Do C-reactive protein and procalcitonin predict hospital-acquired infection in patients with trauma?

Bulent M. Ertugrul, MD, Aylin Yilmabasar, MD, Ozden Ertugrul, MD, Hatice B. Ayabakan, MD, Sevda Kizilirmak, MD, Sembol Turkmen, MD, PhD.

rauma patients frequently present signs of sepsis such as fever, tachycardia, hyperventilation and leukocytosis even in the absence of infection. The diagnosis of infection in patients with trauma is essential for correct patient management. However, over utilization of antibiotics can lead to the emergence of multiresistant organisms, increased toxicity, and increased cost. The C-reactive protein (CRP) is currently the most widely used parameter to support the diagnosis of infection. As routine laboratory tests often provide inadequate discrimination in the diagnosis of infection in patients with trauma, there is a need for inflammatory agents that are reliable enough to differentiate hospital-acquired infections (HAI) from other types of inflammation both requiring different forms of therapy. In adults and children, infection, and sepsis have been found to be associated with increased serum levels of calcitonin precursors. Procalcitonin (PCT) concentrations are very low in healthy individuals, but have been shown to increase markedly after endotoxin administration during severe systemic infection and septic shock.¹ In this regard, we designed a prospective study to define the value of PCT and CRP concentrations and white blood cell (WBC) count in the diagnosis of HAI in patients with trauma admitted to the surgical intensive care unit (ICU).

The study included 41 consecutive adult patients with trauma admitted to emergency surgical ICU at Istanbul University, Istanbul Medical Faculty Hospital, Turkey. All of the patients' age, gender, type of trauma, glasgow coma score (GCS), Acute Physiologic Assessment and Chronic Health Evaluation (APACHE) II Score, and Sequential Organ Failure Assessment (SOFA) score were recorded. All patients were examined for signs and symptoms of infection at the time of admission and daily thereafter by an infectious diseases consultant, and the diagnosis of an HAI was made according to the criteria defined by the Centers for Diseases Control and Prevention. Informed consent was obtained from all patients. Infected patients at the time of admission to ICU, patients with penetrated abdominal trauma, patients who underwent recent abdominal surgery

560 Saudi Med J 2006; Vol. 27 (4) www.smj.org.sa

Table 1 - The comparison of the markers of infection in the infected group.

Marker	Initial value* (n=21)	Latter value† (n=21)	P-value	
WBC count (/mm ³)	13109.5	13432.9	0.794	
CRP concentration (mg/L)	49.4	167.2	<0.001	
PCT concentration (ng/mL)	6.2	4.7	0.106	

WBC - white blood cell, CRP - C-reactive protein, PCT - procalcitonin, *The values obtained from the infected group at the time of admission to intensive care unit, †The values obtained from the infected group at the onset of hospital-acquired infections

were excluded from the study. Venous blood samples were obtained for measurement of serum concentrations of PCT, CRP and WBC count, at the time of admission to ICU (initial), and at the onset of HAI (latter). The PCT concentration was measured by immunoluminometric assay with the commercially available Lumitest® PCT (BRAHMS Diagnostica GmbH, Berlin, Germany). The CRP was measured by immunoturbidimetry with the Turbiquant® CRP test kit (Dade Behring, Marburg, Germany). The normal values for PCT concentrations is 0 - 0.5 ng/ml, for CRP concentrations is 0 - 5 mg/L, and WBC count is 4000 - 9000/mm³. Results are expressed as mean $(\pm$ SD). Mann Whitney U test was used in univariate analysis of independent samples. For paired analysis, Wilcoxon test was used, p < 0.05 was accepted as the level of significance.

There were 34 male (83%) and 7 female (17%)patients and had the following clinical and laboratory findings at admission to ICU: mean age \pm SD was 39.8 ± 19.7 years, mean APACHE II score ± SD was 12.8 \pm 7.1 points, mean GCS \pm SD was 10.9 \pm 4.1 points, mean SOFA score \pm SD was 5 \pm 2.6 points, mean WBC count \pm SD was 14521.5 \pm 6043.2/mm³, mean CRP concentration \pm SD was 54.1 \pm 45.4 mg/L, mean PCT concentration \pm SD was 4.6 \pm 1 ng/mL. Thirteen patients had only head trauma while 3 patients had only abdomen, one patient only chest, and one patient only extremity trauma. The rest of the patients (n=23)had multi-trauma at admission to ICU. Hospitalacquired infections were diagnosed in 21 (51%) patients. Mean date of infection diagnosis \pm SD was 6.6 ± 3.5 days. Among infected patients, ventilator associated pneumonia was diagnosed in 12 (29.1%) patients, bacteremia in 3 (7.3%), catheter-related infection in 2 (4.9%), meningitis in 2 (4.9%), intraabdominal abscess in 1 (2.4%), and pyelonephritis in 1 (2.4%) patient. Among the initial findings of all patients' age, gender, APACHE II score, GCS, SOFA score, WBC count, CRP and PCT concentrations were not significantly different between the infected and non-infected groups. The initial CRP and PCT concentrations and WBC count and the values obtained at the onset of HAI in the infected group were listed in Table 1. Only serum CRP concentrations obtained at the onset of HAI increased significantly compared with the initial values in the infected group (p < 0.001). The recognition of HAI in trauma patients is difficult as no single marker of inflammation allows the establishment of the diagnosis. In this regard, we prospectively investigated the benefit of a new innovative marker PCT and a conventional marker CRP together with WBC in diagnosis of HAI in patients with trauma admitted to a surgical ICU.

