International Journal of Occupational Medicine and Environmental Health, Vol. 10, No 3, 259–265, 1997

ORIGINAL PAPERS

DETERMINATION OF TISSUE POLYPEPTIDE ANTIGENS (TPA) AND CARCINOEMBRYONIC ANTIGEN (CEA) IN SERUM: ITS VALUE IN THE PRELIMINARY CANCER RISK ASSESSMENT IN ASBESTOS EXPOSED WORKERS

WALDEMAR LUTZ, BOŻENNA KRAJEWSKA and BOŻENA PIŁACIK

Department of Laboratory Diagnostics
The Nofer Institute of Occupational Medicine
Łódź, Poland

Key words: Asbestos, Serum TPA and CEA

Abstract. Seeking the changes at the cellular level or at the level of cellular metabolism products, present in the biological fluids, in order to detect early stages of the carcinogenic process is an essential step in preventing cancer development among asbestos exposed workers. Carcinogenic biomarkers such as tissue polypeptide antigens (TPA) and carcinoembryonic antigen (CEA) were found very useful in this attempt.

The objective of this work was to identify individuals at critical cancer risk in the population of workers exposed to asbestos and to evaluate the value of TPA and CEA determinations for this particular purpose.

The study was carried out in the group of workers exposed to asbestos (n = 274). Age, exposure duration, smoking habits and the kind of job performed, were concidered in the analysis of the results.

To sum up, it should be concluded that in 22 persons exposed to asbestos TPA values exceeded the cut off concentrations, established on the basis of the studies performed in the control group, and CEA value accounted for 10 ng/lm. Statistically significant differences in the percentage of TPA increased values between two groups under study were indicated. Such a relationship did not apply to CEA. In the exposed group, an evident effect of the age and exposure duration on the number of persons with TPA concentrations above the cut off, was also revealed. These changes show a growing tendency and statistical significance for TPA only. Smoking had a great impact on the occurrence of TPA increased concentrations.

Three kinds of jobs were considered: operation of the production line, white collar workers and miscellaneous'. The significant differences in TPA concentrations between the operators and miscellaneous, and between white collar workers and miscellaneous were found. Therefore, it may be concluded that a similar percentage of TPA increased values was observed in the group of operators and white collar workers.

The study allowed to identify, among those exposed to asbestos, 22 persons who should be covered with target medical care. It also indicated that TPA determination was more useful than that of CEA in this kind of investigations.

Address reprint requests to Prof. W. Lutz, Department of Laboratory Diagnostics, The Nofer Institute of Occupational Medicine, P.O. Box 199, 90-950 Łódź, Poland.

INTRODUCTION

Recently, researchers in the field of occupational medicine have more and more frequently introduced different specific and nonspecific biochemical markers whose changed levels in biological fluids inform about the onset of the carcinogenic process. They seek, among others, cellular macromolecule adducts produced by carcinogenic substances, investigate mutagenic activity or detect cytogenetic changes in the biological material as well as they monitor oncoproteins as biomarkers easily available in the biological fluids (1,5).

At present, studies of biomarkers develop into two directions, some seek changes at the genome level or at the level of protein products which participate in the regulation of cell division and cellular alteration, so called oncogenes (2), others seek biomarkers which reflect changes related to the impairment of intra- and intercellular communication (8,9). The latter parameter has been applied, and has been recognised in occupational medicine due to easy available biological material (blood, urine), feasibility of covering large populations and relatively low costs.

Particular interest is arised by these neoplastic markers which reflect the promotion stage of the carcinogenic process, namely this stage which shows the features of reversibility. Two neoplastic biomarkers should be mentioned here: tissue polypeptide antigens and carcinoembryonic antigen. They belong to the group of biomarkers which are used to evaluate early health effects of chemical carcinogens.

Carcinoembryonic antigen (CEA) appears, among others, in the biological fluids due to neoplastic transformation (10) which results from unblocking and depression of so called 'silent genes' and synthesis of proteins not existing in the cells before the onset of this process.

Tissue polypeptide antigen (TPA) appears in the biological fluids as a result of cellular release under conditions of an intensified proliferation (3). It is considered that resting cells do not contain TPA and even if they do it is in small quantities. This protein appears, and its concentration increases in cells just before their division, and the largest quantity of TPA can be found in cells during mitosis. Both TPA and CEA may appear many years before the manifestation of overt symptoms of neoplastic disease.

This work aimed at defining the incidence of increased TPA and CEA concentrations in workers exposed to asbestos with special reference to exposure duration and tobacco smoking.

