Failure to wean due to steroid psychosis

Fahmi Y. Khan, MD.

Since their introduction as therapeutic agents, corticosteroids have been associated with psychiatric symptoms ranging from mood disturbances to (florid) psychosis. By the time there have been reported psychotic reactions in patients receiving steroids or after sudden withdrawal of long time corticosteroids therapy. In this report a 40-year-old male patient known to have bronchial asthma since childhood, presented to the Accident and Emergency Department with marked shortness of breath. His medical history was otherwise unremarkable. Ventolin (β2 agonist) and Atrovent (anticholinergic) was delivered via nebulizers and methylprednisolone was given at a dose of 60 mg intravenously (IV), every 6 hours. The patient's condition deteriorated over the next hours and he was subsequently electively ventilated via cuffed endotracheal tube and transferred to the medical intensive care unit (MICU).

In the MICU, the patient was put on mechanical ventilator and was given the following drugs: nebulized Ventolin 60 mg, every 6 hours IV, methylprednisolone 60 mg, and remifentanil IV. No muscle relaxants were used. On the following days, the patient became stable and he was prepared for weaning by tapering the dose of sedatives (midazolam and remifentanil). Remifentanil was stopped initially, while the patient remained calm, then midazolam was tapered gradually. As soon as the dose of midazolam decreased below the therapeutic level, the patient showed interrupted appearance of excitation and aggressiveness and fought with the ventilator, thus weaning was postponed. Investigations, including electrolytes, arterial blood gas, liver function test, chest x-ray and renal function tests were normal. Attempts to wean the patient continued but failed, as the patient became aggressive without sedatives, which makes the weaning process more difficult. Weaning failure were suspected due to steroid psychosis, methyl-prednisolone was withdrawn and haloperidol was administered, while the patient was kept on midazolam and bronchodilators. Psychotic symptoms, consisting of interrupted appearance of excitation and aggressiveness were gradually eliminated and completely disappeared at approximately 7 days after onset. On the following days, the patient behavior became reasonable, haloperidol and midazolam were stopped and weaning succeeded.

Glucocorticoid therapy causes psychiatric side effects in many patients. The frequency of occurrence varies from study to study. Although psychiatric side effects occur most commonly in women and middle-aged patients, no clinical features have been identified to predict which patients are at risk. Patients with a family history of depression or alcoholism are at increased risk for affective diseases when given glucocorticoids.

In one prospective but uncontrolled study of 50 patients for example, large doses of glucocorticoids, given for various ophthalmologic indications, induced hypomanic symptoms in approximately 30% and depressive symptoms in about 10% by the end of one week. A second report found that patients treated with prednisone doses of 5-40 mg/day for at least one year had a partial loss of explicit memory, elderly patients were more susceptible to memory impairment with less protracted treatment. The systemic side effect of steroids such as diabetes, glaucoma, osteoporosis, are well known to physicians. The most prominent psychiatric side effects of this drug consist of emotional liability, anxiety, distractibility, interrupted appearance of excitation and aggressiveness, pressured speech, sensory flooding, insomnia, depression, perplexity, agitation, auditory and visual hallucinations, intermittent memory impairment, mutism, disturbance of body image, delusions, apathy and hypomania. The mechanism by which glucocorticoids produce psychiatric symptoms is probably multifactorial, including both direct and indirect effects on the brain.

Our patient who had no previous history of psychiatric problems, developed psychotic symptoms, consisting of interrupted appearance of excitation and aggressiveness 2 days after steroid initiation. When steroid was stopped the psychotic symptoms, were gradually eliminated and completely disappeared approximately 7 days after onset. The time and course of events suggested that steroid was the cause of the psychotic symptoms, which cause weaning to fail in this patient, since no other causes could explain the psychotic reaction. Dose reduction or discontinuation of the systemic corticosteroid is associated with improvement in psychiatric symptoms in many studies. Lithium has been used successfully to both manage and prevent glucocorticoid-associated affective disorders. Other reports suggest valproic acid, neuroleptics such as haloperidol, can also be useful to treat these symptoms. Of particular note, was the fact that tricyclic antidepressants produced an exacerbation or worsening of the clinical state in all patients to whom they were administered.

Thus, steroid psychosis should be considered in the differential
diagnosis, in patients under steroid therapy, who do not wean from mechanical ventilation after 48-72 hours of the resolution of the underlying disease process.

Received 15th February 2005. Accepted for publication in final form 18th May 2005.

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References


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**Paclitaxel in relapsed high risk anthracycline treated breast cancer patients**

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Breast cancer is the most common malignancy afflicting women, and second most common cause of cancer death in women. Considerable progress has been made in the treatment of breast cancer, and mortality is decreasing in developed countries. Despite this, the majority of breast cancer patients will develop metastases and eventually die of the disease. Response to chemotherapy, while frequent, is usually short-lived and the median survival for patients treated with chemotherapy for metastatic disease ranges between 18-24 months.1 The introduction of new agents has improved prognosis in chemotherapy, pretreated patients.2 In 1994, paclitaxel was approved for the treatment of metastatic (or advanced) breast cancer (MBC) following failure with standard anthracycline -based on chemotherapy, or in patients who had relapsed after initial chemotherapy.

In this study, we report our experience with paclitaxel in our patients who relapsed following anthracycline chemotherapy, and who are mostly premenopausal women, as opposed to other studies that included mostly postmenopausal women. The aim of this study is to assess response rate, mean duration of response, median time to progression, and survival rate in MBC patients who received paclitaxel. This retrospective study was performed at Tripoli Medical Center, Tripoli, Libya. Women with a histologically confirmed diagnosis of breast carcinoma and evidence of metastatic disease who were on regular follow up and relapsed after adjuvant treatment, were included in our study. All patients included have an Eastern Cooperative Oncology Group (ECOG) performance status of 0-2. All patients received paclitaxel as single agent in a dose of 175 mg/m² IV infusion over 3 hours every 3 weeks. Premedication with dexamethasone and antihistamine was given prior to the paclitaxel dose. Median of 6 cycles was administered per patients (1-9 cycles). Imaging procedures included chest, abdomen, CT scan and bone isotope scans. These were repeated to assess objective response every 3 treatment cycles. Forty-two patients were included in this study in the period between June 1997-June 2004. The age of the patients ranged from 28-67 years with a median age of 45 years at diagnosis. Premenopausal women represented 61.9% and postmenopausal women represented 38.1%. 58.14% had stage II disease, 25.6% had stage III, 14% had stage IV, and 2.3% were unknown, 86% were node positive, 11.6% were negative and unknown in 2.4%. Histological diagnosis was as follows: invasive duct carcinoma in 81.4%, 11.6% lobular carcinoma, 4.7% medullary carcinoma and inflammatory type in 2.3%. Estrogen and progesterone receptors were studied in 43% of patients where their receptors were positive in 44.4% and 55.6% were negative. Regarding type of surgery, modified radical mastectomy was carried out in 81.4% and lumpectomy and axillary clearance was carried out in 11.6%, and only biopsy was done in 9.3%. In those who had positive lymph nodes, the median number of involved node >4 (5-8 lymph node). Radiotherapy as loco regional treatment as 50 gray over 25 fraction was given to 73%, in those who have more than 3 positive lymph node, locally advanced disease or those who had breast conserving surgery. Tamoxifen tab. 20 mg/day was given to all patients who have estrogen positive or where the receptor status was unknown. Chemotherapy as CAF Cyclophosphamide,
Paclitaxel in relapsed high risk anthracycline treated breast cancer patients

Figure 1 - Overall survival time (months).

