Spinal Cord (1998) 36, 771–773

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Seminal plasma PSA in spinal cord injured men: a preliminary report

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Objective: The aim of the study was to evaluate the impact of spinal cord injury on seminal plasma PSA concentration.
Material: Semen obtained from normal controls ($n=20$) and patients ($n=16$) with spinal cord injury.
Results: The concentration of prostate specific antigen in seminal plasma depended on the level of spinal cord injury, with significantly lower concentrations in patients with spinal cord lesions below T7 compared to both normal age-matched controls ($P=0.007$) and patients with spinal cord injuries at or above T7 ($P=0.017$).
Conclusions: The results add to the previously reported observations of the possible impact of neurogenic stimulation on prostate activity. More studies of neurogenic stimulation in prostate growth and development are warranted to further elucidate the possible impact of neurogenic factors in the development of prostatic diseases.

Keywords: Prostate specific antigen; semen; seminal plasma; spinal cord injuries

Introduction

Prostate specific antigen (PSA) was first isolated from human seminal plasma.[1] PSA is produced almost exclusively in the prostate epithelium and is normally regarded as an indicator of the activity in the prostate gland. Furthermore, changes in PSA measured in serial serum samples correlate to the development of prostatic disease.[2] Prostate development and growth depends on normal androgen supply.[3] *In vitro* studies in animal models suggest that sympathetic activity may induce growth and/or maintain cell survival in the prostate[4] and human prostate cancer cell proliferation is inhibited by alphaadrenergic blocking agents.[5]

The aim of this study was to evaluate the seminal plasma PSA concentrations in patients with spinal cord injuries (SCI) compared to normal controls, and to evaluate the impact of level of spinal cord injury on seminal plasma PSA-concentration.

Material and methods

Semen was obtained from 20 normal, healthy and fertile controls following masturbation and 16 SCI patients undergoing either vibratory or electrostimulation to induce ejaculation as described by Sønksen *et al*[6] and Ohl *et al*.[7] Details about the patients included are given in Table 1. Before assisted ejaculation procedures a urine culture was performed in all SCI patients. Semen was frozen at $-20^{\circ}C$ within 30 min after ejaculation. For PSA measurement, semen was diluted (1 : 10 000 or 1 : 100 000) in PSA-negative female serum and analyzed with the automated PSA method from Abbott Labs., Abbott Park, IL[8,9] performed on an AxSYM (Abbott).[10] Follicle stimulating hormone (FSH), luteinising hormone (LH) and testosterone levels were measured in SCI patients, but not in controls. Seminal plasma PSA concentrations were compared using the Mann-Whitney rank sum test. *P*-values less than 0.05 are considered significant.

Results

The age and seminal plasma PSA concentrations in controls and SCI patients are shown in Table 2. No significant differences in age, completeness of SCI, or time since injury were found between patients with spinal cord lesions at or above T7 compared to lesions below T7. All SCI patients had normal FSH, LH and testosterone levels. No SCI patients had significant bacterial growth in the urine before the ejaculation procedures.

The seminal plasma PSA concentrations were lower in patients with SCI compared to normal age-matched controls, however the difference did not reach a significant level, ($P=0.08$). No difference in seminal plasma PSA was found between patients with lesions at or above T7 and normal controls.

Seminal plasma PSA concentrations in patients with lesions below T7 were significantly lower than concentrations found in controls, ($P=0.007$), and in patients with lesions at or above T7, ($P=0.017$). No

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Table 1 Spinal cord injured patients

Age	*Duration of injury (years)*	*Level of lesion*		*Method*	*Seminal PSA conc. (mg/L)*
Lesions at or above T7					
31	9	C2	Compl.	PVS	892
28	10	C5	Compl.	PVS	271
29	6	C5	Compl.	PVS	440
33	13	C6	Compl.	PVS	1534
21	4	C6	Compl.	PVS	1437
31	12	C7	Compl.	PVS	243
31	29	T6	Compl.	EEJ	780
32	2	T6	Compl.	PVS	330
36	1	T7	Incompl.	PVS	440
45	29	T7	Compl.	PVS	480
Lesions below T7					
44	18	T8	Compl.	EEJ.	140
27	7	T8	Compl.	EEJ.	110
42	20	T12	Compl.	EEJ.	944
34	12	T12	Compl.	EEJ.	46
25	9	T12	Incompl.	EEJ.	108
29	7	T12	Compl.	EEJ.	71