The mean PCT values at admission to ICU were 4.62 ng/ml, CRP values were 54.14 mg/L, and WBC values were 13521.46/mm³, and all those were above the reference ranges. Early elevation of PCT and CRP concentrations and WBC count may be related to tissue damage after trauma. Wanner et al,² pointed out that mechanical trauma causes elevated PCT levels depending on the severity of the injury. Levels were in the peak on day 1 to 3 and fall thereafter. The PCT is a sensitive marker of sepsis and severe multiple organ dysfunction syndrome in injured patients. Routine PCT analysis appears to be useful in the early recognition of post-traumatic complications. A secondary rise in PCT appears to indicate superadded bacterial sepsis. On the other hand, in our study, there were no significant differences between the initial and the latter PCT concentrations and WBC counts in the infected group while the difference for CRP was statistically significant. It is clear that early diagnosis of HAI prevents the development of sepsis. There were only 3 bacteremics patients in our study. In these patients, CRP exhibited an increase but not PCT except in one bacteremic patient and only this patient met all sepsis criteria. We evaluated the course of PCT and CRP concentrations and WBC counts in the infected group and took their initial values as the control group. Our aim was to diagnose HAI at the very early stages of the infection. So, these tests were not repeated in the non-infected group. It is possible that in the infected group, PCT levels had began to rise by the time the initial levels were taken and had began to fall by the time the latter levels were taken. This will explain why the initial PCT levels were higher (nearly reaching statistical significance) in the infected than in the non-infected group and why the PCT levels were higher on the initial sample than on the latter. In our study, CRP assessment has proven more helpful in the prediction of HAI compared with PCT and WBC counts. Miller et al³ reported that CRP but not WBC is useful in determining the presence of infection in trauma patients. In a study performed by Ugarte et al⁴ it was reported that CRP remains to be the best discriminant test due to its good sensitivity and specificity, and could discriminate between infected and non-infected patients. They recommended that PCT should not replace CRP as a marker of infection in ICU patients, but the combination of both parameters can indicate the presence of infection with greater specificity. There had been similar results in a study performed by Mimoz et al.⁵ They evaluated 21 blunt trauma patients and found that at the late posttraumatic period (day 7) while CRP concentrations remain elevated in all patients, PCT concentrations were only raised in septic patients. Recently a metaanalysis was performed by Simon et al.⁶ This analysis included 12 published studies that evaluated PCT and CRP for the diagnosis of bacterial infection in hospitalized patients. They concluded that the overall accuracy of PCT markers is higher than that of CRP markers to differentiate bacterial infections from other non-infective causes of systemic inflammation. They evaluated a heterogeneous patient population with different age groups with different types of infections from different areas of the hospitals unlike our study group.

Sepsis may lead to a lethal multiple organ failure in trauma patients, especially in cases of delayed diagnosis of infection. Together with the clinical symptoms, CRP is a useful marker for the rapid identification of HAI in patients with trauma.

Acknowledgment. We thank M. Carin, H. Eraksoy, K. Taviloglu and N. Cakar for their assistance.

Received 3rd October 2005. Accepted for publication in final form 25th January 2006.

From the Department of Infectious Diseases and Clinical Microbiology (B. Ertugrul), Adnan Menderes University Medical Faculty, Aydin, Clinical Biochemistry Laboratory (Yilmabasar, O. Ertugrul, Ayabakan, Turkmen), Social Insurances Institute Okmeydani Training Hospital, and the Department of Anesthesiology and Reanimation (Kizilirmak), Istanbul Medical Faculty, Istanbul University, Istanbul, Turkey. Address correspondence and reprint requests to: Dr. Bulent M. Ertugrul, Department of Infectious Diseases and Clinical Microbiology, Adnan Menderes University Medical Faculty, Aydin, Turkey. Tel. +90 (532) 6456621. Fax. +90 (256) 2146495. E-mail: mbulentertugrul@yahoo.com

References

1. Meisner M. Pathobiochemistry and clinical use of procalcitonin. *Clin Chim Acta* 2002; 323: 17-29.

- 2. Wanner GA, Keel M, Steckholzer U, Beier W, Stocker R, Ertel W. Relationship between procalcitonin plasma levels and severity of injury, sepsis, organ failure, and mortality in injured patients. *Crit Care Med* 2000; 28: 950-957.
- Miller PR, Munn DD, Meredith JW, Chang MC. Systemic inflammatory response syndrome in the trauma intensive care unit: who is infected? *J Trauma* 1999; 47: 1004-1008.
- Ugarte H, Silva E, Mercan D, De Mendonca A, Vincent JL. Procalcitonin used as a marker of infection in the intensive care unit. *Crit Care Med* 1999; 27: 498-504.
- Mimoz O, Benoist JF, Edouard AR, Assicot M, Bohuon C, Samii K. Procalcitonin and C-reactive protein during the early post-traumatic systemic inflammatory response syndrome. *Intensive Care Med* 1998; 24: 185-188.
- Simon L, Gauvin F, Amre DK, Saint-Louis P, Lacroix J. Serum procalcitonin and C-reactive protein levels as markers of bacterial infection: a systematic review and meta-analysis. *Clin Infect Dis* 2004; 39: 206-217.