adriamycin, and 5-flourouricil were given to 85.7% every 3 weeks from 6-9 cycles, and 14.3% received CMF. Cyclophosphamide, methotrexate, and fluorouracil, as they have contraindication to adriamycin with cardiac function impairment. The median time to relapse was 19.5 months (95% confidence interval [CI], 14.5-27%). The most common sites of relapse were in bone 66%, and visceral metastases in 63.4% (lung 22%, liver 27% and brain 14.6%), pleura in 5%, lymph node in 12.2%, and local recurrence in 39%. Overall response rate after paclitaxel was 22/42 (54%) (95% CI, 43-69%), wherein 13/42 (32%) (95% CI, 18-46%) had complete response, and 9/42 (22%) (95% CI, 9%-35%), had partial response or stable disease. Nineteen out of 42 (46%) (95% CI, 31%-61%) had no response or progressive disease. The response rate of our study was consistent with other studies such as Sato et al study (weekly paclitaxel was administered) with 40.5% (95% CI, 29, 4%-51.7%) and Acuna et al study (both paclitaxel and vinorelbine used as first line chemotherapy) with 60% (95% CI, 46%-74%). The response rate was also significantly better than that reported by Bishop et al with 29% (95% CI, 21%-39%), O'Shaughnessy et al with 25.6% (95% CI, 20%-30.9%), and Albain et al with 22% (95% CI, 17%-27.2%), possibly as these studies include older women (median age was 53 years). The median age of our patients was 45 years, 28/42 (66.7%) of patients relapsed and median time to progression after paclitaxel was 6 months (95% CI, 3.5%-10%), which is similar to the study of Bishop et al, 5.3 months (95% CI, 4.1%-5.6%), O'Shaughnessy et al 3.5 months (95% CI, 2.9%-4.0%), Albain et al 2.9 months (95% CI, 2.6%-3.7%), Sato et al 4.8 months and Acuna et al 7 months. The median duration of response (from detection of response until relapse or death) was 9 months (95% CI, 6.5%-12%), which is similar to O'Shaughnessy et al study 7.2 months (95% CI, 6.8%-8.6%). The median survival after paclitaxel was 11.5 months (95% CI, 9%-15%). Figure 1, which is consistent with Bishop et al study 17.3 months (95% CI, 12.6%-21.4%). Over all median survival (from diagnosis to death) was 34.5 months (95% CI, 28%-41%). In terms of therapy-related toxicities of paclitaxel administration, 12% had grade 3 febrile neutropenia and anemia, and 4.7% developed grade 3 peripheral neuropathy. Bishop et al reported febrile neutropenia and infection or both in 10% of paclitaxel patients and grade 3 peripheral neuropathy in 9% of patients. O'Shaughnessy et al reported grade 4 neutropenia in 6.6% of patients and grade 4 anemia in 0.4% of patients. This study confirm the tolerability of paclitaxel therapy in Libyan women with advanced or metastatic breast cancer. Given the above information, it appears that a dose and schedule of 175 mg/m² by 3 hour infusion every 21 days is both effective and well tolerable, and a reasonable therapeutic choice. In our study, we used paclitaxel as a single agent. This is because there is no good evidence, that combination chemotherapy is more effective, especially as our women were in a stable condition and did not present with life threatening emergencies. Paclitaxel has significant activity against metastatic breast cancer that extends to patients who received prior chemotherapy.

We conclude that single agent paclitaxel offers a very good option in the management of metastatic breast cancer in women who have been heavily treated with anthracycline and that toxicity is acceptable and manageable.

Received 1st March 2005. Accepted for publication in final form 29th May 2005.

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References


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**Effect of antioxidant serum levels of myocardial ischemia markers in patients with ischemic heart disease after treadmill exercise testing**

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Hedef D. El-Yassin, PhD.

Heavy physical exercise increases oxygen consumption, and potentially initiates formation of reactive oxygen species (ROS), which leads to oxidative stress and cellular damage if not properly counteracted. The increase in malondialdehyde (MDA), released after intracoronary platelet aggregation might be a biochemical marker of coronary artery disease (CAD). Meanwhile, oxygen-derived free radicals after temporary coronary occlusion causes myocardial stunning. Exercise leads to an increase in metabolic rate, production of ROS, and compromised antioxidant defense systems. The development of treadmill exercise testing, has allowed early and better evaluation of electrocardiogram (ECG) results, during and after exercise testing for the detection of ischemic changes. We undertook the present study to determine whether the plasma antioxidant status could help in confirming the diagnosis of CADs in borderline cases of treadmill exercise testing results. Also, whether changes in the parameters involved could help in the early detection and possible prevention of CADs especially in people with a family history.

We selected 62 subjects (42 patients and 20 control). We positively diagnosed all patients with CAD. We instructed all not to take any cholesterol lowering drugs and stop taking β-blockers or calcium channel blockers 3 days before doing the exercise test. We applied the Bruce protocol, starting with an initial work rate low enough for the least able subject. Progression continued until we reached the rate suitable for the most vigorous subject. We used stages of 3 minutes duration, permitting 5 different exercise intensity levels, which may be spaced more closely in terms of work rate and thus, may be more precise in measuring maximal functional capacity. We terminated the test on any evidence that further exercise might be harmful to the subject. The exercise endurance in males was approximately 11.5 minutes and in females 7.6 minutes. We only included patients with true positive exercise results in this study. After the return of all parameters to recovery, we asked the patient to hyperventilate for 2 minutes, and we took a 12 lead ECG, which may reproduce the ST-depression in suspicious positive cases.

We took blood samples immediately before, and half an hour after finishing the exercise test. The biochemical tests included: lipid profile total cholesterol (TC), triglycerides (TG), high density lipoproteins (HDL), low density lipoproteins (LDL) and very low density lipoproteins (VLDL), serum very low density lipoproteins cholesterol (VLDL-C), and low density lipoproteins cholesterol (LDL-C) was calculated by Friedewald formula. The formula is only valid at serum triglyceride concentration of less than 400 mg/100 ml.

We measured lipid peroxidation in the form of MDA, a secondary product of lipid peroxidation. Its measurement is based on the colorimetric reaction with thiobarbituric acid. We measured uric acid, and albumin as antioxidants and the last parameter was creatine kinase. The heart rate progressively increases with every stage as maximal aerobic exercise capacity is reached, then it reaches a plateau like the oxygen consumption curve. There was a progressive increase in systolic blood pressure with increasing exercise intensity and very little change in diastolic pressure. At peak exercise it ranged from 162-216 mm Hg, while the diastolic may fall slightly in younger age groups, however, in middle-aged people this may rise not to exceed 10 mm Hg. A pathological fall in systolic blood pressure is highly specific for severe CAD. Failure of systolic blood pressure to rise reflects an inadequate elevation of cardiac output especially in left main stem disease, or equivalent coronary disease, and in 3 vessels disease.

The results of the positive exercise test revealed that the ECG changes of ST-depression will be found mainly in the bipolar leads. Only 2 cases out of 55 positive cases showed changes in the standard leads (3.6%). There was a significant rise of mean albumin level in the post-exercise samples of the control and patient groups (Table 1).

The pre-exercise samples of the patients group showed lower levels of albumin than the control group. The percentage rise in the control group more than the patient group. Albumin is considered a sacrificial antioxidant, and the hypervolemia resulted after exercise account for the increased...
level of albumin post exercise in the control and patient groups. The lower percentage of increase in the patients group is due to overuse as an antioxidant.