PVS: Penile vibratory stimulation. EEJ: Electroejaculation

Table 2 Age and seminal plasma PSA concentrations in controls and SCI patients

	No	*Age (years) Median/range*	*Seminal PSA mg/L Median/range*
Controls	20	34 years/25–48	535/238–2379
Patients			
At or above T7	10	31 years/21–45	460/243–1534
Below T7	6	32 years/25–44	109/46–944

significant differences in seminal plasma PSA concentrations were found, when comparing ejaculates obtained by either vibratory or electrostimulation.

Discussion

PSA is secreted in high concentrations by the epithelium in the prostate, and is involved in the liquefaction of the seminal coagulum formed at ejaculation.[11] Seminal plasma PSA concentration is approximately 10^5–10^6 times higher than PSA concentration in serum and the majority of PSA in seminal plasma is present in the catalytically active single-chain form.[12]

Prostate growth and development of prostatic diseases depends on age and androgen supply.[3] Other factors, however, may modify the impact of androgens, such as a low 5-alpha-reductase activity found in Japanese men, which may be part of the explanation for the lower prostate cancer incidence in Japan.[13]

The prostate normally contains a number of neuroendocrine cells and it has been suggested, that neuroendocrine stimulation may affect prostate growth and differentation.[14,15] The number of neuroendocrine cells in the prostate is increased in benign prostatic hyperplasia compared to normal glands.[14] Further, neuroendocrine cells can be found in the majority of prostatic carcinomas.[15] The neuroendocrine cells are often found in close relation to afferent nerves and produce a number of bioactive hormone-related substances of which some act as growth stimulators,[16] while others like somatostatin can inhibit trophic or growth factor activity.[15]

The neurogenic stimulation of the male accessory sexual glands including the prostate arises from sympathetic nerves from the thoracolumbar spinal cord (T11–L2) and from parasympathetic nerves from the sacral spinal cord (S2–4).[17,18] When analyzing the impact of the SCI level we found seminal plasma PSA concentrations to be significantly lower in patients with lesions below T7 compared to patients with lesions at or above this level. More logically a spinal cord cut-off level at T10 would have been expected. However, previously it has been demonstrated, that seminal somatostatin levels in patients with SCI depended on the level of spinal cord injury, with significantly higher levels in patients with lesions below T6.[19] This finding suggests that the neurogenic stimulation of somatostatin is dependent on nerve fibres arising above this level. In addition, semen analyses from SCI men have demonstrated significantly better sperm motility in patients with lesions at or above T6 compared to lesions below this level.[20] PSA is in our study lower, although not significantly, in patients with spinal cord injuries compared to healthy controls. It is noteworthy that patients with normal testosterone levels and SCI below T7 had significantly lower seminal PSA than both normal controls and SCI patients with lesions at or above T7. This finding suggests that some neurogenically mediated factor plays a role in the PSA production. The inverse correlation between high somatostatin and low seminal plasma PSA concentrations found in patients with spinal cord lesions below the level of T6/T7 suggests that this spinal cord level represents a crucial point in the neurogenic stimulation of the prostate gland.

PSA has been demonstrated to degrade, when serum samples are stored.[21] Most likely a similar degradation will occur in seminal plasma when these samples are stored. The observed difference found in seminal plasma PSA concentration, however, is unlikely to be explained by storage, as the handling of samples were identical in the two groups. Serum PSA concentration increases in patients with urinary retention, lower urinary tract infections, and prostatitis,[22,23] conditions frequently present in patients with SCI. The impact of these conditions on seminal plasma PSA has not been elucidated. However, if seminal plasma PSA were to increase, this would tend to diminish the difference in

seminal plasma PSA concentrations by producing higher seminal plasma PSA in the patients with SCI.

Serum PSA concentrations have been demonstrated to vary when measurements are repeated.[24] To what extent seminal plasma PSA concentration varies is not known, and studies including more patients and repeated measurements are ongoing.

Further studies on the possible effect of neurogenic stimulation of prostatic development and growth are warranted, and may possibly add to our understanding of both neuroendocrine differentiation and aetiological factors in the development of prostatic diseases.

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