



Editorial – referring to the article published on pp. 549–554 of this issue

Micronutrients and BPH

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Descriptive epidemiology suggests that the incidence and prevalence of prostatic diseases vary significantly in different areas of the world [1–3]. Possible reasons for such wide variations have been explored and nutritional factors were found to play a role together with genetic, behavioral, occupational, and environmental ones. Epidemiologic studies of benign prostatic hyperplasia (BPH) have been hampered by the lack of a valid definition of the disease. Neither BPH nor benign prostatic enlargement or benign prostatic obstruction can be used in population-based studies; lower urinary tract symptoms (LUTSs) have often been used as a surrogate definition of BPH but their etiology remains multifactorial. The need for prostate surgery has been rarely considered as a proxy for BPH because it limits the population to a subset of patients.

Current knowledge of the etiology of BPH includes a number of putative factors. An inverse relationship has been observed between smoking and the risk of BPH and is considered to be dependent on the fact that smokers are less likely candidates for surgery because there is little evidence of a hormonally mediated effect of smoking on BPH; the effect is considered to be weak and has no practical implications [1]. The association of obesity, particularly body mass index, and BPH has been investigated and considered possible although firm evidence is lacking. Alcohol consumption and liver cirrhosis seem to be inversely associated with the risk of BPH but data remain weak. The importance of

family history has been evaluated notwithstanding the difficulty in separating genetic from environmental factors; a 3.3-fold increased risk for monozygotic twins may reflect a difference in genetic predisposition [1]. A common etiology for LUTS/BPH and hypertension has been proposed but further research is needed. The possible relationship of the “metabolic syndrome” and BPH has been investigated, looking for a possible link between hypertension, obesity, and BPH, but results are controversial [1]. Racial differences in the risk of BPH surgery and severe symptoms have been documented although the influence of cultural differences and access to health care facilities should also be considered [1].

Although we all agree that “to prevent is better than to cure,” medicine and particularly urology remain focused on treatment. Prevention is a very trendy subject that has generated a consensus and attention but relatively little funding. Actually, clinical research in the area of preventive medicine is poorly supported when compared with pharmacologic treatment; among the different reasons we have to acknowledge that the former is basically of interest for academic research, whereas the latter is mainly sponsored by industry. Interestingly, the definition of chemoprevention in the National Institutes of Health Web site limits the area of intervention to neoplastic disorders. The importance of preventing cancer is self-evident although the health and economic consequences of preventing highly prevalent benign disorders is probably of

similar relevance. Analysis of the peer-review literature on chemoprevention reveals 4208 papers on prevention and prostate, 3681 of which are about prostate cancer prevention with only 130 related to BPH. No information is available on the relationship of chemoprevention of benign and neoplastic disorders of the prostate, but the two subjects are not necessarily independent.

Nutritional factors are considered to be of importance in maintaining good health. In particular, fruits and vegetables are known to have a chemopreventive effect and a daily dose of 400–600 g/d is recommended. According to the National Cancer Institute bulletin, about 400 compounds have been listed as potential chemopreventive agents and about 40 of these are currently under clinical evaluation [4]. Different mechanisms for the observed chemopreventive effects have been described including antioxidant effects, anti-inflammatory activity, modulation of steroid metabolism, antibacterial and antiviral effects, modulation of detoxifying enzymes, stimulation of the immune response, and antineoplastic effects. Some of the potentially beneficial substances have been included in alternative remedies and herbal medicines that now represent a growing market worldwide but are sometimes distributed without any prescription and in the absence of rigorous testing of their safety and activity [5]. In the ever-changing field of medicine, urology is facing a new challenge because our specialty is not only about surgery but also the practicing urologist is becoming the patient advisor to maintain the urogenital system in good health.

Dietary factors include different issues such as the total caloric intake, macronutrients (carbohydrates, proteins, and fat) and micronutrients (vitamins and minerals). Data from epidemiologic studies provide evidence of a possible significant relationship between dietary habits and the incidence of prostate disorders but do not suffice, per se, to justify a widespread adoption of new dietary habits. From a statistical standpoint, as long as we accept a 5% chance that the observed difference is due to chance, a post-hoc analysis of a 100 different parameters is likely to identify five positive associations. Such consideration does not weaken the outcome of epidemiologic research but rather warns against data that are not confirmed in subsequent studies and stresses the importance of properly designed and conducted studies. Having said that, epidemiologic data constitute the rationale for prospective, randomized, clinical trials that can provide a definitive answer to the possible beneficial effect of dietary factors. The etiology of

BPH is elusive. Androgens maintain a permissive but not a causative role. The effect of dietary habits is difficult to investigate because they are rarely evaluated using validated questionnaires, as in the paper from the Mario Negri Institute. Furthermore, the biochemistry of vegetables and fruits is quite complex and sometimes the therapeutic effect of the dietary factor that is considered to be the active component may fail to replicate the therapeutic effect of the parent vegetable/fruit. Interestingly, the administration of lycopene, one of the active components of the tomato, which is considered to be responsible for the beneficial effect of a diet rich in tomato on the risk of prostate cancer, did not prove to be as effective as tomato supplementation [6].

The paper from Tavani and coworkers suggests that the risk of BPH surgery decreases significantly with increasing intake of carotene [7]. The risk also tended to decrease with the intake of vitamin C and iron. On the other hand, the risk tended to increase with the intake of sodium and zinc. None of the other antioxidants or retinol were associated with the risk of BPH surgery. The results of epidemiologic studies must always be weighed against the current knowledge of the organ/disease physiopathology. Both β -carotene and vitamin C derive from vegetables and fruits and have antioxidant properties so that their effect against oxygen-reactive species can be considered to be of importance. Interestingly, none of the other antioxidants derived from fruits and vegetables seemed to play a role so that the mechanism by which carotene and vitamin C play a beneficial role remain unclear. The lack of a protective effect for retinol seems to exclude a possible protective role for vitamin A. The case of zinc is relatively easier because its concentration is decreased in prostatitis and prostate cancer but increased in BPH. Intracellular zinc levels are increased by testosterone and zinc is known to modulate 5- α -reductase activity. Dietary habits may change over time but timing of exposure is an important issue in chronic conditions that take decades to develop, such as BPH.

At present, identifying risk factors for BPH seems to be of importance for understanding how BPH develops rather than for preventing the development of the condition. In Western countries technologic food highly prevails over biologic ones and 6–7 kilos of food additives are consumed each year per person without little knowledge as to their effect on the human body. The use of food additives to prevent the development of chronic disorders (ie, iodine supplementation of salt) is very rare but

highly effective. More money seems to be poured into the research for improving the taste, odor, and aesthetics of food than in studying the effect of dietary habits on chronic disorders. The economic consequences of disease prevention using micronutrients may be formidable and more important in developing countries where both calories and essential nutritional factors are insufficient and health care facilities scarce than in the Western world where the diet is usually well balanced, the caloric intake is too high, and access to health care facilities available.

Urology is taking the lead in the field of chemoprevention. A large study has been completed by the National Cancer Institute providing convincing evidence as to the possibility of reducing the risk of cancer by 25% using finasteride [8]. An even larger study is currently underway to evaluate the role of selenium and vitamin E in reducing the risk of prostate cancer [9].

The relationship between lifestyle and health is an exceedingly serious subject that often becomes trivialized in newspapers and magazines but remains a fundamental issue in medicine. Funding for clinical research into the etiology of chronic disorders and their prevention should be substantially increased because the return on investment may be higher than expected.

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