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Review Article

Oral Adjuvant System-for Immune Augmentation by Oral Route for Preventing the Virus Pandemic

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Abstract

Background: A newly emerged corona virus diseases are necessary to make international cooperative work for the regulation of this virus. Prolonged IRS promised to induce immunological dysfunction with qualitative and quantitative. These condition resulted in age-related disabilities, yet, only a small part of affected individuals seek medical attention. Several studied have described complementary and alternative medicine (CAM) as effective strategies for improving leukocyte subset through safety root such as hypothalamus system, hot-spring hydrotherapy and some other menu in CAM. The purpose of this study was to provoke.

Purposes: In this report, we discuses to the immunoglobulin classes for preparing newly development of virus vaccine.

Pathology of Virus Disease: Hence, the viruses are absolutely dependent system for generation of own species, they need to find host cell, such as hepatic cell by hepatic virus. Immunological attack by IgG antibody to infected hepatic cell induced hepatitis in the host. In other words, there was no pathogenic abnormality only by invention by hepatic virus in hepatic cell.

Points of Discussion for Development of Virus Vaccine: Immunoglobulin classes are absolutely important for prevention of virus infection as first line of defense.

Conclusion: The present report suggest that the immunoglobulin class IgA, secretory IgA is the most important to development of newly development of virus vaccine.

Keywords: *Virus Disease; Vaccine; COVID-19; Oral Adjuvant; Immunoglobulin Class; IgA; IgM; IgG; Secretory IgA*

Abbreviations

CAM: Complementary and Alternative Medicine; IRS: Immune Regulatory Syndrome; SDT: Shi-Quan-Da-Bu-Tang; BYT: Bu-Zong-Ye-Qi-Tang

Introduction

Despite our defenses system, innate and adaptive in the overwhelming problems of possessing this dual system, the innate and adoptive do not seem to guard or even prevent the development of one internal threat to survival [1-4]. However, every individual in the world exposes to the risk of immunomodulatory state in daily life from both internal and externals [5-11]. The factors that influence the acquired immune activity are systemic metabolic disorder such as medical side effect in cancer, diabetes mellitus, malnutrition, extreme exhaustion, stress and aging. Together with recent advances in understanding the pathogenesis of infectious diseases and identification of new therapeutic solutions, the prevention of the disease, especially that of virus one, remains suboptimal, and this clinical form is still associated with a high risk of opportunistic infection by immune-deficient status. Several studies reported the acquired immune-deficient condition yet to values persistent for defense systemic network. So, we have to select appropriate menu to regulate immune function through leukocyte storage. The menu has been summarized and listed as CAM: complementary and alternative medicine. In this script, we plan to collect evidence and judge them with the content suggested in the case of immune deficient status and others. In other words, as a judging standard, setting immunologic factors as main items, we will judge superior and inferior of the factors and timing in each physiological factors [12-15].

Recommending not only quantitatively, but also qualitatively to evaluate "balance of the lymphocyte which is the associate of the white blood corpuscle and the polymorph" as a standard of the immunological factors. Every creature in the world including human exposes to the risk of immunodeficiency in daily life.

A vertebrate animal acquired two ontogenically and phylogenically defense systems and ontogenetically, innate and adaptive. Despite these defense systems overwhelming problems of possessing these dual systems, the innate and adoptive does not seem to guard or even prevent the development of one internal threat to survival. Several studies have indicated the immuno-modulative, cardio-protective, anti-viral, anti-oxidative, hepato-protective, antitumor, anti-diabetic the activities of the bioactive compounds contained in them. We have been trying to regulate the immune responsiveness through much mature for fragile in daily stress and so on. In this article, we would like to show the regulatory mechanism of the hot spring hydrotherapy. The circumstance, the balneotherapy using the effectiveness of hot-springs hydrotherapy, except for cases of contraindication, has been medically useful approved to be effective in many stress-related disorders and the improvement of dysfunction of the biological rhythm disturbance as well as chronic disease. The mechanism of effects has been reported in many studies, but many things are still unclear. We had prepared the native non-specific gourd line outside of the skin and/or mucous membrane. However, the gourd line is easily broken by accidental affair. However, nonspecific and specific attack system had been prepared as lympho-reticular line of defense.

About adjuvants

With a standard program of vaccination, a multiple stimulation had been standard for establishing immune response to the target microorganisms.

