

THE OCULAR SURFACE IN THE PATIENTS WITH PROSTATE CARCINOMA

* JOSEPH CHISARI - **ANTONINO GRAZIANO - **M. PAOLO GRAZIANO

*Center of Ocular Microbiology University of Catania - **United Department of Surgery University of Catania

[Superficie oculare in pazienti con carcinoma prostatico]

SUMMARY

Objective: Evaluation of tear film in patients with prostate CA were subjected to chemo-immunotherapy.

Materials and methods: 20 patients were evaluated in two groups with prostate cancer with systemic therapy with signs of ocular discomfort, visual impairment, signs of foreign body, abnormal lacrimal apparatus. Scores were performed for bacterial infections, testing Schirmer.

Results: The demographic characteristics of patients included in our study are shown in Table n. 1. The figures n. 1 and 2 highlight the average values of tear secretion test obtained in the two study groups "A" patients with prostate cancer. Group "B" after treatment.

Conclusions: The significant change in tear tests (Schirmer I, Schirmer II and BUT) obtained in the two study groups A and B shows an alteration of the ocular surface with a significant reduction in the tear film. L'alteration of this structure results in a variety of ocular disorders in different pathogenesis, including dry eye syndrome is certainly very good.

Key word: Carcinoma; lachrymal film; ocular microbiological

RIASSUNTO

Obiettivo: Valutazione del film lacrimale nei pazienti affetti da ca prostatico, sottoposti a chemio immunoterapia .

Materiali e metodi: sono stati valutati 20 pazienti divisi in due gruppi affetti da carcinoma prostatico con terapia sistemica con segni di disconfort oculare, alterazione visiva, segni di corpo estraneo, alterazione dell'apparato lacrimale. Sono stati eseguiti valutazione per infezioni batteriche, test di schirmer.

Risultati: Le caratteristiche demografiche dei pazienti inseriti nel nostro studio sono evidenziati nella tabella n. 1. Le figure n. 1 e 2 mettono in evidenza la media dei valori dei test della secrezione lacrimale ottenuti nei due gruppi di studio "A" pazienti con carcinoma prostatico. Gruppo "B" dopo trattamento.

Conclusioni: La significativa modificazione dei test lacrimali (Schirmer I, Schirmer II e BUT) ottenuti nei due gruppi di studio A e B evidenzia una alterazione della superficie oculare con riduzione significativa del film lacrimale. L'alterazione di questa struttura determina una varietà di disordini oculari a patogenesi diversa, di cui la sindrome da occhio secco è sicuramente la più importante.

Parole chiave: Carcinoma, film lacrimale, infezione oculare

Introduction

Prostate cancer predominantly affects elderly men, compared with other cancer species. The global age-adjusted morbidity rate of prostate cancer (age-adjusted morbidity rate: percentage of patients per 100 000 men per year) is 19.8, which stands as the third highest following 37.5 for lung cancer and 24.5 for gastric cancer. The morbidity of prostate cancer greatly varies across regions in the world. The morbidities of prostate cancer in advanced countries are generally more than three times as high as those in developing countries. In Japan, the age-adjusted morbidity of prostate cancer in men (based on the 1985 population) is 19.9, which is the sixth highest following those of gastric cancer, lung cancer, colon cancer, hepatic cancer and rectal cancer. However, it is forecast that the incidence of prostate cancer will become the second most prevalent following lung cancer by 2020 in Japan^(1,2). The global age-adjusted mortality rate of prostate cancer is 8.2, which is the fifth most prevalent following

33.7 for lung cancer, 19.1 for gastric cancer, 14.2 for hepatic cancer and 10.7 for colon/rectal cancer. In Japan, the 2001 age-adjusted mortality rate of prostate cancer in men is 8.4, which is the eighth highest following lung cancer, gastric cancer, hepatic cancer, colon cancer, pancreatic cancer, esophageal cancer and rectal cancer. The number of Japanese men dying of prostate cancer accounts for 4.2% of all Japanese men dying of any cancer. Prostate cancer can be latent as it is sometimes detected incidentally by microscopic investigation of biopsy specimen collected during any interventional procedure. The incidence of latent prostate cancer increases along with the advancement of age. However, the incidence of latent prostate cancer is similar across regions of the world , in contrast to the overall morbidity of prostate cancer.³ It is generally believed that latent prostate cancer does not commonly grow into clinically apparent cancer, however, some of the latent prostate cancers may slowly grow into a clinical cancer^(4,6). Since prostate cancer and benign prostatic hypertrophy (BPH)

occur due to similar etiologies and at similar ages, both prostate cancer and BPH may be identified simultaneously in the same man. It has been reported in Japan and other countries that prostate cancer was found in 4-7 % of men presenting to the outpatient sections of hospitals with dysuria^(7,8).

