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A CONCEPTUAL REVIEW OF VRANAGRANTHI ACCORDING TO AYURVEDA AND CONTEMPORARY SCIENCE

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ABSTRACT

Acharya vagbhata in Ashtanga sangraha has mentioned Vraṇa Granthi, while explaining the types of Granthi. As stated by vagbhata, Due to injury to the wound, apthya sevana by vraṇita and improper wound dressing there is Vitiation of Vāta and Rakta, followed by accumulation and drying up of vitiated Rakta in the site of the wound leading to the formation of an elevated structure associated with burning sensation and itching. This hard structure formed is called as Vraṇa Granthi.[1] The pathogenesis of Vrana granthi is similar to that of Keloid. Keloidal scarring is one of the most frustrating clinical problems in wound healing. Keloids form following dermal injury and exhibit exuberant, indefinite growth of collagen.[2,3] Keloid management can be difficult and frustrating, and the mechanisms underlying keloid formation are only partially understood. Despite the growing literature investigating reliable methods for keloid management, no standardized guidelines or treatment protocols are supported by academic governing bodies. Using original and current literature of Vranagranthi and keloid, this comprehensive review presents the major concepts of Vranagranthi [keloid] pathogenesis and their treatment options.

KEYWORDS: Vranagranthi, Keloid, Hypertrophic scar.

INTRODUCTION

Vrana Granthi was described by Acharya Vagbhata in Ashtanga Sangraha while describing the different types of Granthi. According to him, vitiation of vata and rakta results from wound injury, apthya sevana by vraita, and improper wound dressing. This is followed by an accumulation and drying up of vitiated rakta at the site of the wound, which creates an elevated structure that is accompanied by burning and itching.

In modern science vranagranthi can be correlated with keloid and hypertrophic scar. Scars are often described as being atrophic, hypertrophic and keloid. An atrophic scar is pale, flat and stretched in appearance, often appearing on the back and areas of tension. It is easily traumatized as the epidermis and dermis are thinned. Excision and resuturing may only rarely improve such a scar. A hypertrophic scar is defined as excessive scar tissue that does not extend beyond the boundary of the original incision or wound. It results from a prolonged inflammatory phase of the wound.

A keloid scar is defined as excessive scar tissue that extends beyond the boundaries of the original incision or wound. Its etiology is unknown, but it is associated with elevated levels of growth factor, deeply pigmented skin, an inherited tendency, and certain areas of the body (e.g. a triangle whose points are the xiphisternum and each shoulder tip).

In the current study, an effort is made to comprehend the Predisposition, Causes, and Pathophysiology of the formation of Vrana granthi (keloid) as well as numerous preventative measures and strategies for preventing their recurrence after excision.

AIMS AND OBJECTIVES

1. To search and re-evaluate the Vranagranthi in various kinds of Ayurvedic literature with special references to Keloid and Hypertrophic scar.
2. To evaluate and elaborate the aetiology, and pathophysiology of Vranagranthi.
3. To elaborate and discuss the management of Vranagranthi.
4. To evaluate and elaborate methods to prevent recurrence of keloid, as per ayurveda.

MATERIALS AND METHODS

The present article is a review of Ayurvedic texts, modern literature, and various research papers. Materials related to Vranagranthi, Keloid and Hypertrophic scar have been collected

from Ayurvedic Brihatrayi, laghutrayi, and other Ayurvedic books. Various modern texts, journals, and Various websites have been searched to collect information on the relevant topics.

Conceptual study

Ayurvedic disease review

Ayurveda consider Keloid as Rakta and mansapradoshaja vikara. In Ashtanga sangraha Uttara tantra acharya vagbhatta has mentioned Vraṇa Granthi while explaining the types of Granthi. The main causative factors are Apathya sevana by vranita and improper wound dressing.

Nidana (Causative factor)

1. Apathya sevana by Vranita (Wounded person) during the wound healing process or after complete healing of wound.
2. Vata and rakta Prokapaka Ahara and vihara sevana.
3. Improper wound dressing or leaving the wound open leading to a moist wound.
4. External trauma over wound caused by stone etc.