There was a significant increase in the mean level of uric acid in post-exercise samples of the control and patients groups (Table 1). The percentage increase in the control group (17.6%) is more than double the increase in the patients group (6.6%). This is due to uric acid is considered an antioxidant, and it scavenges radicals and inhibits lipid peroxidation. This suggests a defect in the antioxidant status of the patient group, and high lipid peroxidation levels.³ A significant increase in the mean level of creatine kinase was found to exist in the post-exercise of control and patient group. The percentage increase in the patients group was 55% while in the control group was only 49%. The rise could be more pronounced after days, or even weeks.⁴

Oxygen free radicals generated in vivo react with polyunsaturated fatty acids and form new radicals (peroxyradicals), which initiates a chain reaction of lipid peroxidation in the presence of oxygen. Therefore, MDA level is an indicator of free radicals generated in the human body. The level of mean MDA showed a significant increase in the post-exercise samples of both control group and the patients group (p<0.05) (Table 1). The rise in the female patients (19%) is more than the male patients (16%), which could be due to wider deprivation of antioxidants in the female group of patients. The pre-exercise values show higher levels in the patients group (ischemic heart disease) than in the control group.

From the previous speculation and the present observation, it might be postulated that the high MDA level in ischemic heart disease cases is attributed to the circulating fractions of membrane lipids peroxidation products in addition to serum lipids. Decreased serum total antioxidant status is associated with increased MDA levels in coronary atherosclerosis.³ A significant drop in the level of LDL in the post-exercise levels of the control group and in the post-exercise levels of the patient group as seen in Table 1. The percentage of decrease is more in the male patient group than in the others (~76%). Low-density lipoprotein is a major vehicle in distributing cholesterol from the liver to other tissues. The significant increase in the HDL level of post exercise level of the patient group is shown in Table 1. Testosterone increases with exercise, thus will decrease HDL formation. Significant correlation is found between HDL and MDA in the pre-exercise male control group. A significant drop in the level of VLDL in the post-exercise control group and in the post-exercise female and male patient groups is shown Table 1. Meanwhile, a significant decrease in the level of TG in the post-exercise samples of the control group and in the post-exercise level of the patient group can also be seen in Table 1. Both resistance training and moderate aerobic exercise increase serum testosterone levels of untrained subjects after 15-20 minutes. Testosterone will increase the formation of HDL, in males and in females, which will increase the metabolism of TG. With the utilization by myocardial cells for energy, this will account for the decrease in level of TG in the post-exercise blood samples. A significant decrease in the level of TC in the post-exercise control group, and in the post-exercise patient group is seen in Table 1.

All the cholesterol circulating in the blood is contained in lipoproteins. Control of body levels depends on the rate of excretion in the bile as cholesterol or bile salts in relation to the rate of

**Table 1** - Lipid profile and some antioxidants measured in both groups (control and patients) pre and post exercise.

<table>
<thead>
<tr>
<th>Levels</th>
<th>Male pre</th>
<th>Male post</th>
<th>Female pre</th>
<th>Female post</th>
<th>Male pre</th>
<th>Male post</th>
<th>Patients pre</th>
<th>Patients post</th>
<th>Female pre</th>
<th>Female post</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin g/dl</td>
<td>4.2</td>
<td>4.43</td>
<td>3.92</td>
<td>4.14</td>
<td>4.022</td>
<td>4.19</td>
<td>3.82</td>
<td>3.95</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uric acid mg/dl</td>
<td>5.66</td>
<td>6.66</td>
<td>4.11</td>
<td>4.79</td>
<td>5.51</td>
<td>5.88</td>
<td>3.89</td>
<td>4.15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cholesterol mg/dl</td>
<td>197.5</td>
<td>156.9</td>
<td>179.9</td>
<td>156.8</td>
<td>207.05</td>
<td>184.41</td>
<td>209.65</td>
<td>186.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triglycerides mg/dl</td>
<td>104.7</td>
<td>85.3</td>
<td>80.4</td>
<td>66</td>
<td>163.95</td>
<td>139.95</td>
<td>138.5</td>
<td>118.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HDL mg/dl</td>
<td>528</td>
<td>581</td>
<td>44.5</td>
<td>49</td>
<td>40.81</td>
<td>43.6</td>
<td>39</td>
<td>42.35</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDL mg/dl</td>
<td>105.76</td>
<td>81.74</td>
<td>119.32</td>
<td>94.6</td>
<td>199</td>
<td>112.9</td>
<td>142.45</td>
<td>120.681</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VLDL mg/dl</td>
<td>21</td>
<td>17</td>
<td>16</td>
<td>13.2</td>
<td>32.8</td>
<td>28</td>
<td>27.7</td>
<td>23.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MDA mmol/l</td>
<td>3.9</td>
<td>4.16</td>
<td>4.66</td>
<td>5.66</td>
<td>3.1</td>
<td>3.38</td>
<td>2.8</td>
<td>3.17</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

HDL - high density lipoproteins, LDL - low density lipoproteins, VLDL - very low density lipoproteins, MDA - malondialdehyde
Antioxidant serum levels in patients with IHD

synthesis in the liver from Acetyl-CoAm, which is regulated by feed back inhibition on reductase hydroxyl -methyl - glutary -CoA (HMGCoA) reductase by excess cholesterol. A high cholesterol diet causes decreased synthesis, and the excess is excreted in bile. The excreted bile salts are very efficiently reabsorbed more than dietary cholesterol.

Significant correlations have been found among the studied parameters in both groups studied, for example, between uric acid and albumin in the post-exercise male control group and in the pre and post-exercise control female group. There was a significant correlation between uric acid and albumin in the pre-exercised male patient group, and post-exercise female patients group. As well as between LDL and MDA in the post-exercise male control group and in the pre-exercise female patients’ and VLDL and MDA in the post-exercise male control group. A significant correlation was found to exist between TG and MDA in the post-exercise female control group.

In conclusion, treadmill exercise testing is a very valuable aid in predicting and following cases of ischemic heart disease. The state of lipid peroxidation and antioxidants level could give a clue to the diagnosis of cases at risk, especially when combined with treadmill exercise testing, and may influence the prognosis and prevention of CAD.

Received 7th February 2005. Accepted for publication in final form 31st May 2005.

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References


Proliferating cell nuclear antigen index and nm23 expression in osteosarcoma in relation to disease-free survival and tumor grade

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Osteosarcoma cases that have similar histological structure and same grade may have variable responses to the identical chemotherapy regimens, and show different prognosis. The current most common indicator of prognosis of an osteosarcoma patient is his response to neo-adjuvant chemotherapy. This is determined by measuring the amount of necrosis within the tumor mass following neo-adjuvant chemotherapy, which is a very difficult task.1 Certain prognostic markers are needed for osteosarcoma patients. Both nm23 and proliferating cell nuclear antigen (PCNA) are the biologic markers those have been documented to have relationships with various tumors.2-5 The nm23 is a tumor suppressor gene that is identified to be involved in tumor metastasis. There are many reports on nm23 expression in tumors; however, literary information is inadequate concerning nm23 expression and osteosarcoma together.1 The PCNA, is a proliferation marker and can be detected by immunohistochemical methods in cells. It has been shown to relate with DNA polymerase delta sub-group and proliferation cannot occur in eucaryotic cells without it.2,4 The purpose of this study was to investigate the PCNA and nm23 expression in osteosarcoma cells and their correlation with disease-free life period and tumor grade in search of new prognostic and predictive factors.

