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Review Article

Dermatology Section

Anogenital Pruritus – An Overview

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ABSTRACT

Anogenital pruritus is defined as intense itching, acute or chronic, affecting the anal, perianal, perineal and genital skin, which is a dominant problem in the course of various cutaneous and systemic conditions. It is one of the common, extremely annoying symptom for which patients attend the Dermatology Outpatient Department (OPD). Anogenital skin is highly sensitive to soaps, perfumes, clothing and superficial trauma and it is more prone for itchy dermatoses as a result of warmth, friction, lack of aeration, sweating and occlusive inner garments. Anogenital pruritus is associated with a wide spectrum of diseases which includes localized infections, infestations, inflammatory dermatoses, allergic and irritant conditions, anorectal diseases, systemic causes, nutritional disorders, psychological and when the cause cannot be found out it is often termed idiopathic. Patients are highly reluctant in consulting the physician for anogenital itch in the early stage, they usually present at a later stage with either atypical manifestations or depigmentation and lichenification, secondary to constant scratching. They often resort to over the counter topical agents, particularly combination products which contain topical steroids. The irrational use of such products results in complications like skin atrophy, striae, incognito etc. A proper clinical history, clinical examination, investigations like scrapping for fungus and itch mite, skin biopsy, patch test and relevant blood investigations to rule out systemic conditions should be carried out, when needed, to arrive at an accurate diagnosis, before treating the patient.

Keywords: Causes, Evaluation, Lichenification, Management, Priritus ani, Pruritus vulvae

INTRODUCTION

Pruritus (itch) was defined more than 340 years ago by the German physician Samuel Hafenreffer as an "unpleasant sensation that elicits the desire or reflex to scratch". It is classified based on neuropathophysiology as pruritoceptive (itch originating from skin - primary dermatoses), neuropathic (itch arising from neuroanatomic dysfunction eg. Nerve entrapment injuries), neurogenic (arising from neurochemical action e.g. opioids) and psychogenic [1]. Pruritus can occur in acute or chronic (over 6 weeks in duration) forms [2], may be generalized involving entire skin or localized to areas such as the scalp, upper back, arms and the anogenital region. The International Forum for the Study of Itch (IFSI) has proposed a classification based on the clinical signs and distinguishing between diseases with or without primary or secondary skin lesions [2]. The first group (Group I- pruritus on primarily inflamed skin) includes patients with underlying dermatologic disease; the second group (Group II- pruritus on primarily non-inflammed skin) includes patients with systemic diseases, pregnancy, drug induced pruritus, neurogenic, neuropathic and psychiatric diseases; and the third (Group III – pruritus with chronic secondary scratch lesions, such as prurigo nodularis) group includes patients with pruritus due to the causes of both first and the second groups. In addition itch may result from co-existence of several diseases or undetermined origin. Anogenital pruritus is defined as an itch localized to the anus, perianal (pruritus ani) and genital skin (males- pruritus scroti, females- pruritus vulvae). Pruritus ani occurs in 1-5% of the adult population, and is more common in males than females [3-6]. The frequency of pruritus vulvae is unknown, but it is evident that most women suffer from it at some time in their lives, most commonly postmenopausally as a result of estrogen deficiency, a primary symptom of the vulvar dystrophies [7-9]. Anogenital pruritus in both sexes is a cause of severe distress and sleep disturbance due to treatment resistant itch-scratch-itch cycle.

PATHOPHYSIOLOGY OF ITCH

Itch Pathway -Itch sensation is received by the unspecialized free nerve endings located close to the dermo-epidermal junction. Itch transmitting polymodal, unmyelinated C fibres enter the dorsal horn of the grey matter of the spinal cord, synapse there with secondary neurons, which cross over to the contralateral spinothalamic tract and ascend to the thalamus. Tertiary neurons relay itch to the level of conscious perception in the cerebral cortex, anterior cingulate and insular cortex are involved in the recognition of itch sensation at conscious levels, whilst the premotor cortical areas participate in intention to scratch.

The important pharmacological mediators of itch sensation include histamine, acetyl choline, substance P, Calcitonin Gene-Related Peptide (CGRP), opioid peptides, proteases, bradykinin, serotonin, platelet activating factor, neurotrophins, prostaglandin E and cytokines [1,10-12].

Recent report has suggested four possible itch pathways: histaminergic-Transient Receptor Potential Vanilloid 1 (TRPV1) positive pathway TRPV1–expressing neurons have been suggested to be the main sensors and mediators of itching; histaminergic-TRPV1 negative pathway; non-histaminergic Proteinase Activated Receptor 2 (PAR-2) pathway; Non-histaminergic serotonin (5-HT) pathway [13].

