromatograph and results expressed as part per million (PPM).

Lactose H_2 BT is a rapid, simple, reproducible and cheap method for diagnosis malabsorption. It is based on the fact that, in presence of lactase, the disaccharide lactose is divided in glucose and galactose, rapidly absorbed by bowel mucosa, without production of hydrogen. When lactase is not persistent, lactose reaches the colon where bacterial colonia induced fermentation with production of hydrogen methane and carbon dioxide.

Lactose BT measures inspired H_2 before and after, every 30 min for 4 hours, lactose administration (20 g per os). The increase of H_2 >20 PPM is index positivity. The sensitivity and specificity approach 100% (5).

Lactulose H_2 BT is employed to evaluated oro-caecal transit time (OCTT) and SIBO. Lactulose is not absorbed in small bowel and is quickly metabolized with production of carbon dioxide, marked with ^{13}C, which is measured in inspired air, with a latency time corresponding to OCTT.

10 g lactulose are administered with measure every 15 min for 4 hours. The positivity of the test is based on one of these features: (I) two discrete peaks with two consecutive H_2 values >10 PPM; (II) production of H_2 at a distance <90 min after lactulose ingestion (6).

Microbiologic methods

Samples were cultured on Schaedler Agar/Schaedler KV Agar with 5% Sheep Blood and Columbia Agar with 5% Sheep Blood (Becton Dickinson GmbH—Heidelberg, Germany) and incubated at 35±2 °C in anaerobic condition, for non-selective isolation of anaerobes and to detect Gram-negative anaerobes, particularly *Bacteroides* and *Prevotella* spp.

Trypticase Soy Agar with 5% Sheep Blood (bioMérieux SA—Marcy l'Etoile, France) was used for cultivating fastidious microorganisms and for the visualization of hemolytic reactions produced by many bacterial species. MacConkey II Agar (bioMérieux SA—Marcy l'Etoile, France) was used to isolate and to differentiate *Enterobacteriaceae* and other Gram-negative rods. *Gardnerella vaginalis* was detected by Gardnerella Selective Agar (Becton Dickinson GmbH—Heidelberg, Germany) with 5% Human Blood.

Samples were also cultured on *Candida* Bromocresol Green (BCG) Agar (MEUS—Piove di Sacco, Italy), a differential and selective medium used for primary isolation and detection of Candida species from clinical specimens.

Cultured were incubated at 35±2 °C in aerobic condition and at 35±2 °C in aerobic atmosphere supplemented with 3–5% carbon dioxide.

Cultures were performed to detect *Mycoplasma hominis* and *Ureaplasma urealyticum* using Mycofast system (Elitech MICROBIO—Signes, France) according to the manufacturers' instructions.

To detect *C. trachomatis* and *N. gonorrhoea* we used BD ProbeTec™ ET (Becton Dickinson GmbH—Heidelberg, Germany) a system based on strand displacement amplification (SDA) that offers proven specificity and contamination control.

Results

Seminal data were consistent with asthenozoospermia, associated or not with oligo-or teratozoospermia in every patient (*Table 1*).

From microbiological examination, the following pathogens were identified: gram+ bacteria (15%), gram– bacteria (31%), *Mycoplasma hominis* or *Ureaplasma urealyticum* (8%) anaerobic bacteria (15%), candida (8%),

Table 1 Mean (± SEM) values of seminal parameters in our 42 patients

Parameters	Value
Volume (mL)	3.4±0.3
pH	7.7±0.1
Sperm count (10^6/mL)	32.3±7.4
Progressive motility (%)	24.3±3.4
Non progressive motility (%)	22.7±4.6
Normal morphology (%)	24.9±3.3

multiple infections (23%).

A positive lactulose BT was present in 33/42 patients and in 73% (24/33) was associated to lactose malabsorption. Five patients had positive response after lactulose, while only 4 had both negative tests.

Discussion

SIBO is a condition characterized by abnormally high bacterial population level in the small intestine, exceeding 10^6 organisms/mL (7-9). Different factors, including the intestinal tract affected, the severity of contamination, the presence of altered motility or anatomical abnormalities of bowel, can influence clinical manifestations. In presence of insufficient intestinal clearance, SIBO is predominantly distal, colonizing ileum and jejunum; prevalent bacteria are enterobacteriaceae. On the contrary, when gastric acid barrier is insufficient, SIBO is often proximal (stomach, duodenum, proximal jejunum) and the dominant flora is represented by Gram positive bacteria, derived from upper respiratory tract (7,10). It is difficult to establish a correct prevalence of SIBO, which is often under-diagnosed. A high prevalence of SIBO has been shown also in irritable bowel syndrome (IBS), contributing to symptoms in such conditions (11). The positivity of BT in IBS has been found to be 30.7%, compared with 3.9% of controls (12). Other studies showed an increased bacterial flora in 43% IBS patients, compared with 12% of healthy subjects, without relation with severity of symptoms (13).

BT represents a valid and non-invasive tool for approaching these disorders (14). They are based on the gas produced by bacterial fermentation, which diffuses into the blood and are excreted in breath samples. Hydrogen is not produced in healthy humans in fasting state, but only after anaerobic metabolism, which can occur during bacterial fermentation. Anaerobic bacteria metabolized carbohydrates, producing CO_2, short-chain fatty acids and hydrogen (15). Individual microbiota and gastrointestinal transit time influence the results of BT (16). Glucose BT is commonly used for the diagnosis of SIBO, since is rapidly absorbed in the proximal small bowel and does not reach the colon; therefore, it is especially useful in high SIBO. Lactulose is a manufactured disaccharide, which is not metabolized, producing fermentation in the colon; therefore, it is useful in low SIBO but also give information on OCTT (14).