Samprapti (Pathogenesis)[4]

As per Ayurveda due to various aetiologic factors, vitiation of Vata and Rakta leads to accumulation and drying up of vitiated rakta in the site of wound.

Aetiologic Factors

↓

Vitiation of Vata and Rakta

↓

accumulation and drying up of vitiated rakta at the site of the wound

↓

formation of an elevated structure associated with burning sensation and itching.

↓

This hard structure formed is called Vraṇa Granthi

Samprapti ghataka

Dosha: Vata,

Dushya: Rakta

Adhishthana: Arudh Vrana (Healing wound), rudh matra vrana (Healed wound)

Vyadhi Marga: Bahya

Rupa (Symptoms)

1. Formation of an elevated structure over Arudh Vrana (Healing wound) or rudh matra vrana. (Healed wound) giving the appearance of grathit vrana.
2. Burning sensation.
3. Itching.

Ayurvedic management of vranagranthi

A. Nidanparivarjana i.e. removal of cause- according to Ayurveda science avoiding causative factors of disease is the foremost step in preventing and treating disease.

1) Avoiding injury to Vrana - External traumatic injury to a healing wound or healed wound is the main cause of keloid formation. Avoiding traumatic injury will prevent keloid formation.
2) Proper cleaning and dressing of wound – increased moisture in wound due to wound discharges
3) And improper dressing also leads to vranagranthi formation.
4) Avoiding apathya sevana by Vranita is also one of the important causes of vranagranthi as per Ayurveda.

B. Shastrakarma: Chhedana

- Acharya vagbhta in vranagranthi chikithsa mentioned that chhedana i.e. excision of vranagranthi should be done in apakva awastha.
- According to Acharya incomplete excision leads to the reccurence of Vrana granthi.[19]

C. Agnikarma

- After chhedana of vranagranthi, Agni karma should be performed until the bleeding stops.
- Acharya Vagbhta mentioned that Agnikarma prevents reccurance of vranagranthi.[19]

Ayurvedic view

1. Avoiding Kshata – Nidana Parivarjana (Avoiding the causes) is the foremost step in treating or preventing any vyadhi (Disease) as per all the acharyas. As Injury is one of the main reasons for Keloid formation, avoiding it will prevent origin of keloid.
2. As Vraṇa Granthi is mainly due to Vraṇa kshata (Injury to wound), apathya sevana (Unwholesome food), ati vyayama (Excess physical exercises) and ati vyavaya (Excess sexual interourse). which are Vāta & Rakta prakopakara nidanas, doing parivarjana of these nidanas can restrict growth/recurrence of keloids.

3. A vraṇita can undergo basti for vāta shamana and Jalaukavacharana to remove sthanika prakupita rakta to avoid formation of keloids and also to avoid its recurrence post shastra karma i.e Excision.
4. Consuming Rasayana medicines to improve one's own immunity.

Anubhut ayurvedic medicines for shaman chikitsa

a. Kaishora Guggulu
b. Kaanchaara Guggulu
c. Manjishthadi Kwatha
d. Gandhaka Rasayana
e. Arogyavardhini Vati
f. Panchatrikta Ghrita Guggulu

Excess healing[4]

Clinically, excess healing can be as significant as wound failure. More operative interventions are likely required for correction of the morbidity associated with excessive healing than are required for wound failure. The clinical manifestations of exuberant healing are protean and differ in the skin (Mutilating or debilitating scars, burn contractions), tendons (Frozen repairs), the GI tract (Strictures or stenoses), solid organs (Cirrhosis, Pulmonary fibrosis), or the peritoneal cavity (Adhesive disease).