Formalin fixed and paraffin embedded tumor tissues of 51 patients were used in this study. Twenty-six of the cases (51%) were women, while 25 (49%) were men aged between 9-26 (median 16) years. Primary localizations were distal femur in 15, proximal tibia in 20, humerus in 11, proximal femur in 4, and radius in one patient. All patients’ records were examined to determine the disease free survival. Specimens were confirmed as osteosarcoma and graded according to anaplasia, pleomorphism and nuclear hyperchromasia. Intravascular invasion for each specimen was also recorded (Figure 1). All patients were treated by neo-adjuvant chemotherapy, radical surgery, and adjuvant chemotherapy. Surgical treatments were amputations for 36, Enneking procedures for 11, resection arthroplasties for 3, and Van Nes procedure for one patient. The follow up period, free from metastasis or recurrence was defined for each patient as disease-free life.
period. Six mm thick sections of each case were made on silicon coated slides from the original paraffin blocks. Immunohistochemical staining for nm23 was evaluated on both neoplastic and non-neoplastic tissues. For nm23 expression, the sections were incubated with polyclonal-sensitivity and specificity tested, primary anti-nm23 antibody, biotinylated anti-rabbit antiserum (Histostain-SP kit, Zymed lab, Inc., San Francisco, California, USA), and avidin dehydrogenase biotinylated horseradish peroxidase complex (Vecstain, Vector, Burlingame, California, USA). The polyclonal anti-nm23 antibody was cultivated against a synthetic oligopeptide recognizing the internal hydrophilic portion of the protein, which lies between bases corresponding to 354 and 404 of human nm23 cDNA (peptide 11). This antibody recognizes the products both from nm23-H1 and nm23-H2.6 The nm23 immunoreactivity of the tumor tissue was graded as low and high according to the number of the stained cells and the intensity of the reaction by 2 independent observers. For PCNA determination, the sections were incubated with monoclonal PC10 epitaph carrying anti-PCNA antibody in IgG structure (DAKO, PC10, Glostrup, DENMARK), and a modification of the immunoglobulin enzyme bridge technique was applied using biotinylated horse anti-mouse antiserum (Vecstain, Vector, Burlingame, California, USA.) avidin dehydrogenase biotinylated horseradish peroxidase complex (Vecstain, Vector, Burlingame, California, USA). The PCNA index as the ratio of reactive to non-reactive tumor cells in a 40 × High Power Field (HPF) was measured for each slide in 10 different HPFs and the mean was accepted as the PCNA index of the specimen. Positive controls were used for each immunohistochemical study session of nm23 and PCNA. The Pearson correlation tests were used for analyzing the data. P-levels less than 0.05 were considered to be significant.

No recurrence was observed in any patients, but distant metastasis was present in 31 after a mean follow up period of 53 months. Twenty patients were disease free at the latest evaluation. Intravascular invasion was determined on 10 specimens out of 51. Thirty cases (58.8%) demonstrated high nm23 expression. There was no significant relationship between nm23 over-expression, and disease-free life period. Weak negative correlation was detected between tumor grade and high expression of nm23 (p=0.050, r=-0.27). Intravascular invasion rate, age, and gender were independent from nm23 over-expression. The PCNA index ranged between 10-90%. The median value was 40%. Those with less than 40% PCNA index (35 cases, Group 1) and those with PCNA index 40% and more (16 cases, 33.3%, Group 2). Disease free life period was significantly longer in Group 2 than Group 1 (p=0.008, r=0.366). No correlation was detected between PCNA index and tumor grade, age, gender, and intravascular invasion (Table 1).

Since the advent of modern chemotherapy, eventually leading to limb salvage surgery, the quality of life and outcome measures of osteosarcoma patients have demonstrated significant improvement. Unfortunately, there are still no certain prognostic markers for osteosarcoma patients other than histological response to neo-adjuvant chemotherapy. This is especially important, since these patients are mostly young individuals with a long life expectancy. New methods are needed to sub classify osteosarcomas relating to their prognosis and drug sensitivity. The purposes of our study were to investigate the role of PCNA index and nm23 reactivity in osteosarcoma and try to find clues for new prognostic tools. The reasons for choosing these 2 biological markers were their previously documented relationship to prognosis, as well as their roles in proliferation and metastasis of tumor cells in some tumors. In this study, although there was no correlation between nm23 positivity and disease free life period, nm23 reactivity seems to be low in low grade tumors. Disease free life survival found to be significantly longer in patients with higher PCNA positivity.

Received 7th February 2005. Accepted for publication in final form 26th May 2005.
Table 1 - Relationship between nm23, PCNA reactivity and clinicopathological features osteosarcomas.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>nm23</th>
<th>PCNA</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Low (%)</td>
<td>High (%)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>12 (23.5)</td>
<td>14 (27.4)</td>
</tr>
<tr>
<td>Male</td>
<td>9 (17.6)</td>
<td>16 (31.3)</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>5 (9.8)</td>
<td>-</td>
</tr>
<tr>
<td>High</td>
<td>21 (41.1)</td>
<td>25 (49)</td>
</tr>
<tr>
<td>DFS (months)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IVI (+)</td>
<td>44.7</td>
<td>36.6</td>
</tr>
<tr>
<td>(-)</td>
<td>15 (29.4)</td>
<td>26 (50.9)</td>
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<td></td>
<td>6 (11.7)</td>
<td>4 (7.8)</td>
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</tbody>
</table>

DFS - disease free survival, IVI - intravascular invasion, PCNA - proliferating cell nuclear antigen, ns - not significant

References


Medicolegal deaths in children and adolescents

Yasar Tirasci, MD, Suleyman Goren, MD, Fuat Gurkan, MD, Ibrahim Uzun, MD

Accidents are the leading causes of death in all industrialized countries, and in a growing number of developing countries. Trauma is a major cause of death in children, especially those between 5-14 years. Fatal injuries are causing increasing concern from the age of one year up to adulthood. An analysis of the causes showed that most were preventable.1,2 The situation in our country, and in our region, is not adequately known. In the present study, we describe the epidemiology of child and adolescent (0-18 years) mortality in Diyarbakir, Turkey over a recent 4-year period, and discuss both the leading causes of injury and available prevention measures.

We retrospectively reviewed all forensic cases referred to the Diyarbakir City forensic section, during the 4-year period 2000-2003. Of these, we analyzed all children and adolescent deaths and included victims younger than 19 years of age in our study. We considered the case file information from the autopsy reports and hospital reports for age, gender, origin, cause and manner of death, season, and the state of hospitalization before death.
Between 1 January 2000 and 31 December 2003, 690 (29.4%) pediatric and adolescent medicolegal deaths were investigated among 2,343 medicolegal deaths. There were 437 (63.3%) males, and 253 (36.7%) females aged from 4 days to 18 years, with a mean age of the 7.83 ± 3.8 years. The majority was in the groups aged 0-5 years (36.7%). There were 567 (82.2%) victims of accidental death, 84 (12.2%) victims of suicide, and 39 (5.6%) victims of homicides. Accidents were most frequently seen as a cause of death in the 0-5 years (44.3%), but homicides (66.7%), and suicides (72.6%) in the 16-18 years age group. Most accidental (66.5%) and homicidal (74.4%) deaths were among males, and suicides among females (63.1%). The most frequently seen cause of death was traffic accidents (32.7%), followed by fall from height (23.7%), and firearm (9.1%) (Table 1). Only deaths due to hanging displayed a female predominance (69.4%). There was an increase in children and adolescent fatalities in the summer season (34.2%). Of these, 325 (47.1%) were dead on arrival at hospital, 53 (7.7%) died during intervention within 24 hours, and 312 (45.2%) died during treatment after 24 hours.

Deaths in the pediatric age groups are a cause of concern as children are the most innocent and harmless of the community. Most deaths in this age group are preventable, and mostly due to trauma. These rates are similar to the previously reported findings in Turkey. In different countries, there was also a male predominance, reported between 56-70%. Boys have a tendency to play outside and participate in activities more than girls that cause greater risk for injuries.

