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Target the Bite: Knowledge on Lyme's Disease

Anjali Kumar[1*] and Jennings Hernandez[1]

[1]Washington University of Health and Science, Belize.

Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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ABSTRACT

Disease agent *Borrelia burgdorferi* has continued to incrementally spread Lyme disease throughout the United States and has become the concern of the general population's health. Ixodes ticks infected with *Borrelia burgdorferi*, that come in contact with any area of the human body, typically stay attached for a period of 36-48 hours in order for them to completely transfer the bacteria into the host. The symptoms manifested typically inhabit the nervous system, musculoskeletal system and the cardiovascular system. New methods in the diagnostic techniques have been in ongoing research including the SYBR Green I/PI assay which quantifies living bacteria after dosage completion along with molecular testing which uses PCR of synovial fluid, blood, tissue biopsy, and cerebrospinal fluid to detect for an imbalance in OspA and its respective chromosomal targets. Current diagnostic measures of ELISA and Western blot are not reliable due to individuals vaccinated with Lymerix testing positive regardless of infection because it is insensitive to early detection, creates false positives and cannot detect chronic Lyme after treatment.

Keywords: ELISA; B. burgdorferi; Lyme disease; Ixodes tick; SYBR assay; PCR; Western blot; Lymerix vaccine.

**Corresponding author: E-mail: anjalikumar731@gmail.com;*

1. INTRODUCTION

Diagnostic testing most commonly uses ELISA in which elevated levels of antibodies against *Borrelia. burgdorferi* are detected. However, based upon Centers for Disease Control surveillance criteria, ELISA is not sufficient to be the sole diagnostic factor for the confirmation of Lyme disease because in the early stages of the disease, the results may come out negative. Hence, further tests are required to confirm diagnosis. The Western blot tests positive for the antibodies to confirm the diagnosis, but based upon CDC surveillance criteria carried out only if ELISA results are found to be positive. Furthermore, for those patients who suffer from Lyme disease, their diagnosis also encompasses the use of PCR in which bacterial DNA is detected in the joints or in other tissue [1].

Nevertheless, the ELISA test does have a drawback in which it is found to be highly insensitive to the early detection of the disease and its reliability has never been standardized for late stage disease. Often, patients complaining of general myalgia and fatigue have a significantly low probability of actually suffering from Lyme disease. However, in such a situation if ELISA renders a positive result, then it is highly probable and likely that it is a false positive outcome. Therefore, there is a manifold increase in chances of a misdiagnosis and furthermore, unnecessary administration of antibiotics. Additionally, it may take up to several weeks before the patient's immune system generates antibodies in a significant quantity. Therefore, the detection of Lyme disease by serological means is not immediate and ultimately results in further prolonging the time before treatment is administered [2]. This is a major contributing factor which accounts for both morbidity (chronic illness) and mortality due to this disease. Furthermore, blood serum analysis even after completion of an administration of antibiotics is that it is not able to detect chronic Lyme disease in which the bacteria survive. Therefore, bacteria cannot be cultured after treatment completion [3].

Lymerix, a Lyme vaccine, had been in brief use between 1998 and 2002, however it was quickly taken off the market due to ineffectiveness and other considerations. This vaccine was based upon the outer surface protein A of *B. burgdorferi* and consequently those who were vaccinated will develop antibodies. Within its first year of usage, numerous cases of adverse reaction were accounted for. Several studies had shown that a great number of people had developed arthritis as a side effect of to the Lymerix vaccine and thus was discontinued from the market [4]. However, all these diagnostic tests are not the most reliable because vaccinated individuals will still test positive, regardless of the fact that they actually have the disease or not and a number of other reasons.

Nevertheless, there is no alternative better test commonly used. Although, research is currently showing hopes of a new and successful means of early diagnosis to prevent the further delay in treatment. A study being conducted by researchers in which an attempt to measure cytokine levels and memory antibodies in which signs of early infection will be detected. It will allow those patients to be followed through the course of the study and determine who is cured and who develops a chronic situation. However, this study is in its very early stages and cannot confirm of any new diagnostic method as of yet.

2. NEW TESTING METHODS

According to researchers, the majority of patients being treated for Lyme disease, their recovery is successful and the *Borrelia burgdorferi* is eradicated from their bodies a few weeks after the administration of antibiotics [5,6]. Commonly used treatment administers the antibiotic doxycycline or amoxicillin however it still remains ineffective in alleviating the disease in its later stages. However, in some individuals the *Borrelia burgdorferi* survives and remains in the body even after the completion of the standard antibiotic dosage. It is estimated that approximately twenty percent of patients suffer from these long term symptoms known as chronic Lyme disease. The question remains which drugs exactly act against the bacteria which survive, even after the dosage completion. This is the main hurdle in new drug research.