Therefore, it is necessary to investigate patients presenting with any urinating trouble to an outpatient section / clinic for the presence of prostate cancer by prostate specific antigen (PSA) testing and digital rectal examination (DRE). Although the determinate risk factor of prostate cancer remains unknown, some plausible risk factors have been identified. Presently the strongest risk factor of prostate cancer is heredity. The risk of prostate cancer is increased if a family has multiple prostate cancer patients or a prostate cancer patient with onset at a younger age⁽⁹⁾.

Since prostate cancer represents an androgen-dependent cancer, the presence of androgens is essential for the onset of prostate cancer. An extrinsic factor that is suggested to contribute to the risk of prostate cancer is the Western style of diet in which animal fat is frequently ingested, although this has not been definitively validated⁽¹⁰⁾. The incidence of prostate cancer is negatively correlated with the regular ingestion of beans and grains and positively correlated with the active ingestion of sugar, milk, and fat⁽¹¹⁾. Selected chemicals, including selenium; lcarotini b; lvitaminsl to, and, d, c landl; isoflavone; and lycopene, are being researched for possible preventive effects against prostate cancer^(12,13). The risk of prostate cancer it is necessary to investigate patients presenting alteration of the lachrymal constituted film by a siege of heterogeneous substances (lipids, protides, mucin, water) that it is integrated to form a biological structure highly specialized in the trophism and in the defence of the ocular surface.

The alteration of this structure can determine a variety of ocular disorders to pathogenesis different, of which the syndrome from eye dry up is surely the most major. The dislacrimal generally, can have provoke by modifications of the lachrymal components l mucinical and lipidic, from factors various as per alterations of the wink, from the use of corneal lenses. The hyposecretion often determines an alteration of the metabolism of the corneal associated epithelium to an instability of the lachrymal film, and this condition it can increase in the subjects with prostate carcinoma. Some studies have shown as the increase of any components of

the lachrymal film in such patients determines a reduction of its stability. Presumably, the alterations that-quantitative of the lachrymal film it determines a consequent modification of the ocular l microbionical with notable reduction of the immune ocular defences, facilitating like that for l of a possible infectious process. In the light of these knowledges are proposed to study the modifications of the ocular surface in the subject with prostate carcinoma with particular attention to alterations of the l microbionical l of the ocular surface and to the lachrymal film.

Materials and methods

Criteria of inclusion

The clinical studies that have been incorporated, as much as possible, the incidence of clinically significant prostate cancer and the progression speed from latent cancer to clinically. For the staging of prostate cancer at diagnosis, not only DRE, a PSA test and bone scintigraphy are performed but also computed tomography (CT)/magnetic resonance imaging (MRI). A chest X-ray is also performed in certain cases. Transrectal ultrasound-guided insertion of an 18-G needle is the standard prostate biopsy procedure for the pathological diagnosis of prostate cancer. Either transrectal or transperineal access is used.

The therapies are currently used for the treatment of prostate cancer: (1) surgery (the radical prostatectomy is performed usually via the retropubic approach, the perineal approach or the laparoscopic approach); (2) pharmacotherapy (endocrine therapy three-month neoadjuvant with regard to the benefits of the longer survival period and its relevance as a treatment for localized advanced prostate cancer. LH-RH agonists, formulations of goserelin or leuprorelin are available). When recurrent cancer chemotherapy include estramustine phosphate, CPA, fluorouracil (FU), and etoposide (ETP). The clinical studies that have for the staging to investigate patients presenting:

- with signs of ocular discomfort (burning, esprit de corps feeling extraneous, dryness and itch)
- (group "A" Ten patients end group "B" Ten patients)
- Any corneal coloration with fluorescein
- Absence of infections of the ocular and attached surface
- Absence of allergic pathology of the ocular surface

Criteria of exclusion

- Preceding ocular surgery
- Alteration of the lachrymal apparatus
- Medical therapy with systemic or topical medicines that alters the lachrymation and/or with topical steroids during the 4 weeks preceding the beginning of the study.