Keloid versus hypertrophic scar

- Hypertrophic scars (HTSS) and keloids represent an overabundance of fibroplasia in the dermal healing process. HTSs rise above the skin level but stay within the confines of the original wound and often regress over time.
- Keloids rise above the skin level as well, but extend beyond the border of the original wound and rarely regress spontaneously both HTSS and keloids occur after trauma to the skin, and may be tender, pruritic, and cause a burning sensation.[4]
- Keloids are 15 times more common in darker-pigmented ethnicities, with individuals of African, Spanish, and Asian ethnicities being especially susceptible. Men and women are equally affected. Genetically, the predilection to keloid formation appears to be autosomal dominant, with incomplete penetration and variable expression.
- HTSS usually develop within 4 weeks after trauma. The risk of HTSs increases if epithelialization takes longer than 21 days, independent of site, age, and race. Rarely elevated more than 4 mm above the skin level, HTSS stay within the boundaries of the

wound. They usually occur across areas of tension and flexor surfaces, which tend to be at right angles to joints or skin creases. The lesions are initially erythematous and raised, and over time may evolve into pale, flatter scars.[4]

Causes of formation of keloid

- Keloids can result from surgery, burns, skin inflammation, acne, chickenpox, zoster, folliculitis, lacerations, abrasions, tattoos, vaccinations, injections, insect bites, ear piercing, or may arise spontaneously.
- Keloids tend to occur 3 months to years after the initial insult, and even minor injuries can result in large lesions. They vary in size from a few millimeters to large, pedunculated lesions with a soft to rubbery or hard consistency. Although they project above surrounding skin, they rarely extend into underlying subcutaneous tissues.[4]

Site of keloid formation

- Certain body sites have a higher incidence of keloid formation, including the skin of the earlobe as well as the deltoid, presternal, and upper back regions.
- They rarely occur on eyelids, genitalia, palms, soles, or across joints. Keloids rarely involute spontaneously, whereas surgical intervention can lead to recurrence, often with a worse result.

Histology of Keloid and Hypertrophic scar

- Histologically, both HTSs and keloids demonstrate increased thickness of the epidermis with an absence of rete ridges. There is an abundance of collagen and glycoprotein deposition.
- Normal skin has distinct collagen bundles, mostly parallel to the epithelial surface, with random connections between bundles by fine fibril strands of collagen.
- In HTSs, the collagen bundles are flatter, more random, and the fibers are in a wavy pattern. In keloids, the collages bundles are virtually non existent, and the fibers are connected haphazardly in loose sheets with a random orientation to the epithelium. The collagen fibers are larger and thicker and myofibroblasts are generally absent.
- Keloidal fibroblasts have normal proliferation parameters, but synthesize collagen at a rate 20 times greater than that observed in normal dermal fibroblasts, and 3 times higher than fibroblast derived from HTSS.[4]

Pathogenesis

- Abnormal amounts of extracellular matrix such as fibronectin, elastin, and proteoglycans, also are produced. The synthesis of fibronectin, which promotes clot generation, granulation tissue formation, and re-epithelialization, decreases during the normal healing process; however, production continues at high levels for months to years in HTSS and keloids.
- This perturbed synthetic activity is mediated by altered growth factor expresion TGFB expression is higher in HTSS, and both HTS- and keloid derived fibroblasts respond to lower concentrations of TGFB than do normal dermal fibroblasts.
- HTSS also express increased levels of insulin-like growth factor I, which reduces collagenase mRNA activity and increases mRNA for types I and II procollagen.
- The underlying mechanisms that cause HTSS and keloids are not known. The immune system appears to be involved in the formation of both HTSs and keloids, although the exact relationship is unknown. Much is inferred from the presence of various immune cells in HTSS and keloids. For example, in both HTSS and keloids, keratinocytes express human leukocyte antigen-2 and intercellular adhesion molecule-1 receptors, which are absent in normal scar keratinocytes.
- Keloids also have increased deposition of immuno- globulin G (IgG), IgA, and IgM, and their formation correlates with serum levels of IgE.
- Antinuclear antibodies against fibroblasts, epithelial cells, and endothelial cells are found in keloids, but not HTS, HTSS have higher T-lymphocyte and Langerhans cell contents. There also is a larger number of mast cells present in both HTSS and keloids compared to normal scars.
- Other mechanisms that may cause abnormal scarring include mechanical tension (although keloids often occur in areas of minimal tension) and prolonged irritation and/or inflammation that may lead to the generation of abnormal concentrations of profibrotic cytokines.[4]

Treatment modalities

Treatment goals include restoration of function to the area, relief of symptoms, and prevention of recurrence. Many patients seek intervention due to cosmetic concerns. Because the underlying mechanisms causing keloids and HTSS remain unknown, many different modalities of treatment have been used without consistent success.