There is a reciprocal influence between bowel diseases and SIBO. Moreover, malabsorption can favour SIBO. Sugar malabsorption can be primary (as adult-type hypolactasia or lactase non-persistence) (17) or acquired (after damage of bowel mucosa) (5), furnishing substrate for bacterial fermentation. However also in primary SIBO, a false positive lactose BT can be observed, even in presence of normal disaccharidases (18). In such cases, the correction of intestinal flora can reverse this false positivity.

Other than malabsorption (especially of lipids and liposoluble vitamins), other consequences can be observed, ranging from translocation of bacteria (usually gram-negative and aerobic bacteria) from gastrointestinal tract to extra-intestinal tissues (19) until sepsis and multiorgan failure (20). Predisposing factors are again reduced epithelial barrier and immunological defense (19,20).

A few data are reported on SIBO in CP. A pilot study in 16 patients showed SIBO and IBS to be common in CP and were beneficially treated using rifaximin therapy (21). This topic is very important since various antibiotics, used in CP, are not effective in such condition, thus explaining the recurrence of prostate inflammation.

Conclusions

Our data show and association between lactose and lactulose BT positivity. The bacterial overgrowth could cause abnormal H_2 production with the consequence of false results in lactose BT. Alternatively the bacterial overgrowth could damage intestinal mucosa, determining transient deficiency of lactase or other proteinic carrier. They also indicated high prevalence of bacterial colonization of small bowel in patients with CP, possibly related to recurrence or chronicity of genitourinary tract inflammation.

The research for these phenomena could be relevant in diagnostic route of infertile patients in whom slight gastro enteric symptoms can be underestimated.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/aoi.2018.05.01). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study protocol was approved by our Institutional Board and written informed consent was obtained from all patients.

References

1. Pasqualotto FF, Sharma RK, Potts JM, et al. Seminal oxidative stress in patients with chronic prostatitis. Urology 2000;55:881-5.
2. Singh VV, Toskes PP. Small bowel bacterial overgrowth: presentation, diagnosis, and treatment. Curr Treat Options Gastroenterol 2004;7:19-28.
3. Nucera G, Gabrielli M, Lupascu A, et al. Abnormal breath tests to lactose, fructose and sorbitol in irritable bowel syndrome may be explained by small in irritable bowel syndrome may be explained by small intestinal bacterial overgrowth. Aliment Pharmacol Ther 2005;21:1391-5.
4. World Health Organization. Laboratory manual for the examination and processing of human semen. 5th Ed. Cambridge University Press, 2010.
5. Swagerty DL Jr, Walling AD, Klein RM. Lactose intolerance. Am Fam Physician 2002;65:1845-50.
6. Rhodes JM, Middleton P, Jewell DP. The lactulose hydrogen breath test as a diagnostic test for small-bowel bacterial overgrowth. Scand J Gastroenterol 1979;14:333-6.
7. Gabrielli M, D'Angelo G, Di Rienzo T, et al. Diagnosis of small intestinal bacterial overgrowth in the clinical practice. Eur Rev Med Pharmacol Sci 2013;17 Suppl 2:30-5.
8. Bures J, Cyrany J, Kohoutova D, et al. Small intestinal bacterial overgrowth syndrome. World J Gastroenterol 2010;16:2978-90.
9. Vesa TH, Marteau P, Korpela R. Lactose intolerance. J Am Coll Nutr 2000;19:165S-175S.
10. Husebye E. The pathogenesis of gastrointestinal bacterial overgrowth. Chemotherapy 2005;51 Suppl 1:1-22.
11. Esposito I, de Leone A, Di Gregorio G, et al. Breath test for differential diagnosis between small intestinal bacterial overgrowth and irritable bowel disease: an observation on non-absorbable antibiotics. World J Gastroenterol 2007;13:6016-21.
12. Lupascu A, Gabrielli M, Lauritano EC, et al. Hydrogen glucose breath test to detect small intestinal bacterial overgrowth: a prevalence case-control study in irritable bowel syndrome. Aliment Pharmacol Ther 2005;22:1157-60.
13. Posserud I, Stotzer PO, Björnsson ES, et al. Small intestinal bacterial overgrowth in patients with irritable bowel syndrome. Gut 2007;56:802-8.
14. D'Angelo G, Di Rienzo TA, Scaldaferri F, et al. Tricks for interpreting and making a good report on hydrogen and 13C breath test. Eur Rev Med Pharmacol Sci 2013;17:90-8.
15. Levitt MD. Volume and composition of human intestinal gas determined by means of an intestinal washout technic. N Engl J Med 1971;284:1394-8.
16. Corazza G, Strocchi A, Sorge M, et al. Prevalence and consistency of low breath H2 excretion following lactulose ingestion. Possible implications for the clinical use of the H2 breath test. Dig Dis Sci 1993;38:2010-6.
17. Enko D, Rezanka E, Stolba R, et al. Lactose malabsorption testing in clinical practice: a critical retrospective analysis and comparison of the hydrogen/methane breath test and genetic test (C/T_13910 polymorphism) results. Gastroenterol Res Pract 2014;2014:464382.
18. Pimentel M, Kong Y, Park S. Breath testing to evaluate lactose intolerance in irritable bowel syndrome correlates with lactulose testing and may not reflect true lactose malabsorption. Am J Gastroenterol 2003;98:2700-4.
19. Berg RD. Bacterial translocation from gastrointestinal

tract. Adv Exp Med Biol 1999;473:11-30.
20. Madl C, Druml W. Gastrointestinal disorders of the critically ill. Systemic consequences of ileus. Best Pract Res Clin Gastroenterol 2003;17:445-56.
21. Weinstock LB, Geng B, Brandes SB. Chronic prostatitis and small intestinal bacterial overgrowth: effect of rifaximin. Can J Urol 2011;18:5826-30.

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