Patients

I have been admitted to study 10 patient with prostate carcinoma with the following systemic therapy:

- (“A” group) and n. 10 elderly patients of masculine sex with ocular ldisconfortl
- (“B” group)

Both croups manifested signs of ldisconfortl and/or ocular dryness (burning, esprit de corps feeling extraneous, dryness and itch). In all the patients will be taken in consideration the subjective symptomatology and the objective signs to the action of the visit of enlistment.

Considered parameters

- Symptoms: esprit de corps feeling extraneous, dryness, itch and burning
- Objective signs: discomfort and/or ocular dryness
- Objective examination of the anterior segment performed by lamp to crack
- Test of Schirmer I (mm/5’)
- Test of Schirmer II (mm/3’)
- Time of breakup of the lachrymal film (BUT, sec)
- Conjunctival tampon to seek aerobes bacteriums and anaerobes.

N° 10 patients	N°. eyes	Sex	Middle age	Range
Group A	20	M	78.5	68-84
Group B control	20	M	75.5	62-81

Table 1: characteristic demographic of patients that have completed the study.

Test of Schirmer I

It applies oneself to the third outside of the inferior eyelid a lstriscettal of graded blotting paper of the length of 35 mm. The patient comes invited to look with god, after 5 min, the strips come removed and it is appraises the portion of paper that results bathed by tears (normal inclusive values between 10 and 15 mm).

Test of Schirmer II

After linstillazione of an every drop 3 minutes, for three times, of anaesthetic (novesina), proceeds as the preceding Schirmer I. test. After 3 minutes are removed the striscette, and the portion is appraised of soaked paper (normal superior values or equal to 10 mm).

Test of B.U.T.

After instillazione of fluorescein to 2% calculates the existing time (normal inclusive values among 10-15 sec.) among the last wink and the beginning of the formation of corneal dry areas (dry spots).

Bacteriological test

Performs the collecting of the conjunctival secretion by a tampon of Hess, for the search of aerobes bacteriums and anaerobes. champions withdrawn by the patients, they came sows in the special grounds of crop and incubated in aerobe atmosphere and anaerobe for the isolation and identification of bacteriums presents, with count differentiated for aerobes and anaerobes. In particular, every bacterial log anaerobe, comes identified biochemically in accordance with the cautious schemes by the “Anaerobe Laboratory Manual”, 4th and., Virginia Polytechnic Institute⁽¹⁾.

Statistic analysis

To data of clinical parameters gotten in our study, among before and after treatment, will be applied the statistic test “t test of student”.

Results

Demographic characteristics of patients inserted in our study are underlined in the table n.1. The figures n.1 and 2 make oneself conspicuous the media of values of tests of the lachrymal secretion gotten in the two “A” day release croups patients with prostate carcinoma and “B” group of elderly subjects control with ocular discomfort. general data in comparison underline the following values respectively among the group to and the b group: Schirmer the 10.2-13.6; Schirmer II 3.8-4.6; BUT 4.2-6.5. Of cultivation examinations have altogether underlined a bacterial initial growth of 7 (51.2 %) logs in the “A” group in comparison to 4 logs (43.8 %) observed in the group checks (table 2). In the table 4 are brought the kinds of aerobes and found anaerobes in patients with prostate carci-

noma in comparison to the group it checks. Data of clinical parameters (show up n. 1 and 2) Schirmer the, Schirmer II and B.U.T., gotten in the two day release croup is express as it mediates and standard deviation (DS) of champions. The statistic significance of differences among the “A” group first and the “B” group after treatment has been calculated applying the statistic test “Student” p 0.001. With regard to the quantity of bacteriums gotten, it has not been possible to apply any statistic test.

N°. pazients (10)	N°. eyes (20)	“A” carcinoma N°	%	“B” control N°	%
Of cultivation examinations	20	10	51.2	10	43.8

Table 2: Total positive of cultivation examinations gotten for eye among the two day release group.

Microorganisms	A carcinoma	B control
Aerobes	4	3
Anaerobes	3	1
Total logs	7	4

Table 3: General number of aerobes isolations and anaerobes from the of cultivation examinations gotten in the two day release group.

Microorganisms	A carcinoma		B control	
	N°	%	N°	%
S. epidermidis	3	23.4	3	46.5
S. aureus	1		0	
Peptococcus spp.	2		1	
Peptostreptococcus spp.	1		0	
Total logs	7	100	4	100

Table 4: Number and percentage of bacterial logs aerobes and anaerobes isolated by subjects with possible SM before and after treatment with lcarbositetilcellulosal.

