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Case Study

Prophylaxes of Aloe Vera Gel to Atopic Dermatitis and Prostatic Hyperplasia: Case Reports

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Abstract

Effect of aloe vera gel extracts on the immunoglobulin E levels in atopic animal models was discussed and exhibited novel strategies for using prebiotic and probiotic to prevent life-related disease. Furthermore, we exhibited three case reports on the beneficial roles of aloe vera juice (AVJ) with bee-products to atopic dermatitis and prostatic cancer. Combination of Kampo medicine and AVJ with bee-products as adjuvant showed synergistic effect to prevent atopic dermatitis and prostatic cancer in host.

Keywords: *Aloe Vera Gel; Aloe Vera Juice (AVJ); Atopic Dermatitis; Prostatic Hyperplasia; Atopic Disease (AD)*

Introduction

Aloe vera gel extracts having moisturizing properties possess antibacterial and antifungal actions that may aid in preventing secondary infection for atopic disease (AD) patients. The most relevant studies relating aloe vera in AD are two animal studies [1,2]. Both studies investigated the effect of aloe vera on the immunoglobulin (Ig E) levels in their AD animal models. The group that applied aloe vera gel extract topically on AD-induced Balb/c mice for 10 days measured a significant reduction in serum Ig E levels compared with the placebo control. On the other hand, the group that fed AD-induced NC/Nga mice with aloe vera gel extracts for 6 weeks resulted in significantly lowered serum IL-5 and IL-10 concentration but increased serum Ig E levels. The results suggest that aloe vera gel modulate immunological responses in AD mainly through influencing IL-5 or IL-10 levels. Medicinal properties of the aloe vera plant may vary due to conditional changes.

Several studies indicated association between allergic diseases and changes in bacterial balance such as increased of *Clostridium* spp., some species of *Bifidobacterium* spp., or decreased of *Bacteroidetes* phylum and some species of *Bifidobacterium* spp. and production of specific short-chain fatty acids due to food type, delivery modes of infant, infant evolvement environment and time of getting bacteria at an early-life age. Gholizadeh., *et al*. [3] exhibited that obesity and diabetes associated with food type, the production of short chain fatty acids undergo fermentation of the intestinal microbiota, metabolic endotoxemia and properties of the immune system. Well-characterized underlying mechanisms may provide novel strategies for using prebiotic and probiotic to prevent and treatment of allergic diseases, obesity, diabetes, and other life-related disorders.

Management of psoriasis with aloe vera extract and microbial diversity associated with atopic eczema

A placebo-controlled, double blind study was exhibited in 60 patients having mild to moderate chronic psoriasis by Seyd., *et al* [4]. The cure rate was 83% with aloe vera cream as compared to 7% with placebo. The intestinal microbiota signatures associated with the severity of eczema in 6-month-old infants were characterized by Nylund., *et al* [5]. The changes in intestinal microbiota composition related to the improvement of this disease 3 months later were assessed. The high diversity of microbiota and high abundance of butyrate-producing bacteria, *Coprococcus eutactus*, were associated with milder eczema, thus suggesting they have a role in alleviating symptoms of atopic eczema. Schwarz., *et al*. [6] postulated that short-chain fatty acids (SCFAs) produced by commensal skin bacteria may activate resident skin regulatory T cells (T regs), the activity of which is diminished in certain inflammatory dermatoses. Sodium butyrate either injected subcutaneously or applied topically onto the ears of hapten-sensitized mice significantly reduced the contact hypersensitivity reaction. This effect was histone acetylation-dependent because suppression was abrogated by anacardic acid, a histone acetyltransferase inhibitor. This indicates that T regs can be induced by SCFAs, suggesting (i) that resident skin microbes may prevent exaggerated inflammatory responses by exerting a down-regulatory function and (ii) that SCFAs may be used therapeutically to mitigate inflammatory skin reactions.

