Prostate Specific Antigen and Prostatic Acid Phosphatase Measurements for the Follow-up of Patients with Prostate Cancer

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ABSTRACT

The clinical application of 84 prostate specific antigen (PSA) and prostatic acid phosphatase (PAP) measurements for the follow-up of 36 patients with treated prostate cancer was retrospectively examined by case study. Clinicians use several risk markers including serum levels of PSA and PAP to monitor prostate cancer progression or stability. These results of PAP and PSA tests were either utilized during the patient's clinical assessment or they were disregarded. In either case, the results would support or counter the physician's clinical decision for patient management. After predictive value analysis it was concluded that measurement of PSA alone is more useful than parallel measurements of PSA and PAP, when utilized together with standard criteria for assessing treated prostate cancer patients.

Introduction

It was observed in a large, urban, teaching hospital that patients were evaluated for follow-up of prostate cancer, after initial treatment, with two serum assays, one for prostate specific antigen (PSA) and the other for prostatic acid phosphatase (PAP). The diagnostic and clinical utility of both PSA and PAP has been much debated. Some researchers think that PSA is a more useful measure of prostatic neoplasm than PAP. Neither PAP nor PSA or both assays used together is a reliable screening test for prostate cancer. Many researchers concur that PSA is a good monitor of successful prostate ablation, whether the prostate is removed surgically or suppressed with medication. Some investigators champion the use of PSA to detect post-prostatectomy metastatic spread of tumor cells. The literature pertaining to the clinical applications of PAP and PSA tests is somewhat confusing and not fully convincing.

This investigation focuses on the clinical utility of measuring two prostate markers for the follow-up of patients with adenocarcinoma of the prostate, after initial therapy, by comparing results of PAP and PSA assays with the decisions on patient management made by the clinician.

Materials and Methods

The clinical records of 146 patients for whom PAP and PSA assays were per-
formed were reviewed. From these charts, 36 patients with diagnosed adenocarcinoma of the prostate had laboratory results for both of these assays. The study population was a select group of males, over 40 years of age. Values of concomitantly ordered PAP and PSA tests were compared to the decisions on patient management made by the clinician.

Patient management was based on evidence of disease remission or progression that was arrived at after consideration of clinical findings, laboratory tests, and other investigative procedures generally accepted. Clinicians directed patient management after classifying the patient either in remission (no evidence of disease progression, [NED]), or as having extension, progression or residual disease (POD). Patients determined to have NED were assigned outpatient status and were scheduled to make periodic visits to the urology clinic. Patients who showed evidence of prostate disease (POD) were admitted to the hospital for additional testing and treatment.

The 36 suitable candidates for the study included 10 patients who underwent a radical prostatectomy, 10 who underwent a transurethral resection of the prostate (TURP), eight who were treated with radiation therapy, three who received antiandrogen therapy consisting of bilateral orchiectomy, one given anti-androgen treatment, and four patients who were managed with both surgical and medical combined antiandrogen approaches.

Eighty-four assays were documented in the patients' charts, i.e., 42 tests were performed concomitantly for PAP and PSA measurements. Serum for the tumor marker analysis was separated from venous blood drawn from ambulatory patients at the same sitting since significant changes in the concentrations of the analytes occur within a short interval of time. No changes in patient management occurred during the sampling interval between PSA and PAP collection.

The PSA assays were performed with the Hybritech Tandem E reagents and Photon II Immunoanalyzer, which uses an enzyme immunoassay methodology.* Samples suspected of producing a “hook effect” were retested after dilution. The cut-off value for abnormal results was that recommended by the manufacturer; PSA values greater than four ng per mL were considered positive results, indicating disease progression. Values of PSA of four ng per mL or less were considered to reflect absence of disease progression (negative results).

The PAP assays were performed by a colorimetric method with the use of a Gilford Stasar III spectrophotometer. The cut-off value for abnormal results was set by the laboratory. Values greater than 0.83 IU per L indicate progressing prostate cancer (positive results), and values of 0.83 IU per L or less reflect disease remission (negative results).

The clinical significance and predictive value of PSA and PAP serum levels in relation to prostate cancer monitoring were investigated in this study.

Results

Thirty-six patients underwent 84 parallel assays for prostate tumor markers, i.e., 42 for PSA and 42 for PAP. For the 10 patients in whom a radical prostatectomy was performed, 12 parallel assays were performed. Nine true negative and three true positive results for PSA were shown when compared to the clinician's patient evaluation. Of 12 PAP results, nine were true negative and three were false negative when compared to the clinical judgment.

* Hybritech, Inc., San Diego, CA 92121.
For the 10 patients in whom a transurethral resection of the prostate (TURP) occurred, 12 parallel assays were performed. There were six true negative, one false negative, and five true positive PSA results when compared to the physician’s evaluation of prostate disease. On the other hand, there were six true negative, five false negative, and only one true positive PAP results when compared to the physician’s assessment.

For the eight patients treated with radiation therapy, nine parallel assays were performed. There were five true negative, three true positive, and one false positive PSA results when compared to the clinician’s impression. The PAP test results showed the same distribution: five true negative, three true positive, and one false positive results in comparison to the physician’s assessment.

For the three patients who underwent bilateral orchiectomy, three parallel assays were performed. Testings for PSA showed two true negative and one true positive results. Prostatic acid phosphatase testing showed two true negative and one false negative results, thereby failing to detect POD in one patient.

