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RESEARCH ARTICLE
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NEMOLIZUMAB IN CHRONIC NODULAR PRURIGO

Dr. Shaktibala Dutta[1], Dr. Navneet Dev[2*], Dr. Jyotsna Sharma[3], Dr. Smriti[4], Dr. Manjeeta Gupta[5], Dr. Deo Narayan Chaudhary[6], Dr. Amit Singhal[7], Dr.Srihari Dutta[8], Amit Kumar

[1]Professor and HOD, Department of Pharmacology, Graphic Era Medical college, Graphic Era Deemed University, Dehradun
[2]Associate Professor, Department of Dermatology, Graphic Era Medical College, Graphic Era Deemed University, Dehradun
[3]Professor & HOD, G S Medical College Pilkuhua
[4]Senior Resident, Department of Pharmacology, Graphic Era Medical college, Graphic Era Deemed University, Dehradun
[5]Senior Resident, Department of Pharmacology, Graphic Era Medical college, Graphic Era Deemed University, Dehradun
[6]Assistant Professor, Department of Pharmacology, Graphic Era Medical college, Graphic Era Deemed University Dehradun
[7]Associate Professor Department of Pharmacology, Graphic Era Medical college, Graphic Era Deemed University, Dehradun
[8]Regional Health Specialist, PHC, UNICEF, MENARO
[9]Assistant Professor, Department of Pharmacology, Government Medical College, Badaun[9]

***Corresponding Author:** Dr. Navneet Dev
*Associate Professor, Department of Dermatology, Graphic Era Medical college, Graphic Era Deemed University Dehradun

Pruritis for more than 6 weeeks along with scratching and presenxe of multiple pruriginous lesions is defined as Chronic prurigo (CPG)[1]. According to the clinical phenotype, CPG is classified into five subtypes:[2]

1. Papular (papules smaller than 1 cm),
2. Plaque (flat plaque > 1 cm)
3. Nodular (equal to prurigo nodularis, nodule > 1 cm)
4. Linear (linear arrangement),
5. Umbilicated (ulcers within the lesions) types.

All these subtypes can co exist together.

CNPG- Chronic Nodular Prurigo is characterized by intensively pruritic hyperkeratotic along with dome-shaped nodules which are more than 1 cm[3]. Pruritic is often persistent with high intensity of itch severity along with burning, stinging and pain. This can have negative impact on their appearance, daily activities, and quality of sleep [4]. Along with this, increased incidence of mental health disorders has been found in some cases.[5]

ETIOLOGY- Can be heterogenous and multifactorial including dermatological, systemic, neurologic, psychiatric or the combination of the above conditions, and unknown[1]. Psychiatric diseases, diabetes, atopic eczema, and allergy are most commonly associated diseases with chronic prurigo[4]. Along with these, co-morbidities such as pulmonary disease, cancer, human insufficiency virus (HIV), and metastatic disease are also associated[5,6].

PATHOPHYSIOLOGY- is multifactorial and complicated. There is interplay between the cutaneous, immune system, and nervous systems in patients with CNPG. Keratinocyte is a big source of growth factors and inflammatory cytokines, which leads to immune activation. There is enhanced infiltration of Th2, Th17/IL-17, Th22/IL-22, eosinophils, and mast cells which initiates the inflammatory process. This promote keratinocytes hyperproliferation. Along with this, neuronal hyperplasia in the dermis further releases neuropeptides, such as substance P, which activate the immune response. The itch-scratch vicious cycle execrates the inflammatory process and scratching causes mechanical damage to peripheral nerve fibers in the epidermis.[7]

TREATMENT- For treatment, recognizing the underlying cause and breaking the itch-scratch cycle are essential . There is no approved systemic licensed treatment for CNPG. Most of the therapies for CNPG are off-label administration. Japanese Dermatological Association[8] and the International Society for the Study of Itch[9], published guidelines for diagnosis and treatment strategies of CNPG .To summarise, topical corticosteroid was effective in the treatment of prurigo with precaution for long-term adverse effects and avoid in treatment-resistant patients. If treatment with topical corticosteroid was insufficient topical vitamin D3 analog, tacrolimus ointment, and topical capsaicin were considered. For systemic treatment, antihistamine is generally the first-line treatment. Ultraviolet light therapy can be used. Gabapentin, pregabalin, antidepressant, and immunosuppressant, such as cyclosporine and methotrexate, can be used. These traditional therapies sometimes showed insufficient responses. There are emerging therapies targeting the pathophysiology of CNPG and have been shown efficacious responses[7]. These includes Aprepitant, Serlopitant, Opioids, Gabapentin/ Pregabalin, Dupilumab, Nemolizumab and Abrocitinib.

Nemolizumab is a humanized antibody targeting IL-31RA. It has shown efficacy in pruritus and its different types[1] and is a treatment option for chronic pruritus now a days[10]. Various studies has been done for its efficacy. Some are listed in Table 1

TABLE 1: EFFICACY OF NEMOLIZUMAB IN DIFFEERENT STUDIES

S. No.	STUDY	DOSE	EFFICACY	ADR	PHASE
1.	Silverberg et al[10]	30 mg / placebo	NRS SCORE -68.8%/ -52.1%	NASOPHARYNGITIS AND UPPER RESPIRATORY TRACT INFECTION	Phase 2 b
2.	Tsoi et al[11]	0.5 mg /kg wt	Effective suppression of downstream inflammatory responses including T_H2/IL-13 and T_H17/IL-17 responses		
3.	Kabashima et al[12]	60mg/ placebo every 4 weeks till 16 weeks	VAS SCORE -42.8%/-21.4% EASI -45.9%/-33.2% DLQI <4 40%/22%	INJECTION SITE RESCTION	PHASE 3 TRIAL
4.	Stander. S et al[13]	0.5 mg / kg S.C / placebo	NRS SCORE 23.5%/ 0 (DAY 3) 55%/22.9% (WEEK 4)		PHASE 2
5.	Stander. S et al[14]	0.5 mg / kg S.C / placebo	NRS SCORE 53.5%/20%	GI SYMPTOMS MUSCULOSKELETAL PAIN	PHASE 2

All these studies showed that the use of subcutaneous nemolizumab helps in reduction in pruritus as compared to placebo. But for determining the durable effect and safety of Nemolizumab. Longer and larger trials are necessary.

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