The Potential Ability of Plaster to Cause Breast Cancer as Indicated by CA15-3 and CEA Antigens in Women Working in Gypsum Factory

(A Short commiuncation)

Ali Abdul Hussein S. AL-Janabi*[1]

1) Department of Microbiology, College of Medicine, University of Karbala, Karbala-Iraq

**Author for Correspondence:* aljanabi_bio@yahoo.com

Received: 28 Dec. 2016, Revised: 16 Feb. 2017, Accepted: 09 Mar. 2017

ABSTRACT

Plaster is an important form of gypsum that mainly used in building construction. Breast cancer was investigated among women exposure to the dust of such material. The levels of CA15-3 and carcinoembryonic antigens (CEA) as indicators for breast cancer were measured in the serum of 120 women working in a plaster factory. All of involved women showed a normal level of CEA, while 12.5% of them had moderately elevated levels of CA15-3. In conclusion; plaster dust has no significant effect to cause breast cancer in working women. Moderately high levels of CA15-3 in some of exposed women may relate to liver diseases.

Key words: Breast Cancer, Plaster, CA15-3, CEA

INTRODUCTION

The gypsum compound that consists of calcium sulfate dihydrate ($CaSO_4.2H_2O$) is widely used in the building constructions [1]. It is very old material which was used in ancient Egypt to build the pyramids [2]. In nature, gypsum occurs as sedimentary material resulting from the condensation of evaporates originating from marine waters or from many industrial processes. At present, gypsum can be produced in different forms, including anhydrite, selenite, calcined gypsum and plaster of Paris [1]. Plaster is an important form of gypsum that is used as a thermal isolation layer or for building walls, protective against external weather conditions [3]. Exposure of the human body to gypsum materials may induce the development of many symptoms, including a bleeding nose, coughing, fatigue, hypertension, diabetes, shortness of breath, and itching of the skin, eyes, or respiratory tract [4-5]. On the other hand, breast cancer was diagnosed in occupational workers who were exposed to the dust of many other industrial materials such as asbestos and wood dusts [6], while it has not been confirmed in workers exposed to gypsum until now [1].

Breast cancer is a very common type of cancer among females worldwide, including Arabic females [7-8]. Early diagnosis of such type of cancer needs to use many of immunological or serological tests based on detecting of several biomarkers such as MUC1, HER-2/neu, estrogen receptor, and progesterone receptor [9]. CA15-3 or MUC1 antigen, related to a large family of glycoproteins, is commonly used as a biomarker to detect breast cancer and its metastasis stages [10-12]. Whereas, carcinoembryonic antigen (CEA), which is another type of glycoprotein antigen is mainly used for diagnosis of colorectal cancer in addition to the breast cancer [13]. Therefore, measurement of CEA levels is important to increase the value of CA15-3 antigen for diagnosis of breast cancer, especially when a metastasis stage [14]. The possible relationship between exposure to gypsum or plaster and development of breast cancer was investigated in women working in plaster (gypsum) factory as indicated by the CA15-3 and CEA antigens.

MATERIALS AND METHODS

Study design

The study was designed as a cohort study to detect breast cancer through the measurement of two serological biomarkers, including CA15-3 and CEA antigens in the blood of voluntary consenting women working in a gypsum factory.

Sample collection

Serum samples were collected from 120 women (age mean; 42 years) who enclosed contact with a plaster material of gypsum factory of Karbala province in February 2015. Other women are working in other parts of the factory, especially in management building that far away from productive sectors were excluded. Working duration in the factory takes about at least 8 hrs without shifting. The factory usually produces various types of plaster from gypsum materials that differ in granular size (fine and

coarse granules) with a production capacity around of approximately 40 tons per hour. The environment of the most productive sectors of the plaster factory was under the control of universal environmental protection rules, but even there gypsum dust can be found accumulated in the area surrounding those sectors. The women volunteers were reported to suffer from different allergic symptoms and some with the liver function disorder.

