



Old Wine in a New Bottle-Focus on Candidial Vaccine



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Abstract

Vaginal *Candidiasis* or vaginal candidial infection is one of the most common infections in reproductive age and older age woman. It is usually managed by first line treatment of azoles and other antifungal antibiotics through oral, topical and intra-vaginal preparations. Followed by if recurrence observed, intravenous preparation also administrated. During the past decades, the incidence of vaginal candidiasis and recurrent vaginal Candidiasis was frequently occurred due to poor/ mis-diagnosis, development of drug resistance, infection by non albicans species, phenotypic and genetic adaptation towards the drug *Candidate*. Even though, there are enormous new antifungal antibiotics was introduced but the incidence of drug resistance was more concern. So in order to overcome this circumstance the researchers are tend to make a new *Candida* to prevent the *Candida* infection. In this review we are trying to achieve the importance *Candida* vaccine thus should provide a better option for candidiasis.

Vaginal Architecture and Candidiasis

Vaginal stratified squamous epithelial cells are the outer most self defence agent against several infectious agents [1]. It was procured the host immune system acted as barrier against sexually transmitted diseases to opportunistic infections. Vagina showing unique micro environment which facilitates the attachment of probiotic organism like *Lactobacillus* [2]. Because of the loosely bounded cells with enriched glycogen afford to cross the endogenous organisms around the layer [3]. However, due to the production of several antimicrobial peptide and other immune molecules primarily protects the vaginal environment [4]. In most cases, a simple columnar epithelium of endocervix is the major site of infection. During the course of normal phase *Candida* living like a commensal organism, but when it becomes uncontrolled growth possible to be a pathogenic organism. Formally *Candida albicans* alone consider as a causative agent of RVVC (Recurrent vulvovaginal candidiasis), but the detailed investigations evidenced the uncommon non albicans species to be the part of the chronicity of the infections [5,6].

Risk Factors of Recurrent Vulvovaginal Candidiasis (RVVC)

Candida albicans and non albicans species are present in lower reproductive tract of healthy women with asymptomatic manner.

The potential risks of vaginal candidiasis are majorly associated with excessive carbohydrate source such as uncontrolled diabetes, hormonal therapy leading to formation of glycogen. Followed by disturbance of vaginal epithelial architecture by vaginal douching, improper usages of vaginal lubricants, frequent sexual intercourse and sexual mediated transformation [7,8]. Most importantly, recurrent and un-prescribed usage of antibiotics, immune-suppressive agents reduces the lactobacilli count which overlooked to regulate the *Candida* homeostasis leading to candidial overgrowth [9].

Virulence Factors of RVVC

Candida species produces wide range of virulence factors that includes production of adhesion molecules (Als1p, Als5p) [10], secretion of several classes of proteolytic enzymes (secreted aspartyl-proteinase (*Sap* 1 to 10) [11,12], heat shock protein, bio-film formation, drug resistance, germ tube formation (Hwp1p, hyphal- and germ tube-specific gene [13,14] and morphological transition. *Candida* cells were grown like oval in shape, in some condition the yeast form was transited in to hyphae form. This form of *Candida* was more pathogenic than the yeast form; also it was linked with other virulence factors like *Sap* and Als proteins [15]. During the infection, the adhesion molecules initiates the adhesion of candidial cells to the host epithelial cells, vigorous proliferation

takes place leads to abnormal and obnoxious growth due to the expression of Hwp1 protein [3,10].

Therapeutic Failure of RVVC

Till 19th century, several antifungal antibiotics were introduced for candidial prophylaxis and their broader classifications of antifungal are azoles, polyenes, echinocandins, allylamines and pyrimidines. These target the candidial cell wall and cell membrane, DNA/ RNA synthesis and arrest the function microtubules [16]. In the past two decades, the incidence of RVVC were enormously increased because of increased and unrestricted usages of azoles [17] and other antifungal antibiotics, rises the incident of disease prevalence through development of drug resistant to *C. albicans* and other non albicans species [18]. In some cases, a group of chaperones reported from *C. albicans* showing reduced accessibility of drug *Candidate*. Among them Hsp90 regulates drug resistance, morphogenesis, bio-film formation and virulence [15].

Development of New Strategies for Candida Vaccination

The family of *Sap* proteins are the major concern of vaginal candidiasis and RVVC, because of increased invasion through the disturbance of vaginal architecture. Among them *Sap* 1, 2 and 3 having the antigenic interaction with better immune response against *C. albicans* and non albicans species [12,19]. The excellent immunogenicity modulation of *Sap* protein family was determined as one among the important factor of developing anti-candidial vaccine. From the last decade, enormous studies highlighted the importance of candidial vaccine in order to prevent the pathogenicity and virulence of the RVVC. The detailed investigations of two different vaccines against *C. albicans* are

- a. Protein that belonging to *Sap* (*Sap* 2) family [20,21] and
- b. *Als* (*Als* 9) proteins have been completed phase I trials and approved for RVVC treatment.

Recently, the data demonstrated the importance of *Sap* 2 against mucosal infections of *C. albicans* with some formulation by virosomes in order to develop better vaccine for candidiasis [21].

Conclusion

Vaccination is one of the best methods of elimination of pathogenesis of several infectious diseases. But in the account of candidiasis, our own immune system recognised *Candida* as commensal organism, so it falls to develop immunogenicity towards the candidial infection. Also there are several controversies were raised against candidial vaccine, because of lower specificity, higher cost and others. However, detailed investigations by the expertise peoples will be the option to eradicate the controversies over the candidial vaccination.

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