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LIMITING FACTORS OF BRCA GENETIC TESTING AT RISK POPULATION

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Abstract

Most of genetic breast cancers are related to carrying a BRCA1 or BRCA2 gene mutation. Clinical observation and statistics show that only a small number of women (which have a genetic risk for carring BRCA1 or BRCA2 mutations) actually do the test. The aim of the paper is to examine which are the psycho-social factors involved in testing decision. Methods: 68 women was devided in two groups. First group contains current or past breast cancer patients, diagnosed under the age of 45. The second group contains clinicaly healthy women, having close relatives diagnosed with breast cancer or being BRCA mutation carriers. The women with psychiatric disorders were excluded. A genogram was made for each woman. Decisional capacity was assess with a psychological tool already validated on Romanian population. A questionnaire was conceived in order to rank the factors. Results: different results were obtain in the two groups. The high cost of testing was considered as first negative factor and it was reported as such by the women already diagnosed with breast cancer; this was followed by the fear related to the fact that descendants can make the disease and by the fear of getting the ilness themselves. Ignorance or lack of medical education, fear of results related to self, inability to take a decision after a positive result and high cost of test were the main psychological and social limiters found in the group of healthy women. Conclusions and discussions: public health policies and insurance policies should be reviewed in order to ensure a better medical education concerning the risk of being carrier for BRCA1/2 and to cover the cost of genetic testing. Also, as weak points can be considered both the genetic and psychological counseling for women at risk.

Key words: *BRCA1/2, breast cancer, genetic testing*

INTRODUCTION

The breast cancer represents a global health problem and is the most common cause of cancer in women. Approximately 1.7 million women are diagnosed each year, representing 12% of all new cancer cases and a quarter of new cases diagnosed in women (Ferlay et al, 2012). Although therapeutic approaches have evolved a lot (Csapo Gheorghe et al., 2016), the breast cancer remains a life-threatening illness. From this perspective, the past decades have made great efforts in the field of etiopathogenesis research. This fact leaded to the possibility of determining a person's risk of developing breast cancer and to take proper preventive measures (Nelson et al., 2012). One of the significant acquisitions in determining risk factors for breast cancer is the ability to highlight the changes related to suppressor genes BRCA1 and BRCA2 (Welcsh et al., 2001; Metcalfe et al., 2008).

Approximately 15% of all breast cancers are believed to be genetic. Currently is easy to determine the possible mutations of BRCA1 and BRCA2 suppressor genes. A large number of patients considered to be at risk could benefit of this method.

Genetic breast cancer is an inherited condition. The risk is passed from one generation to another. Most genetic breast cancers are related to the presence of BRCA1 and BRCA2 genes mutations (Howlander et al., 2014, Nelson et al., 2012). Typically, the proteins produced by the genes BRCA1 and BRCA2 prevent the cells to become malignant by helping to repair the mutations that occur in other genes. BRCA1 and BRCA2 transmission is autosomal dominant. This means that a person inherits one normal copy of a gene and one altered copy of the gene, but the last one is dominant over the normal one. Thus the risk of being a carrier of one of the genes (under conditions in which it exists at one of the parents) is 50%. There is also one chance in two that the descendant is not a carrier. Risk of developing breast cancer in BRCA1/2 carriers in a lifetime can vary between 40 and 72.8% (Cheng et al., 2007, Howlander et al., 2014).

A method used to detect large genomic rearrangements which would disable the two suppressor genes by analysis of deletions and duplications is MLPA (Multiplex Ligation-Dependent Probe Amplification). Blood samples are taken, saliva or, in rare cases - dermal tissue samples or tumor samples. The result may be: positive (it indicates the presence of a mutation), negative, or with uncertain modification (Levine et al, 2001). In Romania, the cost of genetic testing for BRCA1 and BRCA2 are not reimbursed by the health insurance system. The cost of BRCA1/2 genetic testing exceeds at least a third of the average income of Romanian employees. Genetic counseling, which is recommended before and after testing, has additional cost. Topics approached during genetic counseling take into consideration the opportunity/necessity of genetic testing, the implication of the result, whether is positive or not, management of the positive result, the risk of possible detected mutations transmission to progeny (Hartmann et al., 2001).

Women BRCA1/2 carriers receive recommendation for three categories of preventive measures: enhancing screening in order to detect early the breast cancer, chemoprevention with tamoxifen or raloxifen - which blocks the action of the estrogen and surgical measures. This includes salpingo-oophorectomy and prophylactic mastectomy usually followed by breast reconstruction (Guillem et al., 2006). Genetic testing, as it was described above, is simple to done and the implications of the results are major. However, the clinical observations shows that only a small number of women at risk do actually the test. Our aim is to examine which are the

psychological and social factors that influence genetic testing of BRCA1/2 in risk population.

MATERIAL AND METHOD

A number of 68 women at risk have been selected for this research, devided in two groups. First group was made by breast cancer patient under age of 45 (clinical patients). The second group of patients were relatives of first, second or third degree to the patients with breast cancer (non-clinical patients).