MATERIALS AND METHODS

The study covered a group of 274 asbestos exposed workers. Serum TPA and CEA concenterations were measured in all workers. The subjects were interviewed in order to collect information on smoking habits, and duration of employment under exposure to asbestos.

TPA concentration was determined by means of radioimmunometric method using a ready-made kit produced by Prolifigen Sangtec Medical, and CEA by the RIA method of POLATOM Co.

The mean age of the exposed subjects was 42.8 years, and 64% of those under study smoked.

In our own studies carried out earlier (6) in the group of persons nonexposed occupationally to carcinogenic substances, the cut off concentration for neoplastic biomarkers under study, corresponding to 95 percentile, was established at 84.5 U/L for TPA and 6.2 ng/ml for CEA. Setting cut off values helped to analyse the obtained concentrations of markers under study in the exposed group.

Fisher's exact test was used in statistical analysis.

Data on the study group as well as TPA and CEA concentrations are given in Table 1. In the group of 274 workers exposed to asbestos it was feasible to find out what jobs were performed by 231 subjects. This information helped to analyse whether the kind of job performed has any impact on the concentrations of investigated biomarkers. The size of exposure to asbestos expressed by the fibre/year ratio was identified for 97 workers engaged directly in the production of asbestos cardboards and working together in the same production room.

Table 1. Serum TPA and CEA concentrations in asbestos exposed workers

	Mean values	Range
TPA	44.4 (U/l)	20.4 – 158.6 (U/l)
CEA	2.8 (ng/ml)	0.5 – 67.0 (ng/ml)
Age (years)	41.6	21 – 62
Duration of exposure (years)	15.6	1 – 30
Group size	274	

From 1980 asbestos respirable fibres have been measured in the workplace under study. The measurements were taken by the employees of the Department of Aerosoles, The Nofer Institute of Occupational Medicine, Łódź. The mean values of respirable fibre measurements taken at individual workposts during the years 1986 – 90 and the data on the duration of employment under exposure were used to calculate the size of the workers' exposure.

DISCUSSION

The question why asbestos is carcinogenic has not as yet been fully elucidated. It is thought that asbestos fibres may damage macrophages and fibroblasts, which undergo carcinogenic transformation, or that asbestos carconogenesis is the function of the fibre length and the fibre diameter, and depends on the physical and chemical structure of fibres, or that free radicals released due to incomplete phagocytosis of fibres may be responsible for peroxidase and damage of macromolecules.

Our own study was aimed at identifying, among those exposed to asbestos, persons with increased values of serum TPA and CEA concentrations in order to refer them to target medical care. The percentage of concentrations above the cut-off, ie border oncentration, established in the nonexposed group, was most frequently used in our analysis to characterise the group investigated.

The first stage of our study was designed to analyse the effect of the age and duration of employment on the biomarker values. It is well known that the latency of lung cancer induced by asbestos exposure ranges between 20 – 30 years. Fig. 1 gives the percentage of TPA and CEA concentrations above cut off in the group studied.