Scolicidal agents in hydatid cyst surgery

Nadham K. Mahdi, MSc, PhD, Mohammad H. Al-Johar, CABS.

Surgical operation is the treatment of choice for patients with hydatid cyst as chemotherapy is still controversial. Inoculation of a scolicidal agent into the cavity of hydatid cyst to reduce the risk of spillage of viable protoscolices is a major part of the surgical technique. Although numerous scolicidal agents have been used for many years, good evidence for their efficacy in vivo is lacking. Therefore, the effectiveness of some of these agents needs to be tested.

Fresh, fertile hydatid cysts from the liver were obtained shortly after surgical removal in Basrah General Hospital, Basrah, Iraq. The material was allowed to settle in a sterile bottle, and the supernatant was removed. The viability of protoscolices was determined by flame cell activity and vital staining with 1% eosin. Viable scolices show flame cell activity and do not take up the dye.1 The test was carried out on 5 samples. The scolicidal agents examined were hypertonic solution 30%, normal saline 0.9%, betadine, ethyl alcohol 70% and 95%. Two ml of each scolicidal were placed in a test tubes. A drop of protoscolex rich sediment was added to each tube and was mixed gently. Following 5, 10 and 30 minutes of exposure, the viability of the protoscolices was determined microscopically by assessing flame cell activity and lack of vital staining with 1% eosin. Betadine, hypertonic solution 30% and ethyl alcohol 95% were effective in killing the protoscolices within 5-10 minutes time. In contrast, saline solution 0.9%, and ethyl alcohol 70% could not show any lethal effect on the protoscolices even after 30 minutes time. Cyst fluid contains thousands of protoscolices and each one has the potential to grow into a new hydatid cyst. Thus, it has been traditional to inject scolicidal agents into the unopened hydatid cyst due to the risk of spillage into the peritoneal cavity leading to recurrent disease. Hypertonic solutions 30% have become the scolicidal agents of choice over the past years. Although Besim² demonstrated that 5% saline have no effect on scolices, many surgeons recommended the use of 3% saline.^{3,4} Our findings prove that there is no scolicidal effect (100%) can be shown with 20%saline at 5 minutes.² But, it should not be used in patients who have cysts connecting with the biliary tree due to the danger of sclerosing cholangitis.⁵

Betadine is an effective scolicidal agent, as demonstrated in this study, but polyvinylpyrrolidone storage disease, renal shut down, sterile peritonitis and sclerosing serositis are the associated complications and its use is restricted to preoperative local antisepsis of intact adult skin.⁶ Ethyl alcohol is an effective agent at a concentration of 95%. Unfortunately, it can cause caustic damage to the epithelium of communicating bile ducts leading to sclerosing cholangitis and it is strongly concentration dependent,^{2,3,6} as observed in this study. Therefore, the surgeon in practice in our hospitals aspirates the cyst fluid first. If the aspirate is clear, then they would use any effective scolicidal agents without hazard. However, if the aspirate is yellow in color it means there is a biliary communication. So, the risk of sclerosing cholangitis may be the problem of using a certain agent. Therefore, total evacuation and prevention of any contact of germinative membrane with the peritoneal surface are essential as the germinative membrane can contain viable protoscolices despite proper cyst fluid inactivation.

In conclusion, the risk of dissemination of the cyst contents can be avoided by injecting a potent scolicidal agent, which is an important step in hydatid cyst surgery. The best scolicidal agent to be used is betadine. However, experiment in vitro and in vivo results need to be studied further.

Received 30th October 2005. Accepted for publication in final form 25th January 2006.