High levels of butyrate associated with protection against atopy

Significant association between the levels of SCFAs and the infant's diet were identified by Roduit., *et al* [7]. Children with highest levels of butyrate and propionate in feces at the age of one year had significantly less atopic sensitization and were less likely to have asthma between 3 and 6 years. Children with the highest levels of butyrate were also less likely to have a reported diagnosis of food allergy or allergic rhinitis. Oral administration of SCFAs to mice significantly reduced the severity of allergic airway inflammation. The authors suggested that strategies to increase SCFA levels could be a new dietary preventive option for allergic diseases in children. Wopereis., *et al*. [8] studied the gut microbiota of 138 infants at increased risk of allergy, participating in a clinical trial investigating the effectiveness of a partially hydrolyzed protein formula supplemented with non-digestible oligosaccharides on the prevention of eczema. Infants with eczema by 18 months showed discordant development of bacterial genera of *Enterobacteriaceae* and *Parabacterioides* species in the first 26 weeks, as well as decreased acquisition of lactate-utilizing bacteria producing butyrate, namely *Eubacterium* and *Anaerostipes* species, supported by increased lactate and decreased butyrate levels.

The authors identified a potential link between microbial activity and onset of eczema, which might reflect a suboptimal implementation of gut microbiota at specific developmental stages in infants at high risk for allergy. Cait., *et al*. [9] determined whether bacterial butyrate production in the gut during early infancy is protective against the development of atopic disease in children. The authors used shotgun metagenomics analysis to determine whether dysbiosis in butyrate fermentation could be identified in human infants, before their developing allergic disease. The authors found that the microbiome of infants who went on to develop allergic sensitization later in childhood lacked genes encoding key enzymes for carbohydrate breakdown and butyrate production.

Butyrate inhibits human mast cell activation via epigenetic regulation of FcεRI-mediated signaling

Folkerts., *et al*. [10] investigated the effects of SCFAs on mast cell-mediated pathology and human mast cell activation, including the molecular mechanisms involved. Butyrate treatment inhibited allergen-induced histamine release and airway contraction in guinea pig precision-cut lung slices. Propionate and butyrate, but not acetate, inhibited Ig E-and non-Ig E-mediated human or mouse mast cell degranulation in a concentration-dependent manner. Notably, these effects were independent of the stimulation of SCFA receptors GPR41, GPR43, or PPAR, but instead were associated with inhibition of histone deacetylases. Transcriptome analyses revealed butyrate-induced downregulation of the tyrosine kinase BTK, SYK, and LAT, critical transducers of FcεRI-mediated signals that are essential for mast cell activation. Known health benefits of SCFAs in allergic disease can, at least in part, be explained by epigenetic suppression of human mast cell activation.

Oral treatment with aloe polysaccharide ameliorates ovalbumin-induced atopic dermatitis

Na., *et al*. [11] investigated the oral administration of processed aloe vera gel (PAG) containing low molecular weight aloe polysaccharides to treat ovalbumin (OVA)-induced atopic dermatitis (AD) in mice. Oral administration of PAG suppressed total and OVA-specific Ig E production in sera and decreased the epidermal thickness of skin. Numbers of Ki-67-positive cells were reduced by PAG treatment. Expression levels of tight junction genes including those that encode ZO-1, Claudin-1 and Claudin-8, were decreased in AD skin lesions, whereas oral administration of PAG partially restored the expression levels of tight junction genes. In addition, IL-4 and IL-7A mRNA transcript levels were reduced in skin lesions after PAG treatment. The results suggest that oral administration of PAG ameliorated AD, normalized tight junction gene expression and suppressed inflammatory cytokines in AD skin.

Usefulness of cernilton to benign prostatic hyperplasia and chronic prostatitis

Benign prostatic hyperplasia (BPH) is a major problem for the patients, the urologist, and health care systems. Medical treatment of BPH is presently dominated by α-adrenoceptor blockers but plant extracts are used extensively in a number of countries. Although plant extracts may not effectively alter the natural history of clinical BPH, their use is valuable in patients with mild symptoms in a number of patients. Among plant extracts cernilton, the *Graminea* flower pollen extract, is an interesting product. Results of clinical studies using patients with BPH treatment with cernilton have demonstrated a marked reduction in residual urine, prostate volume, and improvement in the rate of urinary flow. In previous paper [12] usefulness of cernilton to BPH was presented, and present review is focused on prostate cancer suppression with aloe-emodin.