Histamine has remained one of the best known pruritogens, and its signaling mechanism is relatively better understood. Histamine receptors are members of the G-Protein Coupled Receptors (GPCR), and four receptors H1 ~ 4 R have been identified. H1R is a major receptor implicated in itch sensation. HIR is coupled with Gq proteins, which upon binding on histamine activates phospholipase Cβ3 (PLCβ3), which in turn cleaves phosphotidylinositol-4-5-biphosphonate (PIP2) into the second messengers diacylglycerol (DAG) and inositol triphosphate (IP3). DAG activates protein kinase Cε (PKCε) which phosphorylates and thereby opens the TRPV1. Activation of TRPV1 leads to channel opening which allows passage of the positively charged ions sodium, potassium and calcium resulting in depolarization. Thereby voltage-dependent sodium channels are activated generating action potentials along the nerve fibre which lead to sensation of itch. Histamine induced itch is mediated by activation of TRPV1 and requires phosphoinositide interacting regulator of transient receptor potential channels (PIRT), a membrane

protein modulating TRPV1 function. PIRT is required for PIP2 dependent activation of TRPV1. In addition, activation of TRPV1 in histamine induced scratching behavior relates to activation of phospholipase A2 and lipoxygenase generated products including 12-hydroxyeicosatetraenoic acid (12-HETE) [13-16].

In the non-histaminergic pathway PAR-2 has been shown to play a crucial role in itching associated with atopic eczema. PAR-2 activation has been shown to increase the release of IL-6 and granulocyte-macrophage colony-stimulating factor from keratinocytes in atopic eczema patients [17]. 5-HT is, like histamine, mainly secreted from skin mast cells in the periphery and is able to activate sensory neurons directly. The action of 5-HT may be partly mediated by cutaneous 5-HT2 receptor. It activates PLC 3 elicits an itching sensation associated with pruritic diseases, such as polycythemia vera and cholestasis [13,15].

AETIOLOGY

Anogenital pruritus may be a manifestation of skin or systemic diseases and it may be acute or chronic. Acute anogenital pruritus is mainly due to infections and allergic or irritant contact dermatitis. Chronic anogenital pruritus is due to papulosquamous disorders, primary inflammatory disorders of genitalia, mechanical causes, malignancies and psychogenic causes [18]. Other than the common causes listed in the [Table/Fig-1], anogenital pruritus may be due to systemic causes like diabetes mellitus, liver disease, leukaemia, lymphoma, renal failure, iron deficiency anaemia, connective tissue disoders, hyperthyroidism, hypovitaminosis and celiac disease [3,19,20]; anorectal diaeases like haemorrhoids, anal fissure, fistula, rectal prolapse, anal papillomas, abscesses and Crohn's disease; bening tumours like seborrheic keratosis, angiokeratoma and bowenoid papulosis; drug reactions; pregnancy secondary to vulvovaginal candidiasis, bacterial infections or preexisting dermatoses: physical causes like waxing burns, shaving injuries and injuries due to insertion of foreign bodies; faecal soilng, urine and sweat; dietary factors - most common are coffee, tea, cola, alcohol, chocolate and tomato, less common are milk, peanuts, citrus fruits and spices; and lumbosacral radiculopathy [21].

EVALUATION

When approaching the patients with anogenital itch a proper history, thorough clinical examination are very important. Appropriate investigations to rule out systemic causes and skin biopsy are done where ever there is a difficulty in arriving at the diagnosis. In the history patients should be enquired about the onset of itch, severity and quality of itch, timing of itch, relieving/exacerbating factors, bathing/skin care history, previous treatments, itchy contacts, pets, sexual exposure, relation to coitus and menstruation, contraception, lubrication, travel history, topical application to identify irritants and allergens, previous history of itch/rash, past medical history like atopy, diabetes mellitus, etc., and medication history.

The physical examination should be primarily focused on the skin, however importance should be given to examine other systems, lymphatics and anorectum to exclude their involvement. Dermatological examination, to look for primary skin lesions and secondary skin lesions resulting from scratching (excoriation, hyperpigmentation and lichenification), should be done to establish the diagnosis. Examine for the presence and the nature of genital and anorectal discharge.