Surgical excision

Excision alone of keloids is subject to a high recurrence rate, ranging from 45 to 100%. There are fewer recurrences when surgical excision is combined with other modalities such as intralesional corticosteroid injection, topical application of silicone sheets. or the use of radiation or pressure. Surgery is recommended for debulking large lesions or as second-line therapy when other modalities have failed.[4] There are several key principles regarding management of the resultant wound bed that are commonly accepted to reduce keloid recurrence. General recommendations for primary wound closure following complete excision include gentle handling of tissue, avoidance of wound bed tension, eversion of wound edges, meticulous approximation of wound edges, and adequate control of infection and bleeding.[5,6,7] For ear keloid skin reconstruction, bilayered banner transposition flaps and double-crossed skin flaps have been described to reduce wound bed tension.[8,9] As an alternative to primary closure after complete keloid excision, the use of full-thickness skin grafts have been shown to be effective in the literature.

Silicone application

Silicone application is relatively painless and should be maintained for 24 hours a day for about 3 months to prevent rebound hypertrophy. It may be secured with tape or worn beneath a pressure garment. The mechanism of action is not understood, but increased hydration of the skin, which decreases capillary activity, inflammation, hyperaemia, and collagen deposition, may be involved. Silicone is more effective than other occlusive dressings and is an especially good treatment for children and others who cannot tolerate the pain involved in other modalities.

Intralesional corticosteroid injections

Intralesional corticosteroid injections decrease fibroblast proliferation, collagen and glycosaminoglycan synthesis, the inflammatory process, and TGFß levels. When used alone, however, there is a variable rate of response and recurrence, therefore steroids are recommended as first-line treatment for keloids and second-line treatment for HTSs if topical therapies have failed. Intralesional injections are more effective on younger scars. They may soften, flatten, and give symptomatic relief to keloids, but they cannot make the lesions disappear nor can they narrow wide HTSs. Success is enhanced when used in combination with surgical excision.

Serial injections every 2 to 3 weeks are required. Complications include skin atrophy, hypo-pigmentation, telangiectasias, necrosis, and ulceration.

Cryotherapy

Cryotherapy involves the administration of freezing therapy to keloids to reduce scar volume and recurrence. During cryotherapy, the temperature of the keloid scar is lowered below -22°C.[10] Low temperatures have been suggested to induce vascular damage, resulting in cell anoxia, cryonecrosis, and coagulative necrosis.[10,11] Histologic studies after cryotherapy have highlighted several significant changes in scar tissue structure. Posttreatment scar biopsies have demonstrated the reorganization of collagen fibers into a more compact parallel fashion comparable to classic scar and resultant dermal collagen structure.[8,10]

Radiation

Although radiation destroys fibroblasts, it has variable, unreliable results and produces poor results with 10 to 100% recurrence when used alone. It is more effective when combined with surgical excision. The timing, duration, and dosage for radiation therapy are still controversial, but doses ranging from 1500 to 2000 rads appear effective. Given the risks of hyperpigmentation, pruritus, erythema, paresthesias, pain, and possible secondary malignancies, radiation should be reserved for adults with scars resistant to other modalities.[4]

Platelet-rich plasma (PRP)