Proliferative suppression of aloe-emodin through selective targeting in prostate cancer

Aloe-emodin has been found the anti-proliferative effects on breast cancer cells which is through estrogen receptor (ER)-modulating ability. Emodin and aloe-emodin share similar structure with different functions by hitting different targets. Therefore, the molecular mechanisms of aloe-emodin causing cancer death are interesting to explore. Huang and Lin [13] investigated three cancer cell lines: LNCaP, a human prostate cancer cell with androgen receptor (AR) expression; MCF-7 with low expression of HER-2 and AR. In which, MCF-7 cells contain high expression level of estrogen receptor (ER) α. Cells were treated with emodin or aloe-emodin for different time intervals and proliferation was determined. The results indicated that emodin decreased the proliferation of LNCaP and MDA-MB-453 which express high AR protein; however, MCF-7 with low AR protein relatively insensitive to emodin treatment. Oppositely, aloe-emodin decreased cell proliferation in ER-positive MCR-7 cells but had no effects on LNCaP and MDA-MB-453 cells. The authors indicated that aloe-emodin selectively attacks target in cancer cells and had potentials to treat HER-2/ER-positive breast cancer in the future. Liu., *et al*. [14] reported that mammalian target of rapamycin complex 2 (mTORC2) plays an important role in PC3 androgen refractory prostate cell proliferation and anchorage-independent growth. Aloe-emodin inhibited both proliferation and anchorage-independent growth of PC3 cells. Protein content analysis suggested that activation of the downstream substrates of mTCRC2, AKT and PKC α, was inhibited by aloe-emodin treatment. Pull-down assay and *in vitro* kinase assay results indicated that aloe-emodin could bind with mTORC2 in cells and inhibit its kinase activity. Aloe-emodin also exhibited tumor suppression effects *in vivo* in an athymic nude mouse model. Collectively, the data suggest that mTORC2 plays an important role in prostate cancer development and aloe-emodin suppress prostate cancer progression by targeting mTORC2. Ozenver., *et al.* [15] investigated aloe-emodin as the most cytotoxic compound revealed IC50 values from 9.872 μM to 22.3 μM in drug-sensitive wild-type cell lines and from 11.19 μM to 33.76 μM in drug-resistant sublines, was selected to investigate its mechanism against cancer. Aloe-emodin-induced S phase arrest, ROS generation, DNA damage and apoptosis were investigated. Aloe-emodin deserves further investigation as possible antineoplastic drug candidate.

Case Reports of Atopic Dermatitis

Case report 1: The risk-remission for steroid-induced atopic dermatitis in male student at 20-years

A male student suffered from eczema has been administered steroid-cream and antibiotics since 16-years and he was severe situation at the time of entrance examination, because of his short sleep time. On April 2019 he changed steroid administration to Kampo medicine: Orengedokuto-granule and Aloe vera juice (AVJ) 100 - 200 ml/d and aloe vera cream with propolis. On May 2019, he had well bowel movement and good sleep. He was remittent from eczema on June 2019.