From the Departments of Microbiology and Surgery, College of Medicine, University of Basrah, Basrah, Iraq. Address correspondence and reprint requests to: Prof. Nadham K. Mahdi, Central Post Office 42001, PO Box 1565, Ashar, Basrah, Iraq. E-mail: nadhammahdi@yahoo.com

References

- 1. Smyth ID, Barret NJ. Procedure for testing the viability of human hydatid cyst following surgical removal, especially after chemotherapy. *Trans R Soc Trop Med Hyg* 1980; 74: 649-652.
- Besim H. Scolicidal agents in hydatid cyst surgery: are they really effective? *Second Iraqi-Turkish Medical Week* 2002. p. 1-5.
- Little JM, Deane SA. Hydatid Disease. In: Blumgart LH, editor. Surgery of the liver and biliary tract. Edinburgh; Churchill Livingstone; 1988. p. 955-967.
- Milicevic M. Hydatid Disease. In: Blumgari LH, editor. Surgery of the liver and biliary tract. Edinburgh: Churchill Livingstone; 1994. p. 1121-1150.
- Castellano G, Moreno-Sanchez D, Gutierrez J, Moreno-Gonzalez E, Colina F, Solis-Herruzo JA. Caustic sclerosing cholangitis. Report of four cases and accumulative review of the literature. *Hepatogastroenterol* 1994; 41: 458-470.
- Le Veen HH, Le Veen FR, Le Veen GE. The mythology of povidone-iodine and the development of self-sterilizing plastics. *Surg Gynecol Obstet* 1993; 176: 183-189.

Pregnant women with type 1 diabetes mellitus treated by glargine insulin

Abdulrahman A. Al-Shaikh, MRCP, FRCP.

Pregestational diabetes mellitus complicates approximately 0.2-0.5% of pregnancies. Type 1 diabetes was 35% of pregestational diabetic women and 65% was type 2 diabetes mellitus. Pregnancy in diabetes is associated with an increase in risk to both the fetus and the mother. The risk of complications increased in poor glycemic control and decreased in nearly normal glucose levels. Tight control of blood glucose is mandatory in both type 1 and type 2 during pregnancy. The goals of glycemic control in type 1 diabetes sometimes very difficult especially in brittle's diabetes mellitus. With the use of long acting insulin, such as glargine insulin in addition of premeals, short acting insulin makes the control easier in such patients. There is no clear safety of glargine insulin in pregnancy. With very well-known hazards of high blood glucose during pregnancy without known hazards glargine insulin, we decided to use it in difficult cases of type 1 diabetes.

Type 1 diabetes treated by glargine insulin and became pregnant advised either to continue or to change to other insulin. Pregnant women with uncontrolled type 1 diabetes mellitus treated by insulin other than glargine insulin were also advised to be treated by glargine insulin. The safety of the glargine insulin and the hazards of high glucose during pregnancy were discussed with the patients. Glargine insulin was initiated or continued if the patients agreed and signed the consent forms. The total daily insulin doses were calculated according to the body built (0.7 unit/kg) and 50% of it was glargine insulin given once daily either afternoon or in the evening. The other daily dose was given as a short acting insulin (regular insulin) and was divided into 3 premeals doses. The doses of the glargine insulin and short acting insulin were adjusted according to the blood glucose levels. We aimed to lower the fasting blood glucose less than 100 mg/dl and postprandial less than 130 mg/dl. They were followed in monthly bases during the pregnancy in our clinic and followed by the obstetrician. They had all the antenatal investigation and follow up. Home glucose monitoring pre and post meals were carried out by the patients and reviewed in each visits. Glycosylated hemoglobin was carried out in the first month of pregnancy and every 3 months thereafter. Fetal monitoring by ultrasound was carried out in the first trimester and repeated every 3 months thereafter. The fetal sizes, heart pulses, and any abnormalities were reported by ultrasound. The methods of the delivery, fetal apgar scores and fetal sizes were noted at deliveries.

Eleven patients with type 1 diabetes became pregnant and were treated by glargine insulin. All went through pregnancy without any problems except for one abortion. The dose of glargine insulin ranged between 30-80 units per day. The glycosylated hemoglobin in the first trimester was ranging from 7.8-12.4% (the mean was 9.93%). At the end of the pregnancy, the glycosylated hemoglobin reduced to 5.9-7.4% (the mean 6.54%). All antenatal visits revealed no abnormalities. Fetal heart and sizes were normal through all pregnancy. Mild hypoglycemic events reported 3 times in different patients and managed without any complications. Normal spontaneous vaginal delivery was the way of delivery in 7 patients and 3 by cesarean section due to poor progression and fetal distress. All patients were informed to discontinued the glargine insulin during delivery and treated only by short acting insulin. All fetuses were healthy (4 boys and 6 girls). There was no congenital anomalies found in all of them. Their sizes were ranging between 2.8-4.34 kg (mean 3.26%) (Table 1). All patients except one were discharged from the hospital after 24 hours of delivery.

Type 1 diabetes mellitus is a common disease in our country. Women with type 1 diabetes has the capability to conceive and high blood glucose has many drawback effects on the mother and the fetus.

Patients	HA1c- before glargine insulin (%)	HA1c* (%)	Weight of the baby (kg)	Mode of delivery	Congenital anomalies	Fetal complications
1	9.3	6.7	3.4	SV	Absent	Absent
2	9.7	6.92	3.6	CS	Absent	Absent
3	10.2	7.4	4.34	CS	Absent	Absent
4	9.2	6.5	3.1	SV	Absent	Absent
5	10	6.2	2.9	SV	Absent	Absent
6	12.4	6.8	3.3	CS	Absent	Absent
7	11.6	6.1	2.85	SV	Absent	Absent
8	8.9	5.9	2.8	SV	Absent	Absent
9	7.8	6.2	3.1	SV	Absent	Absent
10	10.2	6.7	3.2	SV	Absent	Absent

Table 1 - Important findings on patients treated by glargine insulin during pregnancy.