However, the secondary type of response sure to induce IgG class antibodies. This IgG class antibody should be required to test virus syndrome. Moreover, reduced visit for clinic is absolutely welcome to each Relevant. At this point of view, it will be stressed to the special adjuvant to viral vaccine so as to induce IgA secretary antibodies.

Repetitive preparation of adjuvant and antigen have to be review

A vaccination as well as immunization of antigen molecule, the vaccination gel are prepared by antigen molecule, adjuvant. The adjuvant for experimental animal is specially prepared by mixing mineral oil in order to make the liquid in soluble. The gel may digested by

the local macrophages/antigen presenting cell. We would like to discuss this text for human use, requiring more cool way for preparing adjuvant. For this purpose hemopoietic herbal decoctions are proved to increase lymphocyte and/or macrophage by famous TCM [16]. We already reported BYT was for macrophage rich adjuvant and STD was for lymphocyte one [17-20].

For the cool administration of vaccine material, preliminary oral administration of herbal decoctions followed by real antigen administration by selected molecule of vaccine material. This kind of approach may successful to the human vaccination in this modern century.

Proposal for oral adjuvant system

We conventionally immunized by foreign microorganism via oral, respiratory and other dermal focus from circumstances. But laboratory immunologist when they need some antibodies, they prepare some special mixture that combined soluble antigen plus mineral oil as adjuvant. The purpose of mineral oil is to retain the mixture in the local site of injection. However, this gel sure to made necrosis to the experimental animal. So, this type of gel is not for human use. Instead, the cool system is necessary for the vaccination for human if possible, cattle and pet animals.

In this text, we propose the special TCM for oral use, before administration of vaccine antigen. We already reported suitable TCM for lymphocyte and macrophage as JDT [21-25]. According to the figure Adjuvant TCM administered prior to vaccine antigen molecule.

Shi-Quan-Da-Bu-Tang (SDT), Bu-Zong-Ye-Qi-Tang (BYT).

Immune response is related to disease

Progress during viral infection

Within epidemic acute virus infection, the efficient viral specific immune response is essential. A vigorous response of helper T and cytotoxic T cells was generated to control and clear viral. viral-specific cytotoxic T cells exhibit antiviral activity by producing IFN-g and cytokine or by directly killing the infected hepatocytes. B cells are co-stimulated by T cells and subsequently produce antibodies to viral surface viral specific antigen.

viral infection relates to the magnitude and quantity of anti-viral immune response [26]. Self-limited acute viral infection. NK cells and NKT cells play important roles in early control of viral, and then a robust response of helper T cells and cytotoxic T cells is generated to control and eliminate viral. B cells co-stimulated by T cells produce anti-HBs, anti-HBe and anti-HBc. These protective antibodies clear viral antigens and virus from the circulation and prevent or limit viral reinfection [27]. Chronic viral infection. Five stages are identified including “immune tolerant” stage with a high-replication of viral-DNA and low-inflammation, “immune active” stage with viral-specific cytotoxic T cell response and antibody production which results in chronic liver injuries, inflammations and liver regeneration, “immune inactive” stage with low-replication of viral and limited inflammation, “immune reactive” stage with chronic hepatitis progressed to liver fibrosis, cirrhosis and HCC and in the late stage of “immune exhaustion.” antigen (HBeAg) and viral core antigen (HBcAg). These antibodies act to clear antigens and virus from the circulation, preventing or limiting viral reinfection [28]. In addition, NK cells and NKT cells efficiently control viral, the activities of which peak earlier than that of viral-specific T cells. During chronic viral infection, the early phase termed “immune tolerant” stage with a high-replication of viral-DNA and low-inflammation during childhood. The progressive loss of immune tolerance leads to the “immune active” stage with viral-specific effector T cell responses during adolescence, which results in chronic liver injuries, inflammation and liver regeneration. Patients may subsequently enter an “immune inactive” stage with low level of viral replication and limited inflammation. Particularly, approximately 20 - 30% of patients in the inactive carrier stage are subject to a

viral relapse, displaying replicative viral and thus enter the "immune reactive" stage with chronic hepatitis that progress to liver fibrosis, cirrhosis and HCC. In the late stage, a series of oncogenic signaling pathways activated by viral result in immune escape and promotes the finally developing HCC [29]. More recently, studies show that viral-immuno-tolerant patients develop HCC (12% in 10 years), while treated "immune active" patients develop HCC (6% in 10 years) with a lower rate. Notably, patients with more cumulative immune-mediated hepatocyte damage would be more susceptible to sensitive group.