Reagents

The CA15-3 and carcinoembryonic antigen (CEA) ELISA kits were purchased from Human Gesellschaft für Biochemica and Diagnostica mbH (Germany).

Assay

Direct antigen ELISA technique which is more sensitive and specific assay was used to measure the levels of CA15-3 and CEA antigens in serum samples. The assay depends on the high affinity of the system biotin-Streptavidin. Each duplicate wells of 96-microtiteration plates that coated with Streptavidin received 25µl of the calibration solution, serum sample, or controls (serum from normal individual and distal water). A 100µl of conjugate B (biotin) was added to each well, followed by mixing for 20-30 Sec and incubated for 60 min at 25$^{\circ C}$. All microtiter wells were automatically washed 3 times by 350µl of the working wash solution. A 100µl of enzyme-labelled antibody was added into the wells to form the final sandwich complex, followed by incubation for 60 min at 25$^{\circ C}$. After incubation, excess conjugate was washed out by 350µl of the working wash solution, then 100µl of substrate reagent was added. The plate was incubated for 20 min at 25$^{\circ C}$, then mixed with 50µl of stop solution for 15 Sec. The absorbance of the final product was measured at 450nm within 30 min by a BioTek ELx800 ELISA reader (U.S.A). The concentrations of the test samples were obtained by means of a calibration curve, which was established from the calibrators supplied with the kit. As mentioned in the manufacturer's instructions, the expected value for CA15-3 antigen ELISA in healthy individuals is ≤37U/ml, while it is <5ng/ml for CEA.

Statistical analysis

Data of all tests were expressed as mean ± SD. The values were analyzed statistically with paired "t" test. The minimum level of (p) value was < 0.01 which is considered a significant level.

RESULTS

The presence of breast cancer in the working women in a plaster production factory was investigated by measuring the levels of CA15-3 and CEA antigens.

From one hundred and twenty women, no one had elevated levels of CEA and all of their blood samples showed a normal value of this antigen (≤ 5 ng/ml). Meanwhile, a total of 15 (12.5%) of women volunteers revealed a non-significant moderately high level of CA15-3 antigen (40U/ml)(Table 1). The insignificant differences (p< 0.01) of women with elevated CA15-3 from a total number were also considered an indicator for eliminating the presence of breast cancer in the body of the women involved.

Table (1): The levels of CA15-3 and CEA in the blood of exposed women to gypsum.

CA15-3 level (U/ml)	No. of women (%)	CEA level (ng/ml)	Total No.
≤37	105 ± 1.2 (87.5%)	< 5	120 (100%)
40	15 ± 0.9 (12.5%)		
Total No.	120		120

Mean ± SD

* Significant differences at P<0.01

Normal value of CA15-3 antigen is ≤ 37 U/ml, and of CEA is < 5 ng/ml.

DISCUSSION

Gypsum is an important source of calcium and sulfur due to its high contents of calcium sulfate dihydrate [1, 15]. Therefore, the exposure of the human body to gypsum has often caused the development of different types of health issues such as irritation in many parts of the human body, especially in the eyes, skin and respiratory tract [1, 4, 16]. Moreover, emission of hydrogen sulfide from gypsum after use as bedding on farms could be another health issue [15].

In the present study, all of the women involved showed a normal value of CEA with a moderately high level of CA15-3 antigen in some of them. Based on the instructions included with the ELISA kit that was used in our study, the normal value of CA15-3 antigen should be equal or less than 37 U/ml. Thus, the moderately high level of CA15-3 antigen (40 U/ml) found in the serum of some of the working women involved could not be considered a significant indicator of the presence of breast cancer. Although CA15-3 antigen is more specific for diagnosis of breast cancer, its level can also increase resulting from some benign diseases such as liver diseases [17]. The women involved with high levels of CA15-3 were given further specific clinical and laboratory analysis to check their health condition. It was found that they were suffering from a disorder in their liver functions. Patients with chronic hepatitis, liver cirrhosis and hepatitis B infection were recorded to have high levels of CA15-3 in 42.9%, 13.3%, 28.5% of them, respectively [17-18]. Thus, we can assume that the elevated levels of CA15-3 antigen in