In this study, deaths were most commonly seen in the 0-5 years age group with 253 (36.6%) cases; and secondly in the 6-10 years age group with 184 (26.6%) cases. Most of the fatalities have been reported in the 0-5 years age group, as in ours, in the literature. In some others, the most commonly reported age was over 11 years. In our study, the most common deaths were accidental in 567 (82.2%) cases, suicide in 84 (12.2%), and homicide in 39 (5.6%). Suicide and homicide are major public health concerns, as significant causes of preventable deaths. However, effective strategies for the prevention of these deaths are difficult. In the study of Rimsza et al., there were 70.8% accidents, 11.4% suicides, and 17.8% homicides. In most others, the results were similar. In our series, deaths due to accidents (66.5%) and homicide (74.4%) were more prevalent among males, while suicides were more frequent among females (63.1%). In another study on suicides in children and adolescents in our region, the female rate (71%) was also reported to be much higher than males. When considering all ages including the children and adults, the situation was similar in our region for suicides with a female rate of 58%. In most other studies, there was a male predominance of marginally higher rates.

In the present study, the most common causes of fatalities were motor vehicle accidents (MVA) in 225 (32.7%) cases, fall from height in 163 (23.7%), and firearm in 63 (9.1%) cases. In our country, traffic accidents were also found to be the most frequent cause of death in previously reported studies. In other studies from different countries, the most common cause of death was reported as MVA in 36-64.2% of the fatalities. In the United Arab Emirates, Bener et al. reported MVA as the most common cause, followed by drowning and burning. Most falls were from balconies or rooftops due to the tendency of people to sit and sleep on these places during the hotter months of the year. In the current study, deaths had occurred most commonly in the summer in 236 cases (34.2%).

In conclusion, the main methods of reducing trauma-related deaths are either improving treatment of the injured patients or preventing the injuries. Prevention of MVA and fall from height could help in reducing mortality in children in our region, given that more than half (MVA 32.7% and fall from height 23.7%) of the deaths were related to these accidents.

Received 22nd February 2005. Accepted for publication in final form 29th May 2005.

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### Table 1 - Type of mechanism leading to deaths among children and adolescents.

<table>
<thead>
<tr>
<th>Type</th>
<th>Male</th>
<th>Female</th>
<th>Total n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Traffic</td>
<td>161</td>
<td>64</td>
<td>225 (32.7)</td>
</tr>
<tr>
<td>Firearm</td>
<td>42</td>
<td>21</td>
<td>63 (9.1)</td>
</tr>
<tr>
<td>Stabbing</td>
<td>8</td>
<td>2</td>
<td>10 (1.4)</td>
</tr>
<tr>
<td>Hanging</td>
<td>11</td>
<td>25</td>
<td>36 (5.2)</td>
</tr>
<tr>
<td>Fall from height</td>
<td>103</td>
<td>60</td>
<td>163 (23.7)</td>
</tr>
<tr>
<td>Drowning</td>
<td>26</td>
<td>15</td>
<td>41 (5.9)</td>
</tr>
<tr>
<td>Electrocution</td>
<td>16</td>
<td>17</td>
<td>33 (4.8)</td>
</tr>
<tr>
<td>Burning</td>
<td>23</td>
<td>23</td>
<td>46 (6.7)</td>
</tr>
<tr>
<td>Poisoning</td>
<td>21</td>
<td>19</td>
<td>40 (5.8)</td>
</tr>
<tr>
<td>Stroke</td>
<td>6</td>
<td>1</td>
<td>7 (1)</td>
</tr>
<tr>
<td>Suffocation</td>
<td>4</td>
<td>2</td>
<td>6 (0.9)</td>
</tr>
<tr>
<td>Accident at work</td>
<td>4</td>
<td>-</td>
<td>4 (0.5)</td>
</tr>
<tr>
<td>Crushing</td>
<td>7</td>
<td>4</td>
<td>11 (1.6)</td>
</tr>
<tr>
<td>Babies</td>
<td>1</td>
<td>-</td>
<td>1 (0.1)</td>
</tr>
<tr>
<td>Animal kicking</td>
<td>4</td>
<td>-</td>
<td>4 (0.6)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>437</td>
<td>253</td>
<td>690 (100)</td>
</tr>
</tbody>
</table>
Evaluation of antisperm antibodies in infertile men associated with varicocele. Pre and post varicocelectomy

Abdolrasool Mehrsai, MD, Mojaba R. Valojerdi, Msc, PhD, Homan Djaladat, MD, Gholamreza Poormand, MD

In this prospective study, 27 varicocele associated infertile men undergoing microsurgical inguinal varicocelectomy were included. Varicocele was determined by physical examination and Doppler ultrasonography and was categorized by a single examiner with the patient standing as follows: grade 1, palpating an impulse in the scrotum during a Valsalva maneuver; grade 2, tortuous veins palpated without Valsalva maneuver; and grade 3, visible through skin. All other probable causes of infertility, like female factor, were excluded through evaluation including history, physical examination, and laboratory tests including complete blood count, urea, electrolyte, and urine analysis. Hormonal studies (serum follicle-stimulating, luteinizing hormone, and testosterone) were carried out if there was severe oligospermia (density <10 x 10^6/ml) or if there was any indication with regards to history and examination. Semen analysis and antisperm antibodies were measured by the spermMar test performed preoperatively and postoperatively at 6 months. Any risk factors, like history of trauma, torsion, cryptorchidism, vasectomy or vasectomy reversal, genitourinary infection and previous inguinal surgery were also considered. Semen was collected by masturbation into sterile, wide mouthed containers approximately 72 hours after the last abstinence. By the time of liquefaction, the sample was divided for semen analysis and sperm antibodies assay. Semen analysis was performed routinely and using x40 of microscope, Neubauer hemacytometer and papanicolaou staining method. The different parameters of sperm such as motility, density, and morphology were examined. Seminal and sperm antibodies [immunoglobulin G (IgG), immunoglobulin A (IgA)] were measured by 2 methods of direct and indirect spermMar test (Ferti Pro NV, Belgium).

In the direct spermMar test, one drop of semen was placed on a microscope slide adjacent to a drop of latex reagent and a drop of antisperm either IgG or IgA. The 3 drops were mixed together with a cover slip and was then used to cover the mixture. After 2-3 minutes, the slide was examined under a microscope and the percentage of motile sperm bound to the latex beads was scored. According to the manufacturer, a score of 40% or more indicates a high probability of immunologic infertility, and a score of 1-39% indicates that immunologic infertility is suspected.

In the indirect spermMar test, blood and seminal plasma were first inactivated by heating at 56°C for 30 minutes and then diluted with 1/4 Ham’s F-10 medium containing 10% Albuminar-5 (containing 5% human serum albumin, Blood Research Center, Tehran, Iran). Fresh sperm from a fertile donor washed twice and allowed to swim up in Ham’s F-10 medium. Afterwards the sperm concentration was adjusted to 20 x 10^6 sperm/ml with Ham’s F-10. While 100 µl of the suspension of motile donor sperm was incubated with 100 µl of inactivated seminal plasma or serum, which had been diluted in 1/4 Ham’s F-10 medium for 1 hour at 37°C. The sperm were then washed 3 times, re-suspended in 50 µl of Ham’s F-10 medium, and then tested for membrane bound antibodies similar to that of the direct spermMar test. Data were collected and analyzed using Wilcoxon Signed Ranks and ANOVA test.

The mean age of the patients was 28.7 years (23-42 years), and the mean of the infertility duration was 4.29 years (1-11 years). All had left varicocele (grade one: 2 patients, grade 2: 17 patients, grade 3: 8 patients) and 7 had right varicocele who underwent right varicocelectomy as well. Hormonal studies were performed in 6 patients, all of them had severe oligospermia and negative antisperm antibody. It was normal in 4

References

patients, but increased follicle stimulating hormone (FSH) was considered in 2. All patients were followed up for 6 months and none of them had recurrent varicocele on physical or Doppler examination.

After varicocelectomy, the sperm density improved in 62% of varicocele patients. The normal morphology were also improved in 66% and sperm motility were 37% of cases. The mean of sperm density was significantly increased (22.6 ± 1.9 x 10⁶ for preoperative and 32.2 ± 2.8 x 10⁶ for postoperative, \( p<0.01 \)). The mean of abnormal morphology of sperm was significantly improved (74 ± 18% for preoperative and 53.07 ± 12% for postoperative, \( p<0.001 \)). But the improvement of the mean of sperm motility was not significant (30.8 ± 16.8% for preoperative and 34.8 ± 19% for postoperative).