PRP is concentrated autologous plasma that contains supra-physiologic levels of platelets and alpha granules with growth factors and cytokines, such as vascular endothelial growth factor, platelet-derived growth factor, and TGF-β.[1]PRP has been popularized as an adjunctive treatment to help with a variety of dermatologic conditions, including chronic wounds, alopecia, and scars.[14] Recent studies have focused on the role of PRP in altering keloid pathology. *In-vivo* studies with dermal fibroblasts have demonstrated that PRP increased fibroblast proliferation, expression of collagen, and matrix protein synthesis.[15,16] Increased levels of TGF-β in PRP have been proposed to activate a negative feedback mechanism in the TGF-β signaling pathway.[17] Currently, PRP has been studied as a postsurgical excision therapy that is injected into the wound bed. Hersant et al[18] reported 29 percent keloid recurrence at two years when PRP was used intraoperatively during surgical excision and postoperatively in a monthly regimen for three months.[18]

Pressure therapy

Pressure aids collagen maturation, flattens scars, and improves thinning and pliability. It reduces the number of cells in a given area, possibly by creating ischemia, which decreases tissue metabolism and increases collagenase activity. External compression is used to treat HTSs, especially after burns. Therapy must begin early, and a pressure between 24 and 30 mmHg must be achieved in order to exceed capillary pressure, yet preserve peripheral blood circulation. Garments should be worn for 23 to 24 hours a day for up to 1 or more years to avoid rebound hypertrophy. Scars older than 6 to 12 months respond poorly.[4]

Topical retinoids

Topical retinoids also have been used as treatment for both HTSS and keloids, with reported responses of 50 to 100%.[4]

Interferon

Intralesional injections of interferon-y, a cytokine released by T lympho- cytes, reduce collagen types I, II, and III by decreasing mRNA and possibly by reducing levels of TGFB. This treatment is experimental, and complications are frequent and dose-dependent.[4]

5-fluorouracil

Intralesional injections of chemotherapeutic agents such as 5-fluorouracil have been used both alone and in combination with steroids.[4]

Bleomycin

The use of bleomycin has been reported to achieve some success in older scars resistant to steroids.[4]

Combination therapy

The most effective management for keloids is combination therapy, generally excision with adjuvant treatment

1. Surgery plus steroids
2. Carbon dioxide laser plus steroids
3. Surgery plus radiation therapy
4. Surgery plus compression earrings
5. Surgery plus silicone gel sheeting
6. Surgery plus 5-fluorouracil

Images

Fig. 1.2: Ear lobe keloid in female patient.

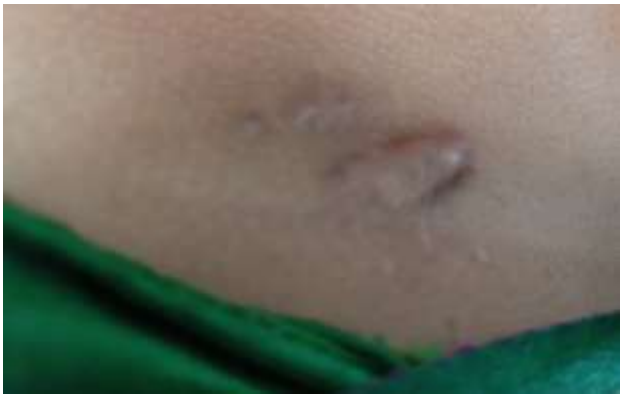

Fig. 1.3: Sternal keloid.

CONCLUSION

Keloids are well known for their high recurrence rate even after surgical excision, or any conventional line of treatment available. Standardized guidelines for keloid management are currently limited by the lack of large, high-quality research assessing the effectiveness of various keloid therapies.

There are now several keloid therapy options available, and new therapies are being researched as well. As of yet, no single therapy has been acknowledged as the gold standard for treating all keloids or for complete scar resolution.

In this review, we have provided a comprehensive summary of the common concepts surrounding keloid formation and discussed, current as well as emerging therapies. Ayurveda treatment modalities have an important role in the prevention and cure of Vranagranthi. Using Ayurveda treatment modalities vranagranthi can be treated effectively. Hence following above mentioned treatment modalities the occurrence as well as recurrence of the keloid can be prevented with a high success rate.

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