Laboratory examination may not be mandatory at the first visit or in patients presenting with primary skin rash, but should be pursued if signs or symptoms of internal diseases are elicited. Screening lab tests like complete blood count, thyroid function test, blood glucose, urea, creatinine, liver function test, stool examination, chest x-ray, ultrasonography of abdomen and age-appropriate cancer screening should be done. Clinical suspicion should drive necessary additional lab tests. Skin scrapping for itch mite, KOH examination for fungus, patch test to identify allergens and skin biopsy should be done wherever there is a difficulty in arriving at the diagnosis [3,18,19,22].

Acute Anogenital Pruritus	Chronic Anogenital Pruritus
Infections. Fungal : Dermatophytoses, *Candida* Bacterial: *Corynebacterium minutissimum*, *Staphylococcus aureus*, group A *Streptococcus* Bacterial vaginosis: *Gardnerella vaginalis*, *Mobiluncus spp.*, *Bacteroides spp*., *Mycoplasma hominus*, anaerobic gram positive cocci Viral: Herpes simplex virus Human papilloma virus Molluscum contagiosum Parasitic: *Trichomonas vaginalis* Infestation:Scabies, Phthirus pubis, Pin worms. Contact dermatitis: Irritant/Allergic (common agenta include local anaesthetics, medicaments, perfumes, cleansers, condoms, garments, sweat, urine, feces).	Dermatoses: Seborrheic dermatitis, Psoriasis, Atopic dermatitis, Lichen sclerosus, Lichen planus, Plasma cell vulvitis / balanitis, Papular acantholytic dyskeratosis, Dermatographism, Atrophic vulvovaginitis Neoplasms: Extramammary Paget's disease, Bowen's disease, Erythroplasia of Queyrat, Syringomas, Hidradenoma papilliferum, Langerhan cell histiocytosis, Basal cell carcinomas. Idiopathic pruritus (lichen simplex chronicus, neurodermatitis, essential pruritus, pruritus vulvae, pruritus ani, pruritus scroti) Psychogenic.

[Table/Fig-1]: Common causes for anogenital pruritus.

APPROACH TO MANAGEMENT

In the management of anogenital pruritus the first priority is to identify any underlying infections, inflammatory dermatoses or irritation. Specific treatment should be given if any primary cutaneous disorder is identified. If it is found to be associated with systemic problems, anorectal or genital disorder appropriate treatment should be initiated [3,18,22]. A simplified treatment protocol for anogenital pruritus is given in [Table/Fig-2].

Pruritus ani (idiopathic) – General and specific measures should be initiated once any of the underlying cause has been excluded. General measures should include limiting constipation with either a high fiber diet or stool softeners and diarrhea if present to be corrected. Vigorous rubbing should be avoided while cleansing after bowel movement and use cotton swabs moistened with warm water instead of tissue paper. In patients with occult fecal leakage similar cleansing method should be followed and usage of bland emollient like petrolatum ointment or 10 to 20% zinc oxide ointment should be applied several times a day [18,22]. Loose cotton inner wear should be preferred instead of tight fitting rough synthetic garments to avoid excess sweating. Bathing with syndets instead of soaps should be advised as a routine and after exercise. Seat cushions made of mesh, wicker or a beaded one is recommended for people who sit for several hours a day to reduce sweating. Irritants and allergens like deodorants, perfumes, antiseptics etc. should be avoided. In patients who do not respond to topical emollients, a short course of mild to medium potency steroids should be initiated for a shorter duration under strict monitoring. Topical capsaicin (0.006%) is found to be highly effective for severe intractable idiopathic pruritus ani [23]. Sedative antihistamines or tricylcic antidepressants are used at bed time.

Identification of any underlying disease, irritants and allergens, current or past skin disorders of atopy. Examination for primary or secondary skin lesions, appropriate investigations to rule out local and systemic causes. Skin biopsy if essential. Examine vaginal secretions for evidence of infection or inflammation. Specific treatment for infections, inflammatory dermatoses etc. if the cause is apparent, in addition to the general measures. For idiopathic anogenital pruritus when no cause can be found out, general measures like proper inner wear, mild cleansers and avoidance of hot water for bathing. Discontinue use of irritants or allergens and medications other than those prescribed. Avoidance of beverages Active measures: Repair of the barrier function - Bland emollients and other topical antipruritic agents in the absence of specific dermatoses. Reduction of inflammation - Initiate trial of topical steroids for those who do not respond to emollients and other agents under strict monitoring. Suppress and break itch-scratch-itch cycle - Antihistamines and antidepressants, for nighttime scratching sedating antihistamines and tricyclics are used. Gabapentin and SSRIs for resistant cases.