Conclusions

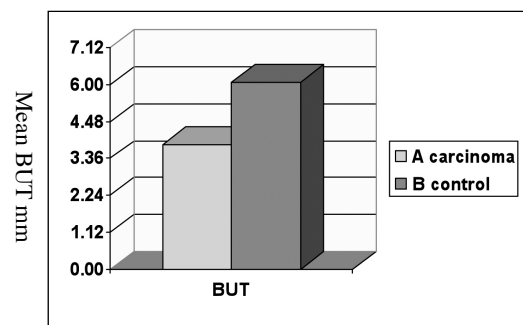
The radical prostatectomy and radiation therapy, are recommended for localized prostate cancer. The long natural history of the disease, due to its low to medium biological aggressiveness, and

the availability of salvage endocrine therapy after failure also prevent a definitive conclusion as to their relative efficacy. A true comparison of the two modalities can only be made possible in a large RCT designed to evaluate overall survival as the primary endpoint in a long-term follow-up.

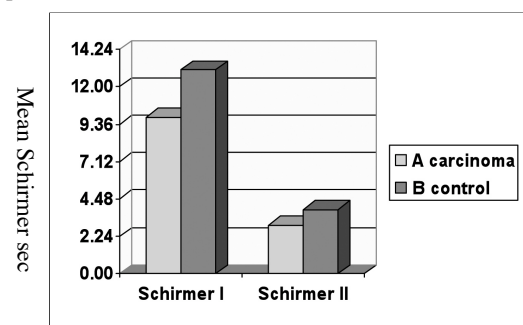
The meaningful modification of lachrymal tests (Schirmer the, Schirmer II and BUT) gotten in the two day release croup to and b underlines an alteration of the ocular surface with meaningful reduction of the lachrymal film. As it is state in preceding searches confirmed 1.2 a lachrymal stable film is the result of the equilibrium of a siege of complex functions harvest in action from the system of the ocular surface.

A fit environment for PH, electrolytic concentration, relative damp and presence of the nutritive fundamental elements it is essential to because the ocular surface power develop its principals work together to an integration of the normal bacterial flora that managed a direct action and indirect of defence of the same surface.

In fact, the function of physical and immunological barrier by the epithelium of the ocular surface is undertaken under the narrow junction of epithelial cells that determines sharpen the versus barrier effect the bacteria with cause disease.



Graphic 1. Break-thyme in the two day release croup A patients with carcinoma and group B control. and after treatment with sodic lcarbositetilcellulosal (per days from the suspension of the treatment). * P 0.001



Graphic 2. Test of Schirmer the and II before and after treatment with sodic lcarbositetilcellulosal 0.5 % (per days from the suspension of the treatment).* P 0.001