Criteria that were included in the study for clinical patients: women, age between 18-45 years old, breast cancer diagnosed unilateral, bilateral or breast cancer concomitent with ovarian cancer, signing informed consent.

Criteria that were included in the study for non-clinical patients: women, age between 18-45 years old, having a first, second or third degree relative with the breast cancer carrier at young age (under 45), having male breast cancer in the family, belonging to Ashkenhazi Jewish population, signing informed consent.

Excluding criteria were: psychiatric diseases, eye and ear impaired, withdrawal of informed consent.

Assessment methods

Genogram – a technique used in psycho-social field in order to collect information about family structure, a kind of family tree. Making genogram during the interview facilitates communication, updating information about ancesters and extinded family cancer.

Decisional capacity – measures two psychological constructs: decider rationality and indecision. Idecision is seen as avoidance of making a choise when the alternatives are known under the time presure. They had 7 minutes to accomplish the test. This tool has 14 items, each item describes a decisional situation. Scores are divided in five normalised classes from class I, very low decisional capacity to class five, very high decisional capacity (Miclea et al., 2009).

Questionnaire – as a method to collect date in simple and quickly manner was designed and it has four categories of data that has to be obtained: demographic data (age, environment, marital status, education level, income level, religious affiliation, ethnicity, foreign languages), questions about breast cancer in extinded family, questions about genetic cancer knowledge (source of this knowledge, contacting a specialist about being BRCA1/2 carrier, what kind of specialist), propositions that describe reasons for the respondent not done yet genetic testing.

RESULTS AND DISCUSSION

Cilinical patients group has a mean age of 43, median age being 41.48 and non-clinical patients group has a mean age of 35 and median age 33.94. The two groups were homogeneous by the point of view of the environment, marital status, education level, income level, religion, ethnicity and foreign languages.

Genogram showed that our subjects had from one to nine breast cancer close relatives. Similar results were obtained by both groups concerning decisional capacity. 11.4% of healthy women and 6.5% of breast cancer women are not informed that breast cancer may be hereditary. Significant diferences were obtained in having information about BRCA genetic test; 83.3% of clinical group has knowledge about BRCA1/2 and only 58.8% of healthy women (p=0.032).

Sources of information were also different. If healty women have information about BRCA carring risk mainly from mass and social media (34.3%), cancer patients are informed mainly by health medical team (54.8%). No subject are informed by booklets, flyer or other written materials. Most of breast cancer patients were informed about BRACA1/2 carrying risk by the medical oncologist (64.5%) and most of the healthy women by general practitioner (22.9%). Only 2.9% of healthy women at risk had a genetic counsseling and none of breast cancer patients. Patients received advice in a higher proportion to do genetic test than their relatives: 95.8% versus 60% (p=0.005).

The hierarchy of the reasons of not doing the genetic test for breast cancer patient is presented in table 1.

Table 1

Arguments raised by breast cancer patients for not doing the genetic test

Hierarchy	Reasons	% of patients
1	Financial reasons	83.33
2	Fear that a positive results would mean that children could be carriers of mutation too	75.00
3	Fear of positive result	20.83
4	Not having enough time	4.20
5	Inability to make a decision in case of positive result	4.17

As we can see, financial reasons are the main argument considering the fact that the genetic testing cost is way above middle income in Romania. So, the patients, despite having been adivised in a very high proportion over 95%), can not afford it.

Breast cancer patient are more concern about their descendants then theirself when it comes to the presence of BRCA1/2 mutation. No wonder, because our sample is made by young breast cancer patients, most of them having from one to four children.

The hierarchy of the reasons of not doing the genetic test for healty women is showed in table 2

Table 2

Arguments raised by healty women at risk for not doing the genetic test

Hierarchy	Reasons	% of patients
1	Fear of positive result	100
2	Inability to make a decision in case of positive result	70
3	Financial reasons	40
4	Fear that a positive results would mean that children could be carriers of mutation too	20
5	Not having enough time	10

Fear of a positive result is the main reason for healthy women at risk for declining the genetic testing. They are already upset, nervous and concerned about their breast cancer relatives so, they would hardly tolerate emotional distress caused by discovering a mutation of their own DNA. As a result, they think about themselves as inable to make such a hard decision as double mastectomy, ooforectomy, taking estrogen inhibitors or enhanced breast controls in case of finding one of BRCA1/2 mutation.

Financial cost of testing is also a signifiant argument.

CONCLUSIONS

This research underline:

- the poor medical education in healthy population, a high percentage of women has limited or no knowledge about genetic breast cancers even when they have young close relatives fighting breast cancer;
- lack of written materials about genetic cancers and BRCA mutations as a source of information for people at risk;
- need for genetic counseling services to advise women in risk group;
- need for psychological counseling of risk population in order to reduce emotional distress related to possibility of being BRCA carrier;
- need for genetic BRCA1/2 testing of women at risk to be introduced in insurance package in order to eliminated this limiter.

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