Tight glycemic control reduced many complications. Normalization of blood glucose concentrations before and early pregnancy reduce the risks of spontaneous abortion and congenital malformations nearly to general population.¹ Macrosomia is one of the most common complication of hyperglycemia during pregnancy and it reduces in those near normal blood glucose.² Frequents measurements of blood glucose are mandatory in women with type 1 diabetes mellitus during pregnancy. Glycosylated hemoglobin values provide the best assessment of degree of chronic glycemic control, reflecting the average of blood glucose concentration during the preceding 6-8 weeks. The lifespan of the red blood cells was shortened during pregnancy and the glycosylated hemoglobin can be measured every 4-6 weeks and even more frequently if the women glycemic control is poor. The recommended targets of glycemic control during pregnancy are as follows, fasting blood glucose of 60-90 mg/dl, one hour postprandial no higher than 130-140 mg/dl, and 2 postprandial no higher than 120 mg/dl. Insulin is only the available treatment of diabetes during pregnancy. Most women with type 1 diabetes require at least 3 injections of insulin per day. The average dose of the insulin in pregnant women with type 1 diabetes is 0.7 unit/kg in the first trimester, often increased to 0.8 unit/kg for weeks 18-26, 0.9 unit/kg for weeks 27-37, and 1 unit/kg for weeks 37 to the term.3 A large maternal weight gain was associated with a greater increase in the insulin requirement. Type 1 diabetes mellitus sometime is very difficult to control and required 3-4 insulin injections with basal long acting insulin. Glargine insulin proved it efficacy in control hyperglycemia in those difficult

cases.^{4,5} Some of our patients with type 1 diabetes have controlled after addition of glargine insulin. Their blood glucose and glycosylated hemoglobin reduced than when they were treated by different types of insulin. Some women with this problem became pregnant, and we have the choice either to continue on same treatments, despite lacking of safety of glargine insulin in pregnancy, or to discontinue the glargine insulin with difficulties to controls other types of insulin. After discussing these issues with the patients, the author decided to continue the glargine insulin with agreements. The backgrounds of using glargine insulin in pregnancy despite there were no reports of safety are difficult cases of type 1 diabetes mellitus. There were no proved complications of glargine insulin while hyperglycemia has many complications during pregnancy.

We conclude from those cases that glargine insulin is safe and effective during pregnancy but more studies are needed.

Received 28th August 2005. Accepted for publication in final form 30th November 2005.

From the Department of Medicine, Faculty of Medicine, King Abdul-Aziz University, Jeddah, Kingdom of Saudi Arabia. Address correspondence and reprint requests to: Dr. Abdulrahman A. Al-Shaikh, Department of Medicine, Faculty of Medicine, King Abdul-Aziz University, PO Box 80215, Jeddah 21589, Kingdom of Saudi Arabia. Tel. +966 (2) 6408272. Fax. +966 (2) 6408113. E-mail: joodshaikh@yahoo.com

References

1. Ray JG, O'Brien TE, Chan WS. Preconception care and the risk of the congenital anomalies in the offspring of women with diabetes mellitus: a meta-analysis. *QJM* 2001; 94: 435-444.

- Mello G, Parretti E, Mecacci F, La Torre P, Cioni R, Cianciulli D, et al. What degree of maternal metabolic control in women with type 1 diabetes is associated with normal body size and proportion in full-term infants? *Diabetes Care* 2000: 23: 1494-1498.
- 3. Steel JM, Johnstone FD, Hume R, Mao JH. Insulin requirements during pregnancy in women with type 1 diabetes. *Obstet Gynecol* 1994; 83: 253-258.
- 4. Rosenstock J, Park G, Zimmerman J. U.S. Insulin Glargine (HOE 901) Type 1 Diabetes Investigator Group. Basal insulin glargine versus NPH insulin in patients with type 1 diabetes on multiple daily insulin regimens. *Diabetes Care* 2000; 23: 1137-1142.
- 5. Hershon KS, Blevins TC. Once daily insulin glargine compared with twice daily NPH insulin in patients with type 1 diabetes. *Endocr Pract* 2004; 10: 10-17.