In a study conducted by Ying Zhang, MD, PhD, [7] an innovative technique was applied to an otherwise standard laboratory exam. The normal test only quantifies the DNA in the samples being examined, but this new technique has allowed scientists to be able to count the number of the remaining bacteria after dosage completion that are alive or dead. The one that are still alive are stained with a green marker and those which have died are stained with a red marker. This method shows positive signs in the future of testing because further examination in this study

has revealed that this technique has already been successful in detecting certain drugs which have been approved in curing other bacteria borne diseases [8].

This innovative technique is known as the SYBR Green I/PI assay. Additionally, this new technique has also shown benefits in the economical market as well. It is not only a lower costing procedure, but also is able to examine thousands of drugs in one time. This is simply due to the fact that this technique does not necessitate the washing of each sample of the lingering bacteria; therefore the living or dead bacteria can be quantified immediately after the completion of the antibiotics administration. This allows for greater accuracy in a less time consuming period. Furthermore, the drugs that were able to be detected in this study were those which directly targeted those lingering *Borrelia burgdorferi* which survived. The only concern which remains is that this method is still in its early stages and trials on humans are yet to be carried out.

There is now hope for these patients because there is another new method which has recently been studied which comprises of molecular testing and assays. This measure was taken in order to raise the level of specificity and sensitivity of Lyme disease [9]. These assays make use of PCR to amplify the DNA sequences of the bacteria that is obtained from the patient's samples [10]. They may be from the synovial fluid of the affected joint or a biopsy of tissue. These samples may also be from blood, urine, or cerebrospinal fluid. In those cases in which there is Lyme arthritis (arthritis which resulted due to an adverse effect of the Lymerix vaccine), the polymerase chain reaction examination reveals an imbalance in ospA and the respective chromosomal targets. This imbalance is observed in the synovial fluid sample.

However, the exact mechanism for which there is an imbalance such that there is a significantly elevated level of OspA in respect to the chromosomal target has not yet been clearly known or investigated. Nevertheless, it is hypothesized that this excessive level of ospA that is detected in the synovial fluids of Lyme arthritis patients is due to the representation and detection by PCR of those blebs of the membrane of ospA which were nonviable.

Lyme arthritis is traditionally diagnosed by patient history and a positive result in and immunoserologic examination. On the contrary, those patients who have persistent arthritis remaining even after administration of an antimicrobial treatment have a confounded result due to the fact that the blood serum examination is not able to differentiate between and an infection which is active or inactive [11]. Therefore, the polymerase chain reaction has shown positive results in being able to detect the Lyme disease causing *Borrelia burgdorferi* bacteria in an elevated quantity in the samples of the synovial fluids obtained from those patients who are suffering from cases of Lyme arthritis which is untreated or inadequately treated. The distinguishing factor is that these patients have ospA remaining behind in their synovial fluid whereas those patients who have received administration of antibiotics yet still have persistent arthritis do not have its ospA or it respective chromosomal target at all or in a percentage which may be detected by the polymerase chain reaction test [12,13].

3. LYME VACCINE IN THE MEDIA

Lyme disease has received immense attention from both the public community and medical community since its initial descriptions of the infection. The well known former Lymerix vaccine was put into focus and received great attention in which media reports were giving emphasis to the countless benefits of this very vaccine. However, its potential side effects and risks were highly trivialized. Residents who were occupying those areas which were known to be endemic were highly influences by media reporters to go and seek advice from their health care providers in regards to receiving this vaccination [14].

Nevertheless, both the rise and fall of the Lymerix vaccine were short lived yet its effects were on the contrary. Briefly after it was given license approval, people who received the vaccination began experiencing adverse effects and the number of such cases that were reported began to rise exponentially. The adverse reactions and side effects were not limited to any single type, but rather a vast range of effects were experienced although, reports of arthritis other musculoskeletal conditions were most prevalent. The direction of the media took a new turn in which these cases of vaccinated individuals presenting with adverse reactions were named by media persons were indentified as "vaccine victims".

4. CONCLUSION

Growing public attention and controversy led to an extensive scrutinizing process of the Lymerix vaccine. Several lawsuits representing thousands of individuals were charged against the vaccine. Claims were made stating that the vaccine was bringing harm and posed a high risk of adverse effects. Additionally, several lawsuits against the manufacturer were stating that crucial evidence for the potential risks of the vaccine was being concealed for a money making business strategy. Ultimately, due to many factors including the ineffectiveness of the vaccine, Lymerix was taken off the market.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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