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Predilection Site for the Meat Lover *Trichinella spp* Larvae and its Pathogenesis and Potency in Human Host

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Author's contribution

The sole author designed, analyzed, interpreted and prepared the manuscript.

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ABSTRACT

Aims: To revisited carefully previously published articles available in the internet regarding predilection site of *Trichinella* spp larvae including their pathogenesis and its potency.
Discussion: By carefully reviewing previously published literature available in the internet regarding the parasite *Trichinella tropism* to its host's striated muscle, the author briefly withdraw some important keypoint to be revealed. The nematode *Trichinella* spp causes serious zoonosis called trichinellosis, a disease affecting striated or skeletal muscles which consider as one of tropical disease. Even though its natural host varied, but infection among live stocks, such as pigs and other animals, which are raising public health concern. Human infection occurs after consumption of raw or undercooked meat or meat products contain muscle larvae of *T. spiralis*. The tropism of the parasite for individual striated muscles and/or striated muscle groups varies significantly. Trichinella spp. has a direct life cycle where all three life cycle stages (the infective muscle larvae, adult, and new born larvae) happen serially in one host only. Intestine-dwelling

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adults of Trichinella produce newborn larvae that bypass the enterocyte, enter the bloodstream and colonize skeletal muscle. The muscle larvae assemble excretory-secretory products which play crucial role in establishing and maintaining persistent parasitism and the host's immune modulation and evasion. It turns out that excretory-secretory products from muscle larvae and mature worm also have hidden medical potential that can be used to treat allergic problems, inflammation-based diseases, autoimmunity and even malignancy.

Conclusion: Trichinellosis is a serious and potentially fatal zoonosis which transmitted through consuming raw or uncooked contaminated meat or its comestibles. Its primary tropism is to the host's striated muscle and infection can persist for a long time facilitated by several reciprocities of its product (e.g., excretory-secretory) with the host's cell and immune system. Fortunately, there are several promising potency in the field of therapeutic and prevention medicine which should be explored intensely.

Keywords: Tropical disease; nematode; tropism; striated muscle; carcasses; trichinosis; trichinelosis.

1. INTRODUCTION

The term tropical diseases encompass all diseases, communicable and no communicable, that occur principally in the tropical countries or tropics, areas that lie between, and alongside, the Tropic of Cancer and Tropic of Capricorn belts [1]. Among those communicable group of disease, neglected helminth infections including trichinellosis or trichinosis, which is still a major health problem [2]. There are eleven known species within the genus Trichinella. These eleven species subdivide into those that invade host muscle cells and encapsulate (surrounded by a collagen capsule) and those that do not encapsulate [3,4]. *Trichinella Spiralis*, the most common species in this genus, belongs to the encapsulated group and causes most human infections and deaths from trichinosis [3]. This genus specifically causing a disease which affecting the host's muscles [1-5].

Even though its natural host varied, but infection among popular live stocks such as pigs [5-8] and other animals, e.g., horses [9], wild game meat (meat from an animal that is typically found in the wild and not raised domestically on a farm for mass consumption; usually free-roaming foragers and hunted for their meat) [10], rats [11], wild birds [12], wild and farmed reptiles [13] etc., which are raising public health concern [14], even though its global burden is much lower than that of other foodborne parasitic diseases (a mean estimated 76 healthy life years lost per billion people per year for human trichinellosis, globally [15].

The aim of this study is to revisited predilection site of Trichinella spp larvae in its host including their pathogenesis and potency along with its comestible implication and effort conducted to prevent transmission.

2. LIFE CYCLE AND PATHOGENESIS

Among many member of helminths which affect human, *Trichinella spp*. are distinctive because it has a direct life cycle [16]; which means that all three life cycle stages of the parasite, namely infective muscle larvae, adult, and new born larvae; Intestine-dwelling adults of Trichinella produce newborn larvae that enter the bloodstream and colonize skeletal muscle [17]. Infection is acquired by consumption of infected raw or undercooked meat or meat based comestibles [3-17].

Under the biochemically pressure of low pH gastric juice, entrapped larvae which is basically anaerobic are released in the host's stomach, followed by the molting process (approximately four times in 30-40-time span) [18,19]. Proteases secreted by Trichinella spiralis intestinal infective larvae directly damage the surrounding junctions of the intestinal epithelial cell monolayer and also arbitrate larval invasion and develop into the adult stage inside the enterocytes of small intestine [20]. The results of study conducted by Song et al [20] stipulate that the parasite enzyme named serine proteases and cysteine proteases play crucial roles in larvae invasion, growth and survival inside the host and that they may be main candidate target molecules for vaccines against larval invasion and development.

After successfully entering enterocyte and become mature, male and female are mating then produce new born larvae [21] are released into circulation and spread throughout the tissues and organs [22] and only those that enter striated muscles mature into muscle larvae [23]. During

the muscular phase, the larvae invade the skeletal muscle fibers inducing a relevant inflammatory reaction aiming for the elimination of the parasite. However, the larvae eventually succeed to build their own home inside the infected myocytes [23]. Muscle invasion results in formation of a capsule surrounding muscle larvae in the region of infected muscles [24]. Once again, this eccentric meat lover Trichinella blessed with the capability to make itself “feel homey like being at home” by way of transforming the infected muscle cell for their own benefit and accomplishing a new type of cell inside the host affected musculature, the so-called nurse cell [25].