Preoperatively, none of the patients were highly probable and positive for antisperm antibodies (ASA) (>40%). However, 7 (26%) patients had low probability and positive for ASA (10-40%). They were as follows: 3 (11%) for direct IgA, 2 (7%) for serum indirect IgG, 1 (3%) for direct IgG and 1 (3%) for direct IgA and seminal indirect IgA. During follow-up of the 7 patients, they were grouped according to ASA changes. Antisperm antibodies titer were reduced in 5 patients (group A), increased in 1 patient (group B) and reduced in a particular antibody type but increased in another in 1 patient (group C) within 6 months after varicocelectomy. In group A, sperm count, motility and normal forms improved postoperatively \( (p<0.05) \). In group B, motility reduced while in group C motility and normal forms was reduced postoperatively \( (p<0.05) \). Out of these, 16 (81%) showed an increase in at least one of ASA types to some degrees postoperatively. This increase was significant for serum indirect IgG antibody: 13 out of 16 patients \( (81\%) \), \( (p<0.01) \). In the latter cases, comparing with preoperation, sperm density \( (24 ± 1.86 \text{ for preoperative and } 30 ± 3.16 \text{ for postoperative}) \), sperm motility \( (28.2 ± 2.6\% \text{ for preoperative and } 37.3 ± 2.1\% \text{ for postoperative}) \), and high abnormal form of sperm \( (68 ± 12\% \text{ for preoperative and } 53 ± 5\% \text{ for postoperative}) \), although none of them were significant.

Considering the risk factors, antibodies had low probability and positive in 2 out of 3 patients with history of significant scrotal trauma and one out of 2 patients with history of varicocelectomy. Follow-up of these patients showed that the antibody titers were reduced postoperatively.

Bouchot et al.\(^1\) showed that sperm motility and normal head spermatozoa density were significantly increased after varicocelectomy. In our study, sperm density improved in 62% of cases. Mean normal morphology improved in 66% and sperm motility improved in 37%. This is in contradiction with other reports, which is the most common improvement in semen parameters occurring in sperm motility after varicocelectomy \( (70\%) \).\(^2\) The debate regarding the efficacy of varicocele ligation for improvement of semen parameters is ongoing. Ozen et al.\(^3\) evaluated 65 infertile varicocele patients. Antisperm antibody was detected with immunofluorescence method in 24.6% of patients. It had no relationship to varicocele grade. Golomb et al.\(^4\) assessed the antisperm antibody with ELISA technique in 32 varicocele infertile patients. It was positive in 90% of patients, in contrast to 41% of control group.

In our study, we found an incidence of sperm-bound immunoglobulin in 26% of infertile varicocele patients and none of them were highly probability and positive with ASA. We did use SpermMar test to evaluate antisperm antibody. SpermMar test has some advantages over immunonud test (IBT).\(^5\) It can be carried out over less motile, unwashed sperm and is more sensitive. Unlike polyacrylamide particles in IBT, latex

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Pre and postoperative sperm density, motility and abnormal forms in 7 varicocele infertile patients with low positive antisperm antibody.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group of patients</strong></td>
<td><strong>Preoperative (mean ± SD)</strong></td>
</tr>
<tr>
<td></td>
<td>Sperm density ( (\times 10^6) )</td>
</tr>
<tr>
<td>Group A (n=5)</td>
<td>14 ± 8 x 10⁶</td>
</tr>
<tr>
<td>Group B (n=1)</td>
<td>35 x 10⁶</td>
</tr>
<tr>
<td>Group C (n=1)</td>
<td>40 x 10⁶</td>
</tr>
</tbody>
</table>

Result of statistical analysis was down only in group A (Wilcoxon Signed Ranks and ANOVA test), \(^*p<0.05\)
particles are the same size in SpermMar kits. SpermMar tests results are reproducible and can be performed by any light microscope even in the office.

Knudson et al. reported antisperm antibody levels in 32 varicocele infertile patients, using immunobead test. In his study, 28% had positive immunobead test among whom IgG was found bound to the surface of the sperm in 100% and 86% IgA. Of the 7 patients who were initially antibody positive, 6 (86%) patients remained positive after varicocele ligation. One out of 15 patients who were antibody negative preoperatively became antibody positive postoperatively. These investigators were not able to show any significant difference between pre and post varicocelectomy ASA level.

In our study, ASA was weakly positive in 7 (26%) patients preoperatively and in follow-up it was reduced in 5, increased in one and in the last patient it decreased in that particular antibody type, but increased in another sub-type. These data and other findings3,4,5 suggest that the incidence of ASA in varicocele infertile patients is still ambiguous, and if it occurs in some cases, varicocelectomy may not always effective. According to the literature, some people believe that men with varicoceles who also have sperm-bound immunoglobulins, have more extensive damage to the seminiferous epithelia than men with varicoceles who lack this finding.6 In our study, antisperm antibody does not have any harmful effect on semen parameters preoperatively. In this regard, we must consider that none of our patients had high probable antisperm antibody that raises the question of whether the low levels of sperm-bound antibody found in our study, will have significant impact on fertility. Furthermore, after varicocele ligation our patients exhibited the same improvement rate in semen parameters regardless of the preoperative antibody status. Assuming pre and postoperative ASA levels, only increase in serum indirect IgG was significant and revealed no significant effect on sperm parameters. It should be mentioned here that serum antibodies such as IgG are nonspecific and can be falsely positive due to many circumstances like fever, medical or systemic disease, surgery, and major stress. However, none of these states occurred in our patients during follow-up.

Heidenreich et al. showed that only vasectomy and previous history of epididymitis could be recognized as risk factors for ASA. In our study, we could find 5 patients with risk factors (3 patients had scrotal trauma wherein 2 of them were ASA positive, among 2 patients who previously had varicocelectomy, one had positive ASA). The ASA level was reduced in all positive cases after varicocelectomy. Like Ozen et al. suggested, we did not find any correlation between varicocele grade and pre and postoperative ASA levels. Seven patients underwent bilateral varicocelectomies. The right varicocele added to the left one did not change the semen parameters and ASA titers significantly.

In conclusion, the relationship among varicocele, antisperm antibody and infertility has always been ambiguous. Varicocelectomy may reduce ASA level. This reduction has good quality effect on semen parameters. Also, it may increase ASA level in some patients. This positive conversion has no adverse effect on semen parameters.

References

The therapeutic value of elective laparoscopic appendectomy in the management of chronic abdominal pain

Seyed V. Hosseini, MD, Marzieh Haghbeen, MD, Hooman Yarmohammadi, MD, Kamran B. Lankarani, MD, Mohammad J. Kaviani, MD, Hamid R. Sharifzad, MD.

Chronic recurrent abdominal pain is among the most devastating symptoms for both patient and physician. Despite the suffering from a real annoying pain, physicians usually cannot find any other abnormality, and the patients express that everything is all right. The introduction of new diagnostic methods and better knowledge of functional abdominal pain and more attention to the abdominal wall as the possible source of pain, has decreased the number of these patients in recent years, but there are still patients who suffer from chronic abdominal pain for which no apparent cause could be found.1 Laparoscopy has been used as both the diagnostic and therapeutic measures for these patients with variable results.1

We designed this prospective study to find the role of this procedure in the evaluation and possible treatment of these patients in our center.