some of the women involved may be related to the presence of liver diseases and not to the breast cancer. This was confirmed by the normal value of the CEA. In a previous study, a CA15-3 antigen found to be elevated more than 30 U/ml in 1.3% of healthy individuals or in patients suffering from other types of cancer diseases such as gastrointestinal malignancies, bronchogenic carcinoma and ovarian carcinoma [19]. Thus, it is important to check the level of other biomarkers like CEA, CA 27.29 antigens or Alkaline phosphatase (ALP) to increase the diagnostic sensitivity of CA15-3 for breast cancer [14, 19-21].

As confirmed in many studies, women in industrial occupations can get breast cancer through exposure to the dust of various types of materials emitted from different industrial processes, contaminated air of the factory, or even from the loading or movement of vehicles within or outside the factory [22-23]. Unlike gypsum dust, which is considered a weak tumorigenic agent [1], many other dusts have been certified to be carcinogenic substances such as asbestos, free crystalline, hexavalent chromium, and certain wood dusts [6]. However, with the exception of some benign diseases, there is no evidence that gypsum or any of its products (e.g. cement) have carcinogenic effects on the human body [1, 24]. Meanwhile, primary experiments on animals for the carcinogenicity ability of gypsum after exposure via inhalation or injection have shown that gypsum has some potential ability to cause cancer diseases, while the studies in humans do not offer any proof. Intraperitoneal injection of gypsum in rats revealed the development of an abdominal cavity tumor in 5% of them, while a heart and kidney carcinoma had been noticed in hamsters after intratracheal administration [1].

CONCLUSSION

occupational exposure of working women with a plaster dust showed an insignificant ability to cause breast cancer as confirmed by measuring the levels of CA15-3 and CEA antigens. Moderately high levels of CA15-3 in some women exposed may result from a liver disease. Other biomedical markers or mammography imaging specifically for breast cancer are recommended for women who are exposed to gypsum in order to confirm the presence or absence of breast cancer.

ETHICAL ISSUES

The author confirms that this paper does not cite from others and not published in other journals.

CONFLICT OF INTEREST

There is no conflict of interest and not funded for this manuscript by any organization.

FUNDING/ SUPPRTING

There is no funding for this research

REFERENCES

[1] Integrated Laboratory Systems (ILS), Inc. Chemical information review document for synthetic and naturally mined gypsum. CAS No. 13397-24-25. 2006. Available at: http://ntp.niehs.nih.gov/.

[2] Olson DW. Gypsum. U.S. Geological survey minerals yearbook. 2001. 35:1-10, Available at: https://minerals.usgs.gov/minerals/pubs/commodity/gypsum/gypsmyb01.pdf.

[3]. Dylewski R, Adamczyk J. The comparison of thermal insulation types of plaster with cement plaster. J Cleaner Production. 2014, 83: 256-62.

[4]. De Medeiros MS, Hurtado-Guerrero JC, Silva LG. Health in the context of the gypsum production area of the city of Araripina, State of Pernambuco, Brazil. Saúde Soc. São Paulo. 2010, 19(2): 358-70.

[5]. Nandi SS, Dhatrak SV, Chaterjee DM, Dhumne UL. Health survey in gypsum mines in India. Indian J Community Med. 2009, 34(4):343-45.

[6]. Van Thienen G, Spee T. Health effects of construction materials and construction products. TTA brochure NRI. 2008, 13-14(1):2- 23.

[7]. Freedman LS, Edwards BK, Ries LA, Young JL. Cancer incidence in four member countries (Cyprus, Egypt, Israel, and Jordan) of the Middle East cancer consortium (MECC) compared with US SEER. National cancer Institute.NIH Pub. No. 06-5873. Bethesda.2001.