Tamoxifen effects on treatment fibrocystic breast disease in women

Seyed R. Mousavi, MD PhD, Michaeal Rezaei, MD.

reast pain in women was first described in D the early 19th century by Sir Astly Cooper, who suggested that women who sought advice for breast pain were "usually of a nervous and irritable temperament".1 This sentiment persisted despite reports by Harris et al,¹ who said that women with breast pain were no more psychoneurotic than those having an operation for varicose veins. Mastalgia remains poorly characterized and not a reason for breast consultation in general practice.¹ The term fibrocystic or cystic breast disease is not a distinctive disease, but rather a term used to represent a group of breast tissue abnormalities that may occur separately or together. While we associate this "disease" with the menstrual cycle, it is important to remember that women can experience palpable breast irregularities regardless of menstruation. Pathologic descriptions of the disease were recorded as early as the 1880 with the term chronic cystic mastitis identified a decade later. Tamoxifen (Nolvadex) has been in use for over 20 years and currently the most prescribed anti-cancer medication in the world. It is an orally effective, synthetic, non-steroidal, estrogen antagonist and agonist agent. In studies and trials, it has been shown to have only limited side effects. It has produced regressions in women with fibrocystic changes, including precancerous ones, and in those with metastatic breast cancer, where its benefits were first observed. It has increased disease free survival (DFS) and overall survival (OS) rates when given as Table 1 - Showed side effects of tamoxifen in different doses.

Dose of Tamoxifen side effects	10 mg	20 mg	Total
Depression (%)	0	2	2
Dizziness (%)	2	4	6
Cephalalgia (%)	2	3	5
Total (%)	4	9	13

an adjuvant systemic type of therapy in women with early breast cancers, and it has reduced the incidence of contra lateral breast cancers.³

We examined the effect of tamoxifen therapy on several patients suffering from fibrocystic disease and mastalgia. The patients were followed and excluded those who had sonography and clinical examination that occurred at or subsequent to the diagnosis of fibrocystic disease. Sixty-two women underwent breast sonography for benign breast disease while in the trial; the remaining 202 women did not. We begin tamoxifen in doses of 10-20 mg daily for 2-4 months; during medication, one or 2 visits in a month is necessary. Over 3 years, tamoxifen treatment reduced the risk of benign breast disease and mastalgia by 78%, breast pain 21%, mild (deep palpation) and severe pain 19% (movement and rest) and moderate pain 38% (between 2). There were 62 women who underwent breast sonography, 85% showed cysts and fibrocystic change. Non-cyclic mastalgia (40%) and cyclical mastalgia (60%) were the most frequent. Thirteen percent of patients experienced some side effects, such as dizziness (6%), cephalalgia (5%) and depression (2%) (Table 1). Relief of pain and tenderness with a dose of 10 mg (11% of patients) and 20 mg (89% of patients) after 2-4 months treatment of tamoxifen were the most frequently reported. In addition, 3(1.1%) patients discontinued the treatment and 78% of patients achieved pain control with the use of this drug. Sometimes referred to as fibrocystic disease, fibrocystic change, cystic disease, chronic cystic mastitis or mammary dysphasia is not a disease, but rather it describes a variety of changes in the glandular and stromal tissues of the breast. Symptoms of fibrocystic breasts include cysts (accumulated packets of fluid), fibrosis (formation of scar-like connective tissue), lumpiness, and areas of thickening, tenderness, or breast pain though sometimes painful, fibrocystic breast condition is not cancer. However,

fibrocystic breasts can sometimes make breast cancer more difficult to detect with mammography. Therefore, ultrasound may be necessary in some cases if breast abnormality is detected in a woman with fibrocystic breasts. According to the American Cancer Society, fibrocystic breasts affect at least half of all women at some point in their lives. Fibrocystic changes are the most common cause of breast lumps in women between 30 and 50 years old. Tamoxifen therapy also reduced the risk for fibroadenoma and fibrosis compared with the placebo group, the tamoxifen group had fewer biopsies and fewer women who underwent a biopsy for fibrocystic disease, hyperplasia, and metaplasia. This resulted in a reduction in the risk of biopsy in women treated with tamoxifen. This risk reduction occurred predominantly in women younger than 50 years.⁴ While in the past 100 years has introduced a variety of terms to describe the abnormality, a consensus for treatment has developed to treat this significant health problem. Any treatment of fibrocystic breast problem is designed to: 1. alleviate breast pain, 2. reduce or remove irregularity and 3. rule out the possibility of breast cancer. Medical treatment can include: 1. Use of sex hormones (estrogens, progestins, androgens). 2. Pharmaceutical use of vitamins (A, B1, E), diuretics, and tamoxifen (an anti-estrogen). In December 11, 2001, researchers from the National Surgical Adjuvant Breast and Bowel Project (NSABP) Breast Cancer Prevention Trial reported that tamoxifen is well described for its ability to reduce the risk of developing breast cancer by 50% in high-risk patients and apparently also dramatically lowers the risk of developing benign breast cancer.⁴ In a study presented by Tan-Chiu et al⁴ at the 24th Annual Meeting of the San Antonio Breast Cancer Symposium, that treatment with tamoxifen reduces adenosis, cysts, duct ectasia, hyperplasia, metaplasia, fibrocystic disease and other benign mass formation by up to 47%. We considered that use of tamoxifen would result in a reduced incidence of benign breast disease in tamoxifen-treated women. In our study, after 2-4 months with doses of 10-20 mg, we removed irregularities and alleviated breast pain in more than 78% of patients. These findings support the therapeutic effects of tamoxifen on breast fibrocystic changes.