The lowest infectious dose of Trichinella larvae is remains unrevealed, but the clinical manifestations of trichinellosis starts to displayed as the number of parasite entering the host increases [26]. Asymptomatic infection could remain silent in human if it is only involving a minimum amount of larvae; Gastrointestinal symptoms manifested as a specific syndrome consist of nausea, diarrhea, vomiting, fatigue, fever, and abdominal discomfort [27], starts very early to develop in case of unintentionally ingestion of hundreds of larvae, perhaps manifest itself clinically within the first 48 hours after consuming contaminated meat. The condition that followed by development of a series of condition which are serious, but scarcely fatal illness [5]. Clinical signs of the disease usually last 4–6 months, rarely longer (up to 2 years).

Chronic form of trichinellosis rarely reported, once in 1983 revealed by two German doctor in their case report regarding biopsies conducted on muscles of five patients with clinical diagnosis chronic neuromuscular disorder, mostly manifested as spinal muscle atrophy. All of them had previous history of acute trichinellosis, the interval between acute parasitic infection and the appearance of the slowly progressive neuromuscular syndrome being of 13 to 26 years respectively. Analysis conducted on the biopsy specimens showed morphological and enzyme-histochemical alteration which indicative the presence of progressive neurogenic muscular atrophy. From the Parasite perspective, distinctive encapsulated but still living, enzyme-positive parasites were clearly identified with definite signs of focal myositis in the muscle portion surrounding the larva. The possibility pathogenesis correlations between the "chronic" trichinellosis and the "degenerative" neuromuscular disorder cannot yet be excluded and this still remains to be an unchartered sea of exploration.

In brief, medication option administered in trichinellosis should include potent anthelmintics, glucocorticosteroids, immunomodulating regimen, and combo-preparations which accommodate and compensate protein and electrolyte deficits [27]. Appropriate anthelmintics (type, dosis and length of treatment) are the principal therapy used for trichinellosis. The option of anthelmintics include albendazole, mebendazole and or pyrantel. Rayia et al [23] proposed Bevacizumab as a new option on therapy of muscle phase of Trichinella spiralis infection [28].

3. THE POTENCY

Infective larvae remain alive in striated muscles of the vulnerable host for years [20]; an evidence supported by the study of Sofronic-Milosavljevic et al which revealed the chronic existence of specific antibody responses that still could be recognized even 30 years post primary infection [29]. In case of invasion by Trichinella larvae against the host’s immune system, it actually arouses a complex immune response; in human host is better designated by humoral immune response [30] rather than the cellular responses; and this emphasize future prospect of the human host’s dynamic humoral response [30] for diagnostic [29] or even vaccine development purposes [31,32] such as reported by Bi et al [32] that revealed the newly identified rTs-ES-1 is potent immunodominant protein secreted by Trichinella stichocytes during natural infection and permits the arousal of fractional protective immunity in vaccinated mice inimical to intentional Trichinella infection. Therefore, findings of this rTs-ES-1 specific protein with the better understanding of its antigenic shift-dynamicity [31] is a potential candidate for vaccine development against trichinellosis. In contrast to what happened inside their vulnerable human host, in animals *T. spiralis* can outstretch a high worm burden without causing prominent clinical symptoms [33].

The initiation of infection depends on first by the annexation of prone intestinal epithelium by infective muscle larvae (ML) and followed secondly with the preservation of parasitism which is marked by the presence of ML in affected muscle cells. The parasite regulatory

protein accountable for enzymatic process of these two steps are very important for future investigation [34].

Excretory-secretory products of invading larvae believed to be originate from stichocyte granules in the stichosome, the secretory organelle of the Trichinella's mature muscle larvae [35]. These excretory-secretory products play a pivotal role in parasite's immune evasion and regulation inimical to the host's innate immune system by way of (1) suppressing NET (neutrophil extracellular traps which primary function as a trap for pathogens and facilitating phagocytosis and cytokine production) production and (2) negatively didacte cytokine secretion. The understanding of this excretory-secretory products function for the larvae or worm provides an encouraging area for manufacturing new intervention strategies in other areas of medicine, e.g., in tackling sepsis induced acute lung injury [36] or allergic plethora [29] or autoimmune condition/diseases such as colitis [37] and even malignancies [29].

These important excretory-secretory products engage mainly in the reciprocity with various host cells: firstly, the immune cells, secondly the enterocytes and thirdly the muscle cells, and, through those interaction establishing their role in parasitism and immune response induction, modulation and even evasion [29-32,34-37]. Through these approaches, this nematode generates a perfect milieu for its own suitability and survival in two ways either by modulation of host immune response or affecting host cell gene expression. Extensive exploration of these molecules is important in order to build better understanding regarding (1) the establishment of triumphant parasitism, (2) the development of novel therapies and (3) preventive treatments for inflammatory based disorder.

4. CONCLUSION

Trichinellosis with its related clinical syndrome must always be considered as serious and potentially fatal zoonosis. Transmission occurs through consuming raw or uncooked meat or its comestibles which contaminated with its muscle larvae. Its primary tropism is to the host's striated muscle and can affect the muscle strength and composition in long term. Infection can persist for a long time facilitated by several reciprocities of its product (e.g., excretory-secretory) with the host's organ specific cells (e.g., enterocytes, myocytes) and immune system. Fortunately, there are several promising potency in the field of therapeutic and prevention medicine which should be explored intensely.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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