References

- 1) Ohno Y, Nakamura T, Oshima T and to the. *The future estimates of cancer prevalence rate in Japan*. In: Oshima A, Kuroishi T, Tajima K (eds).
- 2) Gan Tohkei Hakusho-Morbidity/Death/Prognosis-2004. Shinohara Publisher, Tokyo, 2004; 201-217.
- 3) Yatani R, Chigusa T, Akazaki K and to the. *Geographic pathology of latent prostatic carcinoma*. Int. J. Cancer 1982; 29: 611-16.
- 4) Etzioni R, Feuer EJ and to the. *Asymptomatic incidence and duration of prostate cancer*. Am. Epidemiol j. 1998; 148: 775-85.
- 5) Hiraishi T and to the. *Latent Prostatic Carcinoma*. Clinical Practice Manual for Prostate Cancer, The Japanese Foundation for Prostate Research, Kanehara & Co., LTD., Tokyo, 1995; 13-24.
- 6) Watanabe H. *Studies on the Natural History of Prostate Cancer*. Clinical Practice Manual for Prostate Cancer, The Japanese Foundation for Prostate Research, Kanehara & Co., LTD., Tokyo, 1995; 1-12.
- 7) Fukuta F, Masumori N, Tanaka Y and to the. *The detection rate of prostate cancer in outpatients presenting lower urinary tract symptoms*. Jpn. J. Clin. Urol. 2005; 59: 133-8.
- 8) Lepor H, Owens RS, Roggenbuckler and to the. *Detection of prostate cancer in males with prostatism*. Prostates 1994; 25: 132-40.
- 9) Steinberg GD, BS case, Beaty TH and to the. *Family history and the risk of prostate cancer*. Prostates 1990; 17: 337-47.
- 10) Giovannucci and, Rimm EB, Colditz GA and to the. *A prospective study of dietary fat and risk of prostate cancer*. J. Natl. Cancer Inst. 1993; 85: 1571-9.
- 11) Nakata S, Imai K, Yamanaka H, Yashima H. *Correlation Analysis between Mortality for Prostate Cancer and Dietary Pattern in Japan and the World*. Jpn. J. Cancer Clin. 1994; 40: 831-6.
- 12) Hebert JR, Hurley TG, Olendzki BC and to the. *Nutritional and socioeconomic factors in relation to prostate cancer mortality: to cross-country study*. J. Natl. Cancer Inst. 1998; 90: 1637-47.
- 13) Eichholzer M, Stahelin HB, Ludin and to the. *Tuxedo, moulds c vitamins, and, cancer prostates fatal retinol, carotene and, and: seventeen-year follow-up of the prospective Basel study*. Prostates 1999; 38: 189-98.
- 14) Chisari G., Reibaldi M., Sanfilippo M., *Study of the ocular external ecosystem in diabetic patients with hyposalivation*. Ann Ophthalmol Clin Oculist 2001; CXXVII, 2-3: 113-122.
- 15) Chisari G., Reibaldi M., Sanfilippo M., *Evolution of the etiologic panorama of the ocular external infections*. Boll. Oculistics 2002; 81: 3351-3361.
- 16) Aragona O., Of Stephen G., Ferreri G., Ferreri F., and to the.: *Hypotonic Hyaluronate treatment in type 1 insulin dependent diabetic patients*. Arvo 2000.
- 17) Dogru M., Katakami C., Inoue M., *Tear function and surface changes in noninsulin-dependent diabetes mellitus*. Ophthalmology. 2001; 108(3): 586-92.
- 18) Ozdemir M., Buyukbese MA, Cetinkaya T, Ozdemir G., *Risk factors for ocular surface disorders in patients with diabetes mellitus*. Diabetes Res Clin Pract. 2003; 59 (3): 195-9.
- 19) Yoon KC., Im SK, Seo MS., *Changes of tear film and ocular surface in diabetes mellitus*. Korean J Ophthalmol. 2004; 18 (2): 168-74.
- 20) Sheppard JD. *Guidelines for the treatment of chronic dry eye disease*. Manag Care 2003; 12: 20-25.
- 21) Goebbels M., *Tear secretion and tear film function in insulin dependent diabetics*. Br J Ophthalmol 2000; 84: 19-21.
- 22) Herber S., Grus FH, Sabuncuo P., Augustin AJ, and to the. *Changes in the tear protein patterns of diabetic patients using twodimensional electrophoresis*. Adv Exp Med Biol 2002; 506: 623-626.
- 23) Grus FH., Sabuncuo P., Dick HB, and to the. *Changes in the tear proteins of diabetic patients*. BMC Ophthalmol 2002; 118: 1264-1268.
- 24) Arivazhagan P., Panneerselvam C. *Effect of DL-alpha-lipoic acid on neural antioxidants in aged rats*. Pharmacol Res. 2000; 42(3): 219-22.
- 25) Jun Saito, M., D., et al., *Correlation of corneal sensation, but not of basal or reflex tear secretion, with the stage of diabetic retinopathy*. Cornea 2003; 22(1): 15-18.
- 26) Packer L., Kraemer K., Rimbach G., *Molecular aspects of lipoic acid in the prevention of diabetes complications*. Nutrition 2001; 17: 888-95.
- 27) Ceriello A., MD. *New insights of oxidative stress and diabetic complications may lead to a causal antioxidant therapy*. Diabetes Care 2003; 26: 1959-96.
- 28) L. porch, Gavan NA, Veresiu IA, Orasan R., *In vivo effect of lipoic acid peroxidation in patients with diabetic neuropathy*. 2000; 14(2): 327-330.
- 29) Martin J., Stevens, Irina Obrosova, Xianghui Cao et al., *Effect of DL-a-lipoic Acid on Peripheral nerve conduction, Blood Flow, Energy Metabolism, and Oxidative Stress in Experimental diabetic Neuropathy*. Diabetes 2000; vol 49.

Request reprints from

Prof. ANTONINO GRAZIANO

United Department of Surgery

Hospital Policlinico

University of Catania

Via S. Sofia, 86

95100 Catania

(Italy)