A low incidence of side effects has been reported with tamoxifen, resulting in the proposal to use the antiestrogen as a preventive agent for breast cancer.² Tamoxifen is an effective treatment to control moderate to severe mastalgia and had a reduced incidence of clinically detected benign breast disease.

Received 3rd October 2005. Accepted for publication in final form 4th January 2006.

From Shahid Beheshti Medical Sciences, Shoda Medical Center, Tajrish, Tehran, Iran. Address correspondence and reprint requests to: Dr. Seyed R. Mousavi, Shohada Medical Center, Tehran 45672, Iran. Tel. +98 (212) 2862757. Fax. +98 (212) 2862756. E-mail: seyed29@yahoo.com

References

- 1. Harris JR, Lippman ME, Morrow M, Hellman S. Disease of the Breast. Philadelphia (PA): Lippincott, Raven; 1996.
- 2. Jordan VC. Tamoxifen: toxicities and drug resistance during the treatment and prevention of breast cancer. *Annu Rev Pharmacol Toxicol* 1995; 35: 195-211.
- 3. Leis HP Jr. The role of tamoxifen in the prevention and treatment of benign and malignant breast lesions: a chemopreventive. *Int Surg* 1993; 78: 176-182.
- 4. Tan-Chiu E, Wang J, Costantino JP, Paik S, Butch C, Wickerham DL, et al. Effects of tamoxifen on benign breast disease in women at high risk for breast cancer. *J Natl Cancer Inst* 2003; 95: 302-307.

Family medicine in Turkey. *Need for trainers in general practice*

Okay Basak, MD, Dilek Guldal, MD.

rowing development of family medicine (FM) G in the world revealed the necessity of teaching and learning the philosophy and paradigm of the discipline. With this concern, training the teachers of the FM has become the basic interest of the pioneers of the discipline.¹ The European Academy of Teachers (EURACT) in general practice (GP) supports various training courses.² The objective of the EURACT Teaching the Teachers (ETC) teaching methods in general practice course, which is one of the basic courses of EURACT, is to train peculiar trainers for primary care on the basis of family medicine/general practice (FM/GP) discipline. Family Medicine in Turkey is established as a specialty program in 1985 at the training hospitals of the Ministry of Health (MOH) and spread to universities in 1993.³ Despite many countries, which FM/GP raised on the hands of general practitioners as a new and progressed definition of the discipline, Turkey Specialty Program is established by the government within the preparation in accordance with European community, whereas practitioners had no knowledge on the subject of being a discipline. The word "practitioner" is used for the physicians who works in primary care, without further training after medical school either any specialty including FM/GP or retraining program. However, health reforms in Turkey is also

Course	No. of participants			Where they work					
	Family Medicine Specialist	Practitioner	Resident	Total	Family Medicine Department	Hospital	Primary care	Regional Office of Health Ministry	Other
Kusadasi	28	-	1	29	25	2	1	-	-
Cesme	19	15	1	35	10	5	11	5	3
Aydin	4	14	-	18	2	2	14	-	-
Izmir 1	4	16	-	20	-	-	20	-	-
Izmir 2	2	19	-	21	1	-	17	3	-
Izmir 3	-	19	-	19	-	-	16	3	-
Ankara	21	-	14	35	11	5	5	-	-
Istanbul	25	-	2	27	7	11	7	-	-
Total	103	83	18	204	56	25	91	11	3

Table 1 - Distribution of the participants according to their qualifications and working places.

named as FM reforms, which is basically formed of 3 major parts; general health insurance, privatization, and contractual employment. Using the name FM for 2 new and different issues almost at the same interval caused confusion and chaos regarding what the term is representing for. Many organizations such as Turkish Medical Association and Labor Unions who were against privatization and contractual employment became opposed to FM without knowing the difference between the system and the discipline. This situation became an obstacle for the development of the FM and resulted confusion in understanding even the basic matters of FM/GP. Despite the lack of detailed and consistent policies on this subject, the number of FM specialists gradually increased and started to be recognized in health care provision. Actually, there are FM residency programs at 20 out of 45 medical schools throughout the country, and in 16 training hospitals of MOH, which are localized in 3 big cities.⁴ Although many university FM departments have outpatient clinics, the registered training program based on the training in hospital wards, neglecting the fundamental part of FM training in primary care. Realization of the primary care component of the specialty training requires the preparation of both the primary health care centers, and the teachers practicing in these centers for teaching. However, besides the medical school graduates every year, there are already approximately 35,000 practitioners working in primary care who are expected to be the future family physicians. Due to the huge number of the candidate trainees, MOH have established a short training program that is suggested by WHO.⁵ Since the short training program offered by WHO is mostly based on the teaching in primary care, it raises the need for teachers in primary care. The changes in the medical education towards student, and community-based formation brought the need for trainers in primary care settings. Since the ETC was constructed on the philosophy and principles of FM/ GP discipline, it could be an important and useful tool for removing the ignorance and misunderstandings on FM/GP matters and providing communication among different parties besides training teachers for primary care.