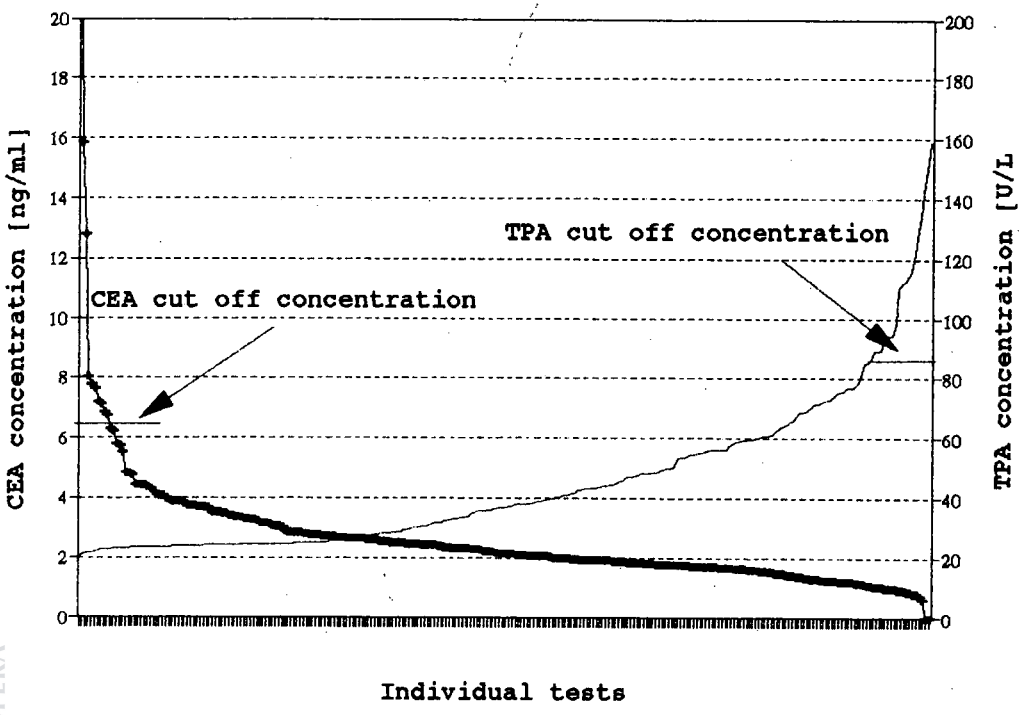

Fig. 1. Distribution of serum TPA and CEA concentrations in asbestos exposed workers.

TPA concentration above cut off was found in 22 workers and CEA concentration in 10 workers. The relationship between the percentage of increased values and the age and exposure duration was analysed. The percentage of TPA values above cut off showed a growing tendency in the successive age groups and it is statistically significant (0.01). CEA values did not show similar relationship. The analysis of the relationship between the increased TPA and CEA values and duration of asbestos exposure revealed the highest percentage of increased TPA values in a 11–15 year exposure interval (15.9%) and CEA values in a 16–20 year interval (9.5%).

Finally, the effect of tobacco smoking on TPA and CEA concentrations was investigated. Smoking is one of the major carcinogenic factors, and in the opinion of some authors (4,7,11) asbestos and tobacco neoplastic synergy is found to be multiplicative.

In the exposed group there were 144 heavy smokers; of this number 15 persons (10.4%) showed TPA concentrations above the cut off. In the group of nonsmokers, the number of those with increased TPA values was twice as low, accountig for 7 persons (5.3%) only. As far as CEA concentrations are concerned, there were 6 smokers and 4 nonsmokers with increased values. The study confirmed the adverse effect of smoking primarily on the occurrence of TPA increased concentrations; the frequency of occurrence was two times higher in smoking workers exposed to asbestos (Fig. 2).

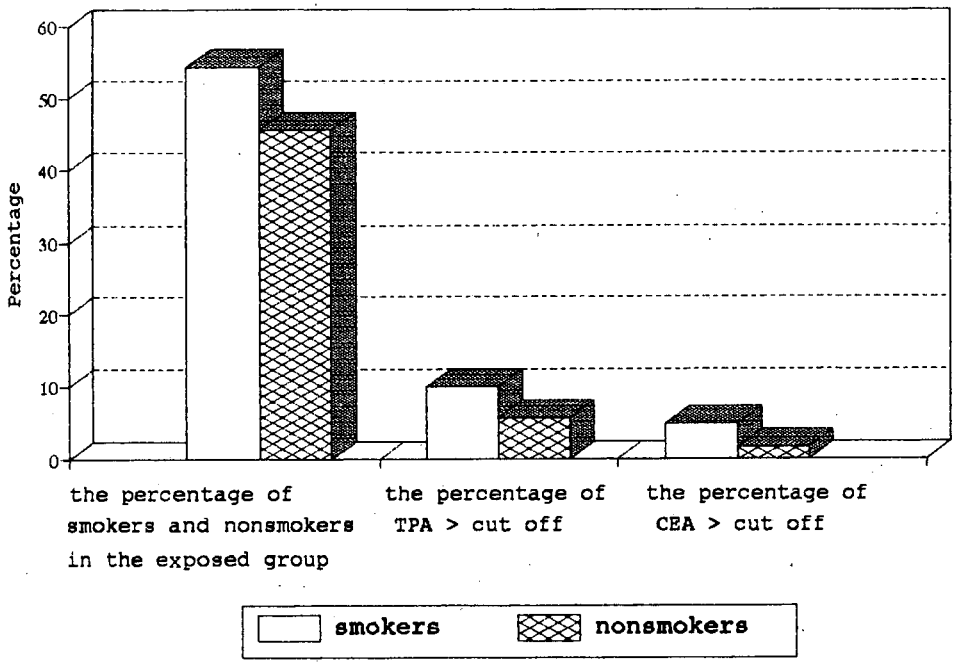

Fig. 2. The percentage of TPA and CEA concentrations > 'cut off' in the group studied, taking into account smoking habits.