[Table/Fig-2]: Management of anogenital pruritus.

Emollients / Moisturizers; Corticosteroids; Calcineurin inhibitors; Cooling agents: shake lotions (eg. Calamine); Anaesthetics: Benzocaine, lignocaine, prilocaine/lignocaine, pramoxine; Antihistamine: Doxepin, diphenhydramine, promethazine, dimetindene, mepyramine; Miscellaneous: Camphor, menthol, phenol, strontium, capsaicin, crotamiton

[Table/Fig-3]: Topical medication for pruritus.

Pruritus vulvae (idiopathic) – General measures include avoidance of exacerbating factors such as sweat, occlusion, irritating cleaning habits and wiping should be always from front to back. Comfortable absorptive cotton innerwear should be chosen instead of tight fitting synthetic materials. Tampons are considered better than sanitary pads during menstruation. Cool compresses may be used as lowering the temperature reduces itch through central inhibitory pathway. Severe scratching may lead to excoriations, lichenification and depigmentation. Oozing excoriated lesions may get infected hence requires topical or systemic antibiotics and astringent soaks like Burow's solution (aluminium acetate). Bland emollients may be tried initially for patients with anogenital itch without skin lesions. The mainstay of treatment for non-specific pruritus vulvae is topical steroids [18,22]. To start with high potency steroids like clobetasol propionate 0.05.% is used twice daily then reduced to once daily and switched over to medium or mild potent steroids according to the response under strict monitoring. Prolonged use of topical steroids should be avoided as it will result in serious side effects like skin atrophy. Intralesional triamcinolone acetonide (15-20 mg) may provide a prolonged relief for resistant cases [24]. Topical calcineurin inhibitors, pimecrolimus 1% cream seems to be an effective and safe treatment modality for pruritus in postmenopausal women with vulvar lichen simplex chronicus [25-27]. Local aneasthetics and other topical antipruritic agents [Table/Fig-3] may be tried according to the therapeutic response [28,29].

Sedative antihistamines like diphenhydramine (25-50mg) or hydroxyzine (12.5-25mg) are given to break the itch-scrath-itch cycle and to prevent the patient from night scratching. In patients who do not respond to these drugs, agents which have antidepressive effects like doxepin (10-25mg upto 75mg) or amytriptyline (25mg upto 100mg) can be used [23]. Amytriptyline is particularly useful in anogenital itch having neuropathic qualities such as stinging or burning. Gabapentin a structural analogue of gamma-aminobutyric acid and selective serotonin reuptake inhibitors (SSRIs) such as fluoxetine, paroxetine, sertaline, fluvoxamine mirtazapine and citalopram may be useful for patients with intractable pruritus resistant to routine therapy [29-31].

CONCLUSION

Anogenital pruritus is a common problem with varied aetiology. It is primarily idiopathic; most secondary causes can be divided into dermatologic, anogenital conditions, systemic causes and psychogenic. A good clinical history, examination and relevant lab tests are important for arriving at accurate diagnosis. Specific treatment is given after finding out the cause and for patients with idiopathic anogenital pruritus management can be accomplished with elimination of irritants and scratching, general control measures and active treatment measures.