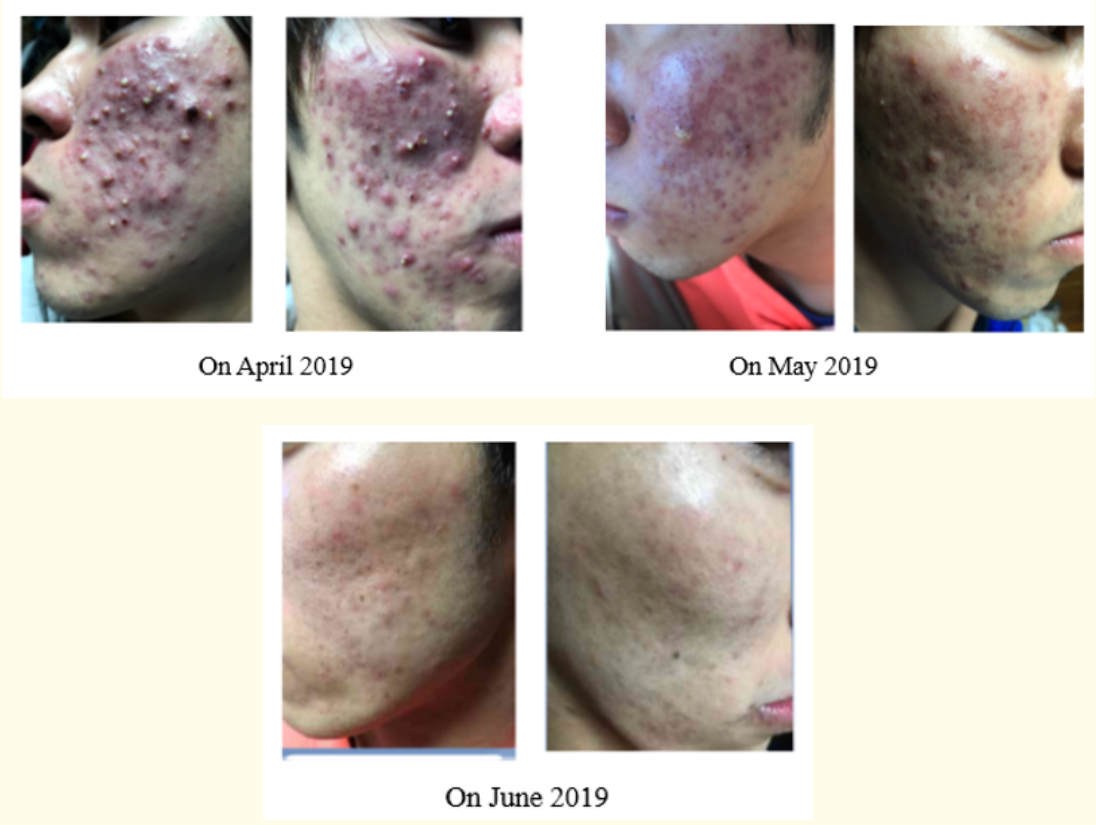

Figure 1

Case report 2: The risk-remission for steroid-induced atopic dermatitis in 30-years male

A 30-years male who had atopic dermatitis as a child, was administered steroid cream over 20 years, had a severe skin-dryness and itching after taking heated pool on Jan 2019. He had Orengedokuto- granule with AVJ 300 - 500 ml/d and AV-propolis cream. He was well remittent from eczema on February 2019.

Case report of prostatic hypertrophy

Case report 3: Prevention of prostate cancer

A 75-years male had been prostatic hyperplasia at high level of PAS and was administered prostatic cancer on June 2019. He was recommended to take Zytiga tablets (predonine tablets) but took AVJ 500 ml/d with bee pollen and propolis from June 2019 to January 20, 2020. The examination resulted in well recovery in PAS and ALP level, and he is well spend healthy days.