Immune response is related to disease progress during viral infection

During self-limited acute viral infection, the efficient viral-specific immune response is essential. A vigorous response of helper T and effector T cells was generated to control and clear viral. Virus-specific effector T cells exhibit antiviral activity by producing IFN-γ and TNF-α or by directly killing the infected hepatocytes. B cells are co-stimulated by T cells and subsequently produce antibodies to viral surface antigen/viral e viral infection relates to the magnitude and quantity of anti-viral immune response [30]. (A) Self-limited acute viral infection. NK cells and NKT cells play important roles in early control viral, and then a robust response of helper T cells and effector T cells is generated to control and eliminate viral. B cells co-stimulated by T cells produce anti-HBs, anti-HBe and anti-HBc. These protective antibodies clear viral antigens and virus from the circulation, and prevent or limit VIRAL reinfection. (B) Chronic viral infection. Five stages are identified including "immune tolerant" stage with a high-replication of viral-DNA and low-inflammation, "immune active" stage with viral-specific effector T cell response and antibody production which results in chronic liver injuries, inflammations and liver regeneration, "immune inactive" stage with low-replication of VIRAL and limited inflammation, "immune reactive" stage with chronic hepatitis progressed to liver fibrosis, cirrhosis and HCC and in the late stage of immune exhaustion". Viral surface antigen and viral core antigen. These antibodies act to clear antigens and virus from the circulation, preventing or limiting viral reinfection. In addition, CD56 cells and CD16/56 cells efficiently viral, the activities of which peak earlier than that of viral-specific T cells. During chronic viral infection, the early phase termed "immune tolerant" stage with a high-replication of viral-DNA and low-inflammation during childhood. The progressive loss of immune tolerance leads to the "immune active" stage with viral-specific effector T cell responses during adolescence, which results in chronic liver injuries, inflammation and liver regeneration. Patients may subsequently enter an "immune inactive" stage with low level of viral replication and limited inflammation. Particularly, approximately 20 - 30% of patients in the inactive carrier stage are subject to a viral relapse, displaying replicative viral and thus enter the "immune reactive" stage with chronic hepatitis that progress to liver fibrosis, cirrhosis and HCC. In the late stage, a series of oncogenic signaling pathways activated by viral result in immune viral-tolerant patients develop HCC (12% in 10 years), while treated "immune active" patients develop HCC (6% in 10 years) with a lower rate. Notably, patients with more cumulative immune mediated hepatocyte damage would be more acceptable to the host cell.

Discussion

While uptake of the HPV vaccine mirrored that of other adolescent vaccines for the first several years after approval and is still increasing, the rate of increase began to lag within three years of introduction, reflecting the myriad controversies and concerns that cropped up during this time. Moreover, disparities in coverage persist, with wide regional and lower coverage among males. Nationwide, coverage among males and females ages 13 - 15 remains significantly below the Healthy people 2020 target of 80%, more than a decade after FDA approval and ACIP endorsement. It is instructive to consider each of the factors that have placed it on a trajectory so unlike that of the viral vaccine. Much of the logistical barrier to HPV vaccination might be overcome if one dose of the vaccine proves non-inferior to two. At the present time, the combination of school-entry mandates and school-located programs for vaccine administration would greatly facilitate access for adolescents requiring multiple doses, as it did for the viral vaccine [31-35]. Mandates also have economic benefits to individuals that could be expected to improve access in populations at highest risk for HPV-associated cancers, given the high cost of the vaccine.

Gender-neutral policies are called for to keep pace with the rising absolute and relative rates of HPV-attributable cancers among men and would likely also aid in normalizing vaccination for HPV by uncoupling it from the culturally fraught area of female adolescent sexuality. Inclusion of males in state mandates may also help to disassociate the vaccine from reports of autoimmune pathology and adverse effects on female fertility. Pharmaceutical companies and healthcare providers have the opportunity to transmit a stronger gender-neutral message and will be aided by research identifying the most successful means of doing so. While global shortages of the HPV vaccine have recently led to calls to temporarily suspend gender-neutral immunization efforts, alternate strategies to maintain the supply of the vaccine, such as suspending marketing to older cohorts, are preferable to tempering efforts to vaccinate males, given low national rates of uptake and the shifting epidemiology of HPV associated cancers. Lastly, younger age of vaccine administration, if approved, may also help to quell concerns regarding both safety and messaging around adolescent sexual behavior.