REFERENCES

[1] Twycross R, Greaves MW, Handwerker H, et al. Itch: scratching more than the surface. *QJM*. 2003;96:7 -26.
[2] Stander S, Weisshaar E, Mettang T, et al. Clinical classification of itch: a position paper of the International Forum for the Study of Itch. *Acta Derm Venereol*. 2007;87:291-94.
[3] Siddiqi S, Vijay V, Ward M, Mahendran R, Warren S. Pruritus ani. *Ann R Coll Surs Engl*. 2008;90:457-63.
[4] Daniel GL, Longo WE, Vernava AM.Pruritus ani. Causes and concerns. *Dis Colon Rectum*. 1994;37:670-74.
[5] Chaudhry V, Bastawrous A. Idiopathic pruritus ani. *Semin Colon Rectal Surg*. 2003;14:196-202.
[6] Hanno R, Murphy P. Pruritus ani: classification and management. *Dermatol Clin*. 1987;5(4); 811-16.
[7] Sener AB, Kuscu E, Seckin NC, Gokmen O, Taner D, Cobanoglu O, et al. Postmenopausal vulvar pruritus-colposcopic diagnosis and treatment. *J Pak ed Assoc*. 1995;45(12):315-17.
[8] Soper JT, Creasman WT. Vulvar dystrophies. *Clin Obstet Gynecol*. 1986;29(2):-431-39.
[9] ACOG. Technical Bulletin Number 39, Vulvar dystrophies. *Int J Gynaecol Obstet*. 1991;35:269-73.
[10] Wallengren J. Neuroanatomy and neurophysiology of itch. *Dermatol Ther*. 2005;18(4):292-303.
[11] Akiyama T, Carstens E. Neural processing of itch. *Neuroscience*. 2013;250:697-714.
[12] Potenzieri C,Undem BJ. Basic mechanisms of itch. *Clin Exp Allergy*. 2012;42(1):8-19.
[13] Nakagawa H, Hiura A. Four possible itching pathways related to the TRPV1 channel, Histamine, PAR-2 and Serotonin. *Malays J Med Sci*. 2013;20(4): 5-12.
[14] Shim WS, Tak MH, Lee MH, Kim M, Kim M, Koo JY, et al. TRPV1 mediates histamine induced itching via the action of phospholipase A2 and 12-lipoxygenase. *J Neurosci*. 2007;27(9):2331-37.
[15] Han L, Dong X. Itch mechanisms and circuits. *Annu Rev Biophys.* 2014;43:331-55.
[16] Jeffry J, Kim S, Chen ZF. Itch signaling in the nervous system. *Physiology (Bethesda)*. 2011;26(4):286-92.
[17] Steinhoff M, Neisiuss U, Ikoma A, Fartasch M, Heyer G, Skov PS, et al. Proteinase-Activated Receptor-2 mediates itch: A novel pathway for pruritus in human skin. *J Neurosci.* 2003;23(15):6176-80.
[18] Weichert GE. An approach to the treatment of anogenital pruritus. *Dermatol Ther*. 2004;17:129-33.
[19] ZuccatiG, Lotti T, Mastrolorenzo A, Rapaccini A, Tiradritti L. Pruritus ani. *Dermatol Ther*. 2005;18:355-62.
[20] Gach JE, Seddon FH. Gluten-sensitive enteropathy associated with genital lichen simplex chronicus. *J R Soc Med Sh Rep*. 2010;1:43.
[21] Cohen AD, Vander T, Medvendovsky E, Biton A, Naimer S, Shaley R, et al. Neuropathic scrotal pruritus: anogenital pruritus is a symptom of lumbosacral radiculopathy. *J A Acad Dermatol*. 2005;52(1):61-66.
[22] Lynch PJ. Lichen simplex chronicus (atopic/neurodermatitis) of the anogenital region. *Dermatol Ther*. 2004;17(1):8-19.
[23] Lysy J, Sisstiery-Ittah M, Shmueli A, Strauss-Liviatan N, Mindrul V, Keret, Goldin E. Topical capsaicin—a novel and effective treatment for idiopathic intractable pruritus ani: a randomized, placebo controlled, crossover study. *Gut*. 2003;52(9):1323-26.
[24] Kelly RA, Foster DC, Woodruff JD. Subcutaneous injection of triamcinolone acetonide in the treatment of chronic vulvar pruritus. *Am J Obstet Gynecol*. 1993;169(3):568-70.
[25] Kelekci HK, Uncu HG, Yilmaz B, Ozdemir O, Sut N, Kelekci S. Pimecrolimus 1% cream for pruritus in postmenopausal diabetic women with vulvar lichen simplex chronicus: a prospective non-controlled case series. *J Dermatolog Treat*. 2008;19(5):274-78.
[26] Sarifakioglu E, Gumus II. Efficacy of topical pimecrolimus in the treatment of chronic vulvar pruritus: a prospective case series --a non-controlled, open-label study. *J Dermatolog Treat*. 2006;17(5):276-78.
[27] Goldstein AT, Parneix-Spake A, McCormick CL, Burrows LJ. Pimecrolimus cream 1% for treatment of vulvar lichen simplex chronicus: An open-label, preliminary trial. *Gynecol Obstet Invest*. 2007;64:180-86.
[28] Elmariah SB, Lerner EA. Topical therapy for pruritus. *Semin Cutan Med Surg*. 2011;30(2):118-26.
[29] Patel T, Yosipovitch G. Therapy of pruritus. *Expert Opin Pharmacother*. 2010;11(10):1673-82.
[30] Stewart KM. Clinical care of vulvar pruritus, with an emphasis on one common cause, lichen simplex chronicus. *Dermatol Clin*. 2010;28(4):669-80.
[31] Yosipovitch G, Bernhard JD. Chronic pruritus. *N Engl J Med*. 2013;368:1625- 34.

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