In a prospective study from May 2002 to July 2004, all patients with chronic abdominal pain (more than 6 months) and without any identifiable cause in their previous evaluations underwent laparoscopic evaluation. The Shiraz University of Medical Sciences Ethics Committee approved the study, and each participants gave an informed written consent after clear explanation of the risks and possible benefits of laparoscopic evaluation of the abdominal cavity. Aside from careful history and physical examination by a gastroenterologist, we evaluated all patients by upper endoscopy, colonoscopy and abdominal and pelvic sonography, which were normal or inconclusive. Routine blood tests including complete blood count, erythrocyte sedimentation rate, C-reactive protein, liver function test, and amylase had to be normal during the episodes of abdominal pain. We excluded from the study patients with known underlying disease, including asthma with chronic steroid therapy, chronic renal failure, coronary artery disease, congestive heart failure, diabetes mellitus, cirrhosis, any neuropsychiatric disorder, those with prior surgery, and pregnant or lactating women. We also excluded patients who fulfilled the Rome II criteria for irritable bowel syndrome and for functional dyspepsia. All patients underwent general anesthesia with orotracheal intubation. We carried out a laparoscopic evaluation of the abdominal cavity with insertion of 3 ports into the abdominal cavity (2 10 mm ports in the supra-umbilical and suprapubic areas and a 5 mm port in the McBurney point). We noted the laparoscopic findings, and performed standard appendectomy for all patients. We sent the appendix for histopathological evaluation. We used the autopsy findings of 80 age and gender matched car accident victims during the same period as the control group and sent the appendixes for histopathological evaluation. The pathologist was blind to the study. We analyzed and computed all the data by SPSS (Chicago, IL) software, version 10, and MS EXCEL (Microsoft, Redmond, WA) software. We used the Fisher exact test for statistical analysis. We expressed values as mean ± SD. We considered a p-value of less than 0.05 as significant.

Among the 80 patients, there were 48 males and 32 females (mean age 38 ± 2 years; range 16-67 years). All patients had suffered from recurrent abdominal pain and were referred to our center for further diagnostic and therapeutic evaluation. The diagnostic tool employed was diagnostic laparoscopy in all patients. There were 80 patients in the control group, who were selected with the same criteria and underwent laparoscopic appendectomy. Table 1 shows the laparoscopic and histopathological findings in 80 patients with recurrent abdominal pain and 80 control group patients.

Table 1 - Laparoscopic and pathologic findings in 80 patients with recurrent abdominal pain and 80 control group patients.

<table>
<thead>
<tr>
<th>Diagnostic tool</th>
<th>Findings</th>
<th>Chronic pain</th>
<th>Control group</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laparoscopic findings</td>
<td>Appendix fibrosis</td>
<td>12</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Appendicular phlegmon</td>
<td>4</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Inflamed appendix</td>
<td>36</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Ovarian cyst</td>
<td>28</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Pathological findings</td>
<td>Moderate inflammation with evidence of chronicity</td>
<td>32</td>
<td>4</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td></td>
<td>Fibrosis</td>
<td>20</td>
<td>4</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td></td>
<td>Follicular hyperplasia</td>
<td>12</td>
<td>4</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td></td>
<td>Non-specific changes</td>
<td>16</td>
<td>12</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS - not significant
abdominal pain for a median duration of 11 months (range 6-36 months). Other symptoms included nausea in 23%, anorexia in 19% and constipation in 15% of patients. Table 1 shows the laparoscopic and pathologic findings. All patients had uncomplicated hospital courses, with the mean hospital stay of 1.5 ± 0.5 days (range of 1-4 days). The mean follow up time was 5.5 ± 0.6 months. All patients were symptom free, except one lady who suffered from one episode of abdominal pain after 3 months postoperatively, which was secondary to ruptured ovarian cyst. Table 1 also shows the autopsy findings in the control group. Abnormal findings were significantly more prevalent in the case group (p<0.05).

We consider recurrent abdominal pain to be a significant problem. Chronic appendicitis and diverticula of appendix are unusual causes of abdominal pain, which may be a significant diagnostic problem. Clinical presentation mostly determines the cause of pain, but in a significant number of patients, the cause remains unclear. Laparoscopic evaluation is a safe and beneficial method for decision making, and it may be a good tool for evaluation of appendicular masses before planning a surgical program. In a study carried out by Agarwala and Liu, they evaluated 1,317 women with chronic recurrent abdominal and pelvic pain with laparoscopy, and reported the abnormal findings of appendix to be endometriosis, acute appendicitis, carcinoid tumors, large mucocele, Enterobius vermicularis infection, benign neumroma, mucous cystadenoma, obliterate of appendicular lumen, and fibrous adhesions. Thirty percent of the cases had normal appendix, in whom pain regressed post appendectomy, and therefore, the appendix was the key organ for abdominal pain. Our study also showed that the most common finding in patients who underwent laparoscopic evaluation due to chronic abdominal pain was related to the appendix. Laparoscopy has been reported to be a safe and effective utility in chronic abdominal pain by several authors. Laparoscopy alone can also reveal the pathologic condition of patients with pain of unknown origin. In our study, all patients benefited from laparoscopic evaluation and appendectomy.

In conclusion, laparoscopic evaluation may be a safe method for evaluation of patients experiencing chronic or unknown abdominal pain and we recommend its use in the evaluation and treatment of chronic abdominal pain.

References


Evaluation of wood’s light and direct smear for diagnosis of pityriasis versicolor and erythrasma

Masood Maleki, MD, AbdolMajid Fata, PhD.

Erythrasma and pityriasis versicolor (PV) are 2 infectious skin diseases of young adults. However, PV can be seen in elderly people and occasionally in children. There are various diagnostic methods including direct smear, scotch tape test and Wood’s light. Although, in most studies and texts there is emphasis on the high diagnostic value of Wood’s light but, some studies reject the diagnostic value of Wood’s light.

In order to evaluate routine laboratory methods of direct smear and Wood’s light; the study was undertaken over a 16 months period (September 2003-December 2004), at the Departments of Mycology and Dermatology, Emam Reza Hospital, Mashhad, Iran. The study population was the patients and volunteer students from Mashhad University of Medical Sciences who referred to Dermatology Clinic, Emam Reza Hospital. Among 215 individuals, 88 patients had skin lesions suspected for PV and 127 for erythrasma. After clinical diagnosis for PV and erythrasma a questionnaire was completed for each patient, they were asked to refer to the Mycology laboratory at Emam Reza Hospital. All of the patients were tested by Wood’s light in a dark room. Fresh smear by potassium hydroxide (10%) was prepared for diagnosis of PV and direct stained smear by methylene blue for erythrasma. The common sites of lesions in patients suffering from PV were trunk and neck. Among 88 individuals suspected to PV, 55 patients (62.5%) showed positive golden yellow fluorescence under Wood’s light, while 59 patients (67%) had positive direct smear. Among 127
patients with suspected lesions for erythrasma, groin was the most common site. Positive orange–red fluorescence was seen in 38 cases (29.9%), while direct stained smear of 40 cases (31.57%) showed Corynebacterium minutissimum (Table 1). Regarding statistical chi-square test, no significant difference was seen between Wood’s light and other methods in the diagnosis of PV and erythrasma (p = 0.001).

Pityriasis versicolor is a superficial mycotic disease, which is common in young people. The well–recognized sites of involvement in PV are the upper trunk, neck, and upper arms, however flexural lesions are not uncommon. Erythrasma is another skin disease with intertriginous lesions. According to our experiments, scrotum was the second highly infected location, while in dermatology text books, scrotal involvement is not common. Although in several studies the value of Wood’s light in the diagnosis of several diseases including PV, erythrasma and pigmented changes of the skin is approved, but in some studies, the diagnostic value of this method is in doubt. In present study the diagnostic value of Wood’s light is highly approved. According to Table 1, 55 individuals (62.5%) showed positive fluorescence under Wood’s light, while 59 patients (67%) had positive direct smear for Malassezia. However, the difference between the 2 tests is not statistically significant. The following factors may affect the result of wood’s light test: 1) the quality of ultraviolet (UV) instrument 2) the amount of room darkness during examination 3) the color of patient’s clothes 4) use of topical drug, lotion, spray, shampoo, and so forth prior to the test. 5) the time of last bathing prior to examination. Considering the above statements, the examiner should have a good knowledge and experience of using wood’s light. False positive and false negative fluorescence may change the result of examination.