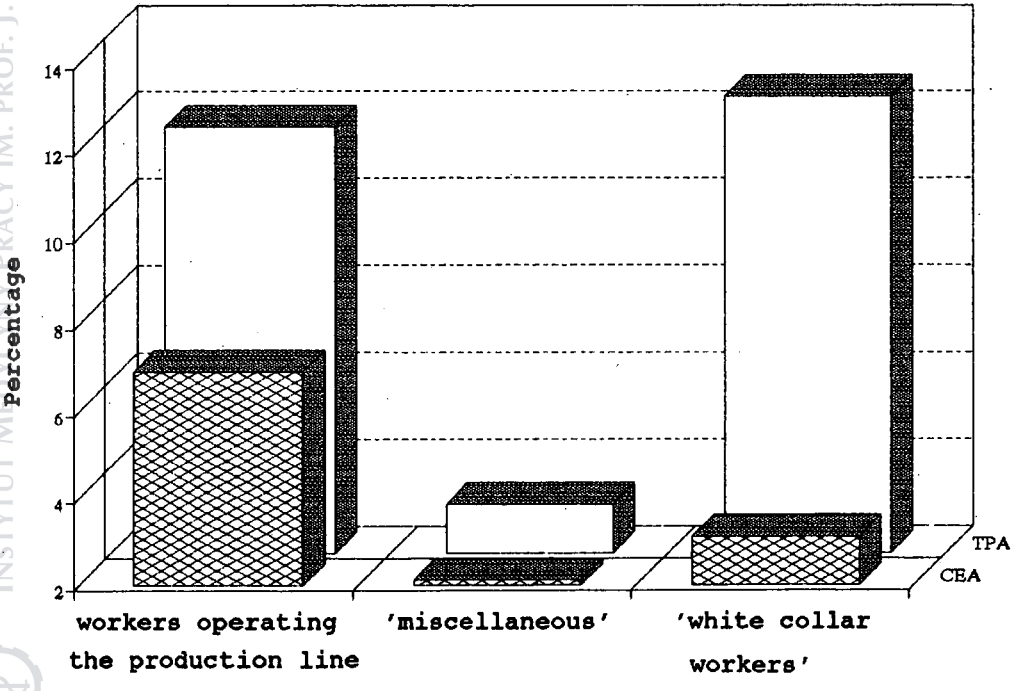

Fig. 3. The percentage of the increased TPA and CEA concentrations in the group studied depending on the kind of jobs performed.

As mentioned earlier, we managed to collect data on workposts of 231 persons. Therefore, it was feasible to evaluate the effect of particular workplaces on TPA and CEA concentrations. Fig. 3 illustrates the percentage of concentrations above the cut-off depending on the job performed. The workers were splitted into three groups: those who operate the production line; clerks and production managers as well as laboratory workers – 'white collar workers'; and those working in different workshops, porters and canteen personnel – 'miscellaneous'. Statistically significant differences in the increased TPA concentrations were found between operators and 'miscellaneous'; and between 'white collar workers' and 'miscellaneous'. Therefore, it may be concluded that both in the group of operators and in the group of white collar workers, the percentage of concentrations above the cut off was similar and it accounted for 11.76% and 12.50%, respectively.

Exposure to asbestos of individual workers was evaluated taking into account the duration of employment under exposure to a given concentration (fiber/cm^3) of asbestos fibres and expressed in the fiber/year ratio. It is thought that the value of no observed adverse effects level (NOAEL), namely 20 fiber/years, should not produce any adverse health effects.

A group of 97 persons engaged directly in the production line and working in the same room was studied. The production line involved the following activities: transport of asbestos bags from the main store-room (30 operations per shift) to crushing mills where asbestos was defiberated; from crushing mills asbestos was conveyed to the hydropulper for further water defibrating, the mass was pomped to mixers where cement and water were added, finally the mixture was formed. The group of 97 persons was composed of 28 workers with exposure above 20 fibre/years (group I); 32 workers with exposure of 10–20 fibre/years (group II); and 37 workers with exposure under 10 fibre/years (group III). The increased TPA concentrations were detected in 7.1% of persons in the group I; in 19.0% group II; and in 5.4% – group III (Fig. 4).