The courses. A total of 8 courses were given in 4 different cities between the year 2000 and 2003. The aims of the courses were to enable participants to assess their own continuing needs as teachers, and to gain the skills required to meet those needs on a continuing basis. Sore throat or hypertension was used as models for teaching, but the course did not target to have medical content. The general strategy and the method of the courses were learning by doing. Due to the different background of the participants, each course was re-formed without changing the fundamental principles, according to needs and expectations of the participants. The features of the discipline and the differences from other disciplines, the concepts such as FM, GP, and necessity for specialty training to work in primary care were the discussion subjects throughout the courses. Each subject was considered as a learning need and formed the structured discussions of follow-up meetings. The last version of the course was translation of the course, not only in the language, but also in needs and necessities of Turkish teachers.

Follow-up meetings. The follow-up meetings could not be performed regularly and systematically in other cities than Izmir due to the limited time of the trainers. We constituted 6 follow-up groups, with 10 participants in each. Four meetings with each of

the groups were conducted by 3 months intervals. At the last meetings, a semi-structured focus groups were conducted, encouraging the group members to share their feelings and thoughts regarding using their teaching skills in their practice and the teaching environment. At the end of each meeting, 2 of the trainers gathered the ideas and feelings of the participants regarding the similar issues from the collected data by thematic analysis. Although the main purpose of follow-up meetings was to share teaching experiences and learning from others, the basic subjects of FM were also discussed. With each group, we focused on 3 main subjects: the origin, philosophy and definition of FM/GP, development of FM/GP in Turkey, and in the world, the clinical method in FM/ GP. The short training program was the focus of all meetings. The features of the participants are given in Table 1. The results of focus group studies were as follows: most of the participants stated that although they could not use their teaching skills regularly, they use communication skills in their daily lives even at home with their spouses and children. Almost all of them pointed out that there had been significant changes in communicating with their patients. They would listen more and be supportive. They stated that their relationship with subordinates changed, as well; they started to share more, and felt as a team more than they used to be. Although the participants did not have residents to train, they enjoyed using their teaching skills for undergraduate students, which they already have. The teaching environment was depressing, and the primary care setting was not relevant to training. There were too many patients, insufficient equipment, and insufficient or ineffective human force. Trainers were not named officially, and various centers without a communication and collaboration among them organized training activities. All those circumstances together were demotivating and frustrating the trainers. No incentives, no recognition, working harder than others, jealousy of the colleagues, unwillingness of the subordinates to work with them were some of the results of being a trainer in the primary care. They were feeling lonely, and losing self-confidence at their practices, outside the meeting group. They had uncertainty regarding the short training program, the future, the health policies, and regarding the discipline.

The EURACT courses initiated the discussion of where the family doctors in Turkey would place themselves as trainers. Conducting the ETC at the national level brought together various advantages. Talking in native language facilitated improving communication skills by using of metaphors, rhymes as well as voice tone, posture, and so forth. Practitioners and family physicians had a chance to understand how close they are, by sharing their experiences and expectations during the courses, and to discuss different aspects of the discipline and equalize the knowledge, develop common understanding, and generate new ideas. In developing countries, it is not possible to encounter all social, historical and economic factors that transform traditional GP to a discipline. Communicable diseases such as measles, water sanitation, and low-income ratios are still problems in such countries. However, high life expectancy rates, high level patient expectations, usage of high technology exists in the developing countries just as in the developed countries. This situation creates very specific problems for establishing and improving FM/ GP in developing countries. That is why we have to use all the tools that we have gotten, by using them for purposes other than they are intended to.

Received 1st October 2005. Accepted for publication in final form 10th January 2006.

From the Family Medicine Department (Basak), Adnan Menderes University Medical School, and Family Medicine Department (Guldal), Dokuz Eylul University Medical School, Turkey. Address correspondence and reprint requests to: Dr. Dilek Guldal, Family Physician, Dokuz Eylul Universitesi Rektorlugu, Cumhuriyet Bulvarı No:144 35210 Alsancak, Izmir, Turkey. Tel. +90 (232) 4648166. Fax. +90 (232) 4648135. E-mail: dilek.guldal@deu.edu.tr

References

- Svab I, Yaphe Y, De Sousa JC, Passerini G. An international course for faculty development in Family Medicine: the Slovenian model. *Med Educ* 1999; 33: 780-781.
- EURACT Presentation Booklet. June 2004. p. 10. Available from URL: http://www.euract.org
- Basak O, Saatci E. The developments of general practice/ family medicine in Turkey. *Eur J Gen Pract* 1998; 4: 126-129.
- Basak O, Saatci E, Ceyhun G. Akademik Aile hekimligi ve gelisme ozellikleri: Turkiye deneyimi. *Turk Aile Hek Derg* 2005; 93: (In Turkish) Accepted for publication.
- 5. Boelen C, Haq C, Hunt W, Rivo M, Shahady E. Education and professional development. Improving health systems: the contribution of family medicine. Singapore: WONCA; 2002. p. 74-117.