While gender-neutral mandates for compulsory HPV vaccination, in conjunction with increased access, would mitigate many of the factors that have limited uptake, these same factors have all but eliminated any push from state legislatures for school-entry vaccination requirements. Most state health departments have mechanisms to enact mandates, as was done and this may be a more tenable pathway for this vaccine. Yet, efforts to press for mandates for the HPV vaccine and future vaccines currently in development are likely to be increasingly held back by the perception of a public health landscape oversaturated with mandated vaccines that place an ever-growing burden on parents, children and school administrators. The artificial vaccine entered the market in a decidedly different climate than the viral vaccine two decades earlier. The number of recommended vaccines had approximately doubled in the interim. At the same time, the spread of anti-vaccine advocacy via the internet and social media platforms has contributed to the rise of vaccine hesitancy on a global scale [36,37]. Vaccines likely to be approved in the coming years will face similar uphill battles for support, given shared features with the VIRAL and Viral vaccines in terms of modes of transmission. Pharmaceutical companies and advocates for these vaccines will need to be circumspect in ensuring that the intervals between, ACIP recommendation, and mandate proposals are effectively used to educate the public and healthcare providers, address access issues, and more fully establish safety profiles after mass implementation of vaccine programs. Author disclosure statement All authors attest they meet the public criteria for authorship. At the same time, there is good reason to suspect that the commonly cited reason for parental refusal of the vaccine of its being ‘‘not necessary’’ for their child, as well as the reluctance of many prompt care providers to press the point with parents, does reflect discomfort with the sexually-transmissible nature of HPV infection. Almost immediately following the vaccine’s approval, a moral dimension figured prominently into debates about its merits and related policy. Notably, while anti-vaccine movements have historically taken hold both among politically liberal groups focused on natural approaches to health maintenance and conservative groups more focused on individual autonomy, political regulations were more starkly drawn over the HPV vaccine and mandate proposals, with more conservative commenters opposing mandates, often by invoking parental autonomy in matters of sexual health and education. Affiliation with religious groups and more frequent religious service attendance have also been associated with opposing the HPV vaccine or favoring older age at vaccination. These political and religious associations can be considered reflective of a perceived irreconcilability.

Between HPV vaccination and messaging around abstinence and sexual transmittance. The effects of these reservations are in turn amplified by providers’ perceptions of them, which, evidence suggests, lead them to anticipate resistance and recommend the vaccine less strongly than other vaccines.

Conclusion

Every creatures in the world including human expose to the risk of immunodeficiency in daily life. The factors that influence the acquired immune activity is systemic metabolic disorder such in diabetes emeritus, malnutrition, extreme stress, senile and side effect by

cellular activity in cancer cell. So, we have to select daily an appropriate menu to regulate immune function through leukocyte storage. The menu had been summarized and listed as CAM: complementary and alternative Medicine. One of the major menu is TCM in western medicine world, some trying to integrate Western Medicine and Eastern Medicine. We have been trying to regulate the immune responsiveness through much mature for fragile daily condition from circumstance stress and so on. The main menu were, acupuncture, hot-spring hydrotherapy, light exercise etc. In this article, we would like to show the regulatory mechanism of the hot spring hydrotherapy. The circumstance, the balneotherapy using the effectiveness of hot-springs hydrotherapy, except for cases of contraindication, has been medically useful approved to be effective in many stress-related disorders and the improvement of dysfunction of the biological rhythm disturbance as well as chronic disease [38]. The mechanism of effects has been reported in many studies, but many things are still unclear. Repeated stimulation may cause fatigue or regulation of nervous system. Fatigue refers to the decrement of response with repeated stimulation [39]. The reports showed that the cutaneous mechanoreceptors showed in excitability as a consequence of repeated mechanical stimulus by the sensitization refers to the response increment resulting from novel, moderate heat stimulation, and it is the main phenomenon in the hypothalamus system. According to HSH research, a part of volunteer reported to locations on the body, controlled by hearing ability, and they felt strong warmth or heat spreading around the stimulating site during HSH. Because the occurrence of this heat-sensitization response is often related to obvious better therapeutic effects, HSH has been widely used to treat various types of symptoms. Although the heat-sensitization response mainly depends on the selection of the sensitive for associating with pathological state, may also be a beneficial way to promote the effectiveness of hot spring hydrotherapy.

Conflict of Interests

No conflict of interest exists in this work.

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