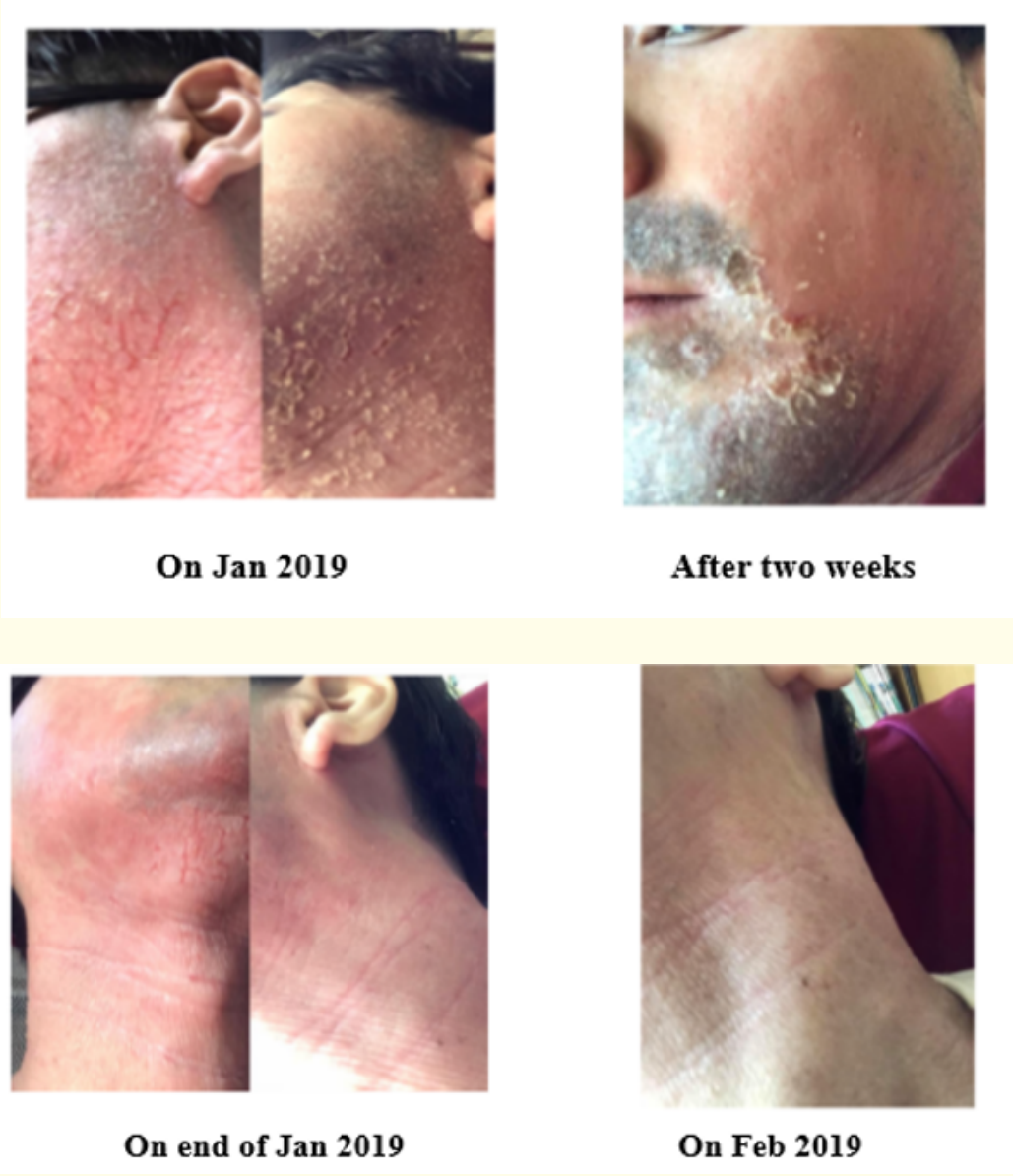

Figure 2

Discussion

As steroid treatment Rinderon-V ointment 0.12% containing betamethasone valerate and gentamicin sulfate, was used in case report 1 and 2. As shown in photography in two case reports, Kampo medicine: Orengedokuto with AVJ and pollen/propolis cream decreased the risk for the steroid-induced eczema. It is suggested that AVJ with pollen/propolis cream support an elastic and healthy skin generation. On

case report 3 a 75-years male was diagnosed prostatic cancer. He tried to ingest AVJ with bee pollen and propolis and was well recovery in PAS and ALP level. It is suggested that AVJ supplemented with bee-products may be remitted to prostatic cancer.

We showed that combinational application of Kampo medicine with successive ingestion of AVJ in which Kampo medicine demonstrates to be a suitable personalized medicine for atopic dermatitis or prostatic cancer and improves gut-microbial ecosystem in host.

Conclusion

Aloe vera gel has anti-inflammation, anti-bacterial, anti-viral properties to cure atopic eczema, and may be a safe and useful alternative to antihistamines and topical corticosteroids.

As shown in the case reports, Kampo medicine in combination of successive ingestion of AVJ with bee-pollen and propolis may decrease the risk for the steroid-induced atopic dermatitis and prostatic cancer. Synergistic effect of Kampo medicine and aloe vera juice with bee-products is fully expected.

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