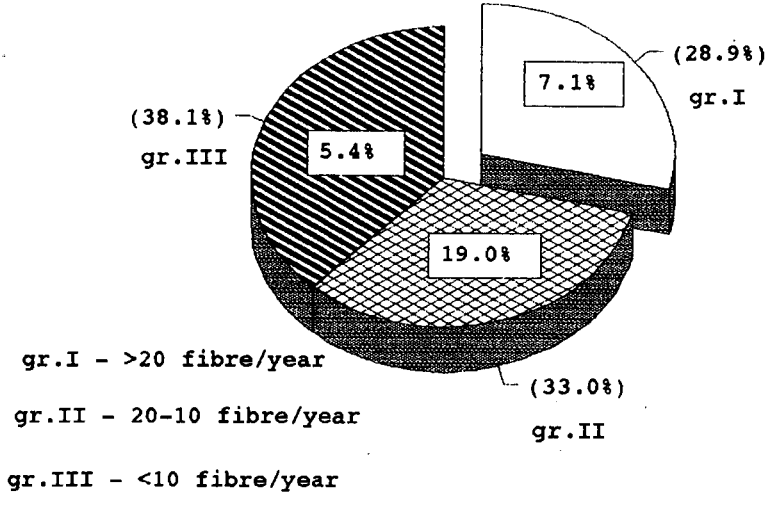

Fig. 4. The percentage of the increased TPA concentrations in asbestos exposed workers depending on the exposure expressed in fibre/years.

CEA concentrations above the cut-off were found in the groups II and III: 6.3% and 9.3%, respectively. A lower percentage of increased TPA values in the group I of the highest exposure is most likely due to considerably lower percentage of smokers. The percentage of smokers in individual groups was as follows: group I – 25%; group II – 59.4%; and group III – 43.2%. This observation confirms again that cancer risk is higher in these asbestos exposed workers who smoke.

CONCLUSIONS

1. The studies carried out in the group of 274 persons indicated more useful determination of tissue polypeptide antigens (TPA) than that of carcinoembryonic antigen (CEA) in the target, comprehensive evaluation of the health condition of the asbestos exposed workers.

2. The percentage of TPA concentrations above the cut off was significantly higher in the asbestos exposed workers than in the control group.

3. A statistically significant growing tendency in the percentage of the increased TPA values in the asbestos exposed workers depending on the age and duration of employment was observed.

4. The effect of tobacco smoking on the concentration levels of studied biomarkers was confirmed. Statistically significant differences for TPA were revealed.

5. The study helped to identify, in the group analysed, 32 persons with higher values of neoplastic markers what should commit health services to more frequent check-ups in this population of workers.

REFERENCES

1. Brandt-Rauf PW. New markers for monitoring occupational cancer. The example of oncogene proteins. J Occup Med 30: 399–404, 1988.
2. Brandt-Rauf PW. Oncogenes and oncoproteins in occupational carcinogenesis. Scand J Work Environ Health 18, suppl. 1: 27–30, 1991.
3. Clippele C, Pluygers E, Baldewyns P et al. The use of Tissue Polypeptide Antigen (TPA) determination in gastrointestinal tract malignancies. Acta Gastro-Enterologica Belgica 11: 52–62, 1987 (in French).
4. Hammond EC, Selikof IJ, Seidman H. Asbestos exposure, cigarette smoking and death rates. Ann Ny Acad Sci 330: 473–479, 1979.
5. Indulski JA, Lutz W, Krajewska B. Biological marker of early health effects in the assessment of risk of cancer in people exposed to environmental carcinogens. Pol J Occup Med Environ Health 6 (2), 149–156, 1993.
6. Krajewska B, Stelmach W, Lutz W, Matych J. Tissue polypeptide antigens and carcinoembryonic antigen in cancer of bladder. Med Pr 46 (1): 7–16, 1995.
7. Loeb LA, Ernster VL, Warner KE, Abbota J, Lazlo J. Smoking and lung cancer: an overview. Cancer Res 44: 5940–5945, 1984.
8. Pluygers E, Baldewyns P, Beaudun M. Carcino-embryonic antigen as a marker of carcinogenesis. J Cancer Res Clin Oncol 16, 94–100, 1990.
9. Pluygers E, Beaudun M, Baldewyns P. Tumor markers for cancer detection. Cancer DCT Prev 9: 495–504, 1986.
10. Seuliar JP. Value of CEA determination in biological fluids and tissues. Europ J Cancer Clin Oncol 7: 1091–1101, 1987.
11. Selikoff LJ, Hammond EC, Churg J. Asbestos exposure, smoking, and neoplasia. J Am Med Assoc 37: 803–809, 1968.

Received for publication: April 21, 1997
Approved for publication: July 7, 1997