The one patient treated medically with an antiandrogenic regimen was accurately identified by both PSA and PAP assays as NED when compared to the physician’s assessment.

For the four patients who received both medical and surgical combined antiandrogen regimens, five parallel assays were completed. The PSA values correlated poorly with the clinician’s evaluation. There were four true negative and one false negative results. The PAP values accurately signaled the four true negative cases, and the one true positive case of disease progression (table I).

The predictive values of PSA, PAP, and both PSA and PAP were compared to the clinician’s assessment of the patient’s disease status (table II). The test sensitivity or probability that an abnormal test result picked up an exacerbation of disease showed PSA to offer the best sensitivity; PAP and both PAP and PSA were not as sensitive. The converse situation, test specificity, which shows the probability that a normal test result indicated absence of disease progression, was equal for both tests.

The probability that a patient has both an exacerbation of disease and an abnormal test result is the positive predictive value. This is measured as the relation between the true positive cases and total number of true positive and false positive results. Prostate specific antigen presents as the better marker to alert the clinician to careful decision making. Conversely, the negative predictive values show the probability that a patient is stable, and the test measurement reflects this condition. Again, PSA is the better marker for reassuring the physician of the patient’s quiescent status.

Test efficiency measures the accuracy of patient classification and compares the number of true tests to the sum of all tests. Prostate specific antigen is the most efficient of the two tests monitored in this investigation.

Discussion

The data show good sensitivity, specificity, and overall efficiency for the PSA tumor marker when used as a sole parameter to monitor prostate cancer (table II). However, the number of patients comprising this study is small, and definitive conclusions cannot be drawn from these data. Many authors agree that PSA is a good, reliable marker of tumor burden once the prostate has been suppressed. This study confirms the conclusions of those investigators. One may speculate that if the number of patients in this study was to be
TABLE I
Prostate Specific Antigen and Prostatic Acid Phosphatase for the Follow-up of Patients with Prostate Cancer

<table>
<thead>
<tr>
<th>Therapy</th>
<th>No. Patients</th>
<th>NED</th>
<th>TN</th>
<th>FN</th>
<th>POD</th>
<th>TP</th>
<th>FP</th>
</tr>
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<tbody>
<tr>
<td>Radical prostatectomy</td>
<td>10</td>
<td>PSA</td>
<td>9</td>
<td>9</td>
<td>3</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>PAP</td>
<td>9</td>
<td>9</td>
<td>3</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Transurethral resection of the prostate</td>
<td>10</td>
<td>PSA</td>
<td>6</td>
<td>6</td>
<td>1</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PAP</td>
<td>6</td>
<td>6</td>
<td>5</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>8</td>
<td>PSA</td>
<td>6</td>
<td>5</td>
<td>3</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PAP</td>
<td>6</td>
<td>5</td>
<td>3</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Orchiectomy</td>
<td>3</td>
<td>PSA</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>PAP</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Anti-hormonal (med.)</td>
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<td>PSA</td>
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<td>1</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>PAP</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combined Med-Surg.</td>
<td>4</td>
<td>PSA</td>
<td>4</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>PAP</td>
<td>4</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Total Number of Tests</td>
<td>42</td>
<td>PSA</td>
<td>27</td>
<td>2</td>
<td>12</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>42</td>
<td>PAP</td>
<td>27</td>
<td>9</td>
<td>5</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

PSA = prostate specific antigen
NED = no evidence of disease
TN = true negative
FN = false negative
POD = progression of disease
TP = true positive
FP = false positive

increased, the results would not differ since similar conclusions have been drawn from other studies.1,2,6,14

Although the distinction between disease progression and remission was a clinical one, we assumed the physician assessment to be the standard for comparison. The patient’s management is determined by the physician’s ability to make appropriate choices from the available data at his disposal. The autopsy will provide the ultimate diagnosis in the long term, but quality control by post-mortem examination was not utilized in this study for obvious reasons.

It is assumed that the values of PSA and PAP in serum are a reflection of the patient’s true clinical status with regard to prostate cancer. Serum levels of both PSA and PAP tend to increase with increasing disruption of the prostate epithelial cell basement membrane.7 False positive PSA values may, in reality, not be so. There is evidence that a rise in PSA values may antedate the symptomatic phase of prostate cancer progression by several months.5,13 If such were the case, the sensitivity of the PSA assay will increase since the clinician made his assessment mainly on the basis of the change in patient symptoms.

The false negative PSA values ostensibly fail to indicate active disease by delivering normal test result. A false negative result could be a manifestation of the “hook effect” which was not
detected, or it may reveal the cautious clinician's lingering doubt and the subsequent overdiagnosis of the patient's symptoms.

It should also be mentioned that some authors feel that the clinical utility of a prostate cancer tumor marker is of dubious value. However, a good marker for prostate cancer progression would assist with monitoring the effectiveness of anti-neoplastic drugs should that therapy option become available. Prostate specific antigen would be a good candidate marker in this respect.

The data presented substantiate the superiority of PSA assay to monitor prostate cancer when compared to PAP or to the combined use of both PSA and PAP. In our judgment, PAP is an obsolete marker of prostate cancer; no additional useful information would be forthcoming by using the PAP test, which is at best redundant. In fact, PAP provides less accurate and more equivocal information than PSA. There is increased cost to the patient without a proportional increase in clinical utility when both PSA and PAP are ordered concomitantly to monitor and assess the status of patients with prostate cancer.

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References