In conclusion, the Wood’s light test is a valuable method for diagnosis of several superficial mycotic diseases. Physicians and especially dermatologists can use it as a simple and easy diagnostic technique for screening of the patients in their private clinics. In order to avoid false positive results, the physician should have good knowledge of UV positive materials and UV light wavelength. The physician should always think about the possibility of mixed infection.

Acknowledgment. The authors wish to thank Dr M. Azim Nejad for his partial assistance in management of patients, Mr. Emad Zadeh for his cooperation in statistical calculations and Mr. M. Akbari and Mr. M. Ganjbakhsh for their assistance in laboratory examinations and Miss S. Bahmani, for drawing the table.

Table 1 - The laboratory results of 88 suspected patients to pityriasis versicolor and 127 patients to erythrasma, Emam Reza Hospital, Mashhad, Iran, 2003-2004.

<table>
<thead>
<tr>
<th>Methods</th>
<th>Pityriasis versicolor n (%)</th>
<th>Erythrasma n (%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wood’s light</td>
<td>55 (62.5)</td>
<td>38 (29.9)</td>
<td>0.001</td>
</tr>
<tr>
<td>Direct smear</td>
<td>59 (67)</td>
<td>40 (31.5)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Students’ perceptions of their undergraduate medical education

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Around the world, there is a continuing debate on medical education. In the 1980s, it was stated that “the aim of medical education is to produce doctors who will promote the health of all people...” The Turkish Medical Association concurs that this aim is not being met in Turkey despite some changes in our medical education. After the 6-year basic medical education, Turkish medical graduates deal with patients in primary care settings without any postgraduate education. The total population of this group is around 30,000 and...
they are called "practitioners." If a Turkish medical student prefers to be a specialist, the student has to succeed in a national examination after graduation. Currently, other than "practitioners", there are approximately 1,300 family medicine specialists, and 700 family medicine residents in Turkey, who are working in primary care settings as well as secondary and tertiary care hospitals. Other specialty groups tend to work in secondary or tertiary care hospitals or in the private sector. As practical sessions in primary care settings take only a little part in medical education, graduates tend to achieve hospital specialty. Students who are exposed to the community can alter their career choices; however, even with increased contact, the majority of the students want to enter hospital-based specialties. Community-based teaching can make some differences, and curriculum style has an influence on the attitudes of medical students. For an effective curriculum for our future doctors, their priorities, needs, and abilities have to be determined. Due to these possibilities, our main aim was to understand the opinions of our students on medical education with regard to primary care, family medicine, and specialty preferences. Our secondary aims were to determine if the family medicine rotation or lectures had any effect on their opinions and to find out if there was a difference between military medical students with the others, since military medical school graduates are employed by the Turkish Army immediately after their graduation.

Four schools, located in 4 different regions of Turkey took part in this study. Edirne Trakya University (ETU) uses classical teaching methods, both Isparta Suleyman Demirel University (ISDU), and Trabzon Karadeniz Technical University (TKTU) use integrated methods, and Gulhane Military Medical Academy (GMMA), as it has different properties, we classified it as military. At ETU and TKTU, the Family Medicine Departments took part in the curricula, while the others did not use it during the study period. In October and November 2001, an anonymous questionnaire, consisting of 13 open- and closed-ended questions was developed and distributed to the fourth and fifth-year students in our medical schools. The study was based on oral informed consent. The fourth and fifth year students were chosen as they have the theoretical and practical basis of medicine as it is taught in Turkey. Students who were absent were excluded in the study. The answers for the open-ended questions were categorized. We evaluated the data according to school, class, gender, and the curricula containing family medicine programs.

Fisher’s exact and independent samples t-tests and ANOVA were used for the statistical analysis.

If a statistically significant difference was determined, Tukey test was used. Statistically significance was defined as $p<0.05$.

During the study period, 596 out of a total of 621 students in the fourth and fifth term of these 4 schools received questionnaires. Four hundred and eighty-two agreed to participate in the study, and 438 (70.5% of the entire group) completed the questionnaires. The mean age was $22.8 \pm 0.1$ (19-29). The students, according to the educational methods are shown in Table 1.

The students generally stated that the practitioners were not clinically efficient (76.5%), but the rate was the highest in GMMA (90.1%). The difference was statistically significant ($p<0.001$). Three hundred and seventy students stated that the community could not efficiently benefit from primary health care services, and there was statistical significance between TKTU and GMMA ($p<0.001$). The TKTU students were more optimistic regarding the efficiency of services. Suggestion for enhancing the benefit from primary health care services generally resulted in "educating the community," however, students from the military school suggested "to improve the primary care teams and equipment" mostly, which was statistically significant ($p<0.05$). Three hundred and twenty-seven students (especially fifth year) thought that their medical education was not sufficient for working in primary care settings. Student attending the military school and those employing classical methods were more cynical about this issue. Students of the latter suggested "more practical training sessions," while military students suggested "bedside education." A total of 260 students preferred family medicine sessions to be included as part of their undergraduate medical education, especially during the internship, and this desire was more common among military students. Although 370 (84.5%) students stated that being successful in the national "medical specialization exam" was not a requirement for "being a good physician" (mostly among fifth year and military students), 91.1% of the whole students would like to specialize. The

### Table 1 - Students according to the term and educational system.

<table>
<thead>
<tr>
<th>Term</th>
<th>Integrated</th>
<th>Classical</th>
<th>Military</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>4th</td>
<td>84</td>
<td>71</td>
<td>40</td>
<td>195</td>
</tr>
<tr>
<td>5th</td>
<td>102</td>
<td>60</td>
<td>81</td>
<td>243</td>
</tr>
<tr>
<td>Total</td>
<td>186</td>
<td>131</td>
<td>121</td>
<td>438</td>
</tr>
</tbody>
</table>
reasons for specialization were "community’s lack of confidence in practitioners" and "self improvement." The answer of "self improvement" was common among girls. The first reason was the leading answer among the fifth year students. More students from TKTU, compared with the other schools, stated that they preferred to work in primary care without specialization. Students mostly preferred to specialize in hospital-based specialties such as internal medicine and obstetrics and gynecology. The major reasons for these preferences were "financial" and "personal interest." The first one was common among boys, while the second one was common among girls. The latter was also more common in TKTU. Only 84 students (19.1%) of the whole group prefer to specialize in family medicine and this preference was less in military school. If they were policy makers, 85 of the students would have established "an efficient referral system," but military students suggested "to change the health care system" more than the others, and TKTU students suggested, "implementing family medicine applications" more than the others. As the Family Medicine Department at TKTU takes more active role in the medical curriculum, this could have affected the answers. If they were curriculum makers, they preferred "to increase the portion of practical sessions in the curriculum," and "to diminish the number of medical schools and contingent."

Considering the results, we can say that our students felt unprepared to work in primary care after graduation, and many preferred to attend hospital-based specialties. The opportunity of military medical school graduates to be employed by the Turkish Army as soon as they graduate seems not to diminish the future anxiety. Students from the schools using integrated methods were found to be more optimistic for their future and working in primary care, especially from the school in which, the Family Medicine Department is playing a large part in the curriculum.

Acknowledgment. We acknowledge Janice O. Vantrease for her grammatical review.

Received 22nd February 2005. Accepted for publication in final form 29th May 2005.

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