[8]. Rizwan MM, Saadullah M. Lack awareness about breast cancer and its screening in developing countries. Indian J cancer. 2009; 46(3): 252-253.

[9]. Misek DE, Kim EH. Protein biomarkers for the early detection of breast cancer. International J Proteomics. 2011, ID 343582:1-9.

[10]. Daniele A, Divella R, Trerotoli P, Caringella ME, Paradiso A, Casamassima P, *et al.* Clinical usefulness of cancer antigen 15-3 in breast cancer patients before and after surgery. The Open Breast Cancer J. 2013, 5:1-6.

[11]. Chourin S, Georgescu D, Gray C, Guillemet C, Loeb A, Veyret C, Basuyau JP. Value of CA15-3 determination in the initial management of breast cancer patients. Annals of Oncology. 2009, 20(5):962-64.

[12]. Duffy MJ, Shering S, Sherry F, McDermott E, O'Higgins N. CA15-3: a prognostic marker in breast cancer. Int J Biol Markers. 2000, 15(4): 330-33.

[13]. Yerushalmi R, Tyldesley S, Kennecke H, *et al.* Tumor markers in metastatic breast cancer subtypes:

frequency of elevation and correlation with outcome. Annals of Oncology. 2011:1-8.
[14]. Laessig D, Nagel D, Heinemann V, Untch M, kahlert S, Bauerfeind I, Stieber P. Importance of CEA and CA15-3 during disease progression in metastatic breast cancer patients. Anticancer Research. 2007, 27: 1963-68.
[15]. Eskildsen T, Glazier N, Gooch C, Czymmek KJ. Gypsum bedding in long-term manure storage may create dangerous conditions. Cvent. 2013. http://www.manuremanagement.cornell.edu/Pages/Topics/Safety.html.
[16]. Brun P, Kunz A, Funke M. Buried under gypsum powder-a rare respiratory complication. Respiratory Medicine. 2013, 8: 36-39.
[17]. Colomer R, Ruibal A, Genollá J, Rubio D, Del Campo JM, Bodi R, Salvador L. Circulating CA15-3 levels in the postsurgical follow-up of breast cancer patients and non-malignant diseases. Breast Cancer Res Treat. 1989, 13(2):123-33.
[18]. Yeganeh-Amirkande S, Assmar M, Ghanaei-Faribors M, Mozafari-Noor A. The frequency of CA15-3, CA125, CA19-9 in patients with hepatitis B and C. Zahedan J Res Med Sci. 2015:29-33.
[19]. Hayes DF, Zurawski VR Jr, Kufe DW. Comparison of circulating CA15-3 and carcinoembryonic antigen levels in patients with breast cancer. J Clin Oncol. 1986, 4(10):1542-50.
[20]. Keshaviah A, Dellapasqua S, Rotmensz N, Lindtner J, Crivellari D, Collins J, *et al*. CA15-3 and alkaline phosphatase as predictors for breast cancer recurrence: a combined analysis of seven international breast cancer study group trials. Annals of Oncology. 2007, 18:701-08.
[21]. Gion M, Mione R, Leon AE, Dittadi R. Comparison of the diagnostic accuracy of CA27.29 and CA15.3 in primary breast cancer. Clinical Chemistry. 1999, 45(5):630-37.
[22]. Clapp RW, Jacobs MM, Loechler EL. Environmental and occupational causes of cancer new evidence, 2005-2007. Rev Environ Health. 2008, 23(1):1-37.
[23]. Galay K. Socio-economic and environmental impact analysis of Khothagpa gypsum mine. J Bhutan Studies. 2008, 18:50-81.
[24]. Manjula R, Praveena R, Clevin RR, Ghattargi CH, Dorle AS, Lalitha DH. Effects of occupational dust exposure on the health status of Portland cement factory workers. International J Medicine and Public Health. 2013, 3(issue 3):192-96.