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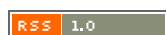
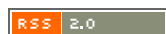
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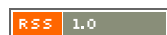
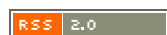
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TREATMENT FOR NEURODERMATITIS – BASED ON PATHOGENESIS OF IT (RETROSPEKTIF STUDY)

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Abstract

Background: Neurodermatitis is a chronic condition with a high recurrence rate. It is critical to avoid repetitive scratching. As topical treatments for neurodermatitis: topical steroids, intralesional steroids, keratolytic agents, and many more are all available. Menthol, camphora, and Liquor Carbonis Detergent can be used in conjunction with topical steroids to enhance their therapeutic effect. The purpose of this journal is to compare the therapeutic efficacy of combination drugs containing 0.05% clobetasol, 3% liquor carbonis detergent, and 2% salicylic acid to standard therapy for neurodermatitis.

Method: This study compares the efficacy of a new treatment therapy utilizing a combination of 0.05 percent Clobetasol, 3% liquor carbonis detergent, and 2% salicylic acid to standard therapy, specifically 0.05 percent Clobetasol. This is a retrospective cohort study conducted at the Indra Clinic. The samples for this study were all cases of neurodermatitis of the skin diagnosed at Indra's clinic between 2016 and 2017. The study's independent variable was the formulation of the drug, while the dependent variable was clinical improvement and the occurrence of side effects.

Results: The cure rate for the 126 respondents who received the combination formulation was 88,9%, compared to 77,5% for the 111 respondents who received standard therapy containing 0.05 percent Clobetasol (p : 0,029).

Conclusion: The innovative therapy of a 0.05% clobetasol mixture with 3% liquor carbonis detergent and 2% salicylic acid has been shown to improve clinical outcomes in patients with neurodermatitis more than the 0.05% clobetasol standard therapy.

Keywords: clobetasol; liquor carbonis detergens; salicylic acid; Chronic lichen simplex

1. INTRODUCTION

Chronic lichen simplex, also known as neurodermatitis circumscripta, is a common and chronic skin disorder characterized by thick, dry, scaly, and hyperpigmented skin that resembles "tree bark." This occurs as a result of a habit of scratching or rubbing the itchy skin area. While Chronic lichen simplex is not dangerous, it can interfere with psychosocial functioning, lowering sufferers' quality of life.(An et al., 2013; Charifa et al., 2020)

The peak incidence of Chronic lichen simplex occurs between the ages of 35 and 50 years. Chronic lichen simplex is more common in

women, with a ratio of 2: 1 between women and men. Patients with a history of atopic dermatitis tended to have Chronic lichen simplex at a younger age, that is, 19 years on average compared to patients without atopic dermatitis, which was a mean of 48 years.(Charifa et al., 2020; Dicky & Listiandoko, 2014)

Some studies say that Chronic lichen simplex is related to psychological factors such as depression, anxiety, emotional stress. In addition, the hypothesis states that Chronic lichen simplex can occur secondary to internal diseases such as renal failure or chronic obstructive biliary disease, Hodgkin's lymphoma, hyperthyroidism,

polycythemia rubra vera, and gluten sensitive enteropathy and other dermatoses as triggers, namely atopic dermatitis, allergic contact dermatitis, stasis dermatitis, insect bites, and xerosis cutis. Other triggering factors can be mechanical irritation (friction with clothes), and environmental factors such as hot weather, sweat, and irritating topical products such as preparations containing benzocaine, tea-tree oil, aloe vera, antiseptic, antifungal, preservative, perfume, lubricants, feminine washers, sanitary napkins and pantyliners. (Lotti et al., 2008; Torales et al., 2016)

Environmental factors such as heat, sweat, clothing friction, and the use of irritants all stimulate type C nerve endings, which are unmyelinated sensory nerves. These nerve fibers transmit mild itching and pain from the skin to the spinal cord and then to the central nervous system. Additionally, diseases that impair the skin's barrier layer can stimulate peripheral nerve endings, resulting in itching. Candida infection, dermatophyte infection, psoriasis, HPV infection, neoplasia, contact dermatitis, parasite infection (scabies and pediculosis), and lichen sclerosus are the most common diseases. (Lynch, 2004)

According to studies, neurotransmitters associated with emotion, such as serotonin, dopamine, or opioid peptide, modulate the perception of itching via a decrease in the spinal pathway, resulting in psychological disorders such as depression and emotional stress causing persistent itching and the desire to scratch the skin. Skin that is constantly scratched will undergo changes, affecting the patient's psychological state and resulting in a cycle of itching scratching. (Dicky & Listiandoko, 2014)

There are several critical steps in treating Chronic lichen simplex, including identifying and treating the underlying disease, reducing inflammatory reactions in the skin, improving the function of the skin barrier layer, and interrupting the cycle of scratching and itching. Topical steroids are anti-inflammatory and aid in the reduction of hyperkeratosis. The use of medium-high potency topical steroids is recommended because they are considered to be more effective and safer for short-term (less than 3 weeks) use than low potency topical steroids. When several weeks of topical steroid use is ineffective, systemic steroids are given. (Dicky & Listiandoko, 2014; Lynch, 2004)

Due to the difficulty in inhibiting the scratch itch cycle, chronic lichen simplex has a high recurrence rate. Apart from medication,

patients should be taught to refrain from rubbing, scraping, and scratching their skin. When the patient feels the urge to scratch, ice cubes or a cold compress should be applied until the itching subsides. This can be beneficial, but only temporarily. Additionally, patients are advised to engage in activities that will divert their attention away from the scratching habit, such as keeping their hands busy while watching television or reading books by holding objects such as rubber balls, and while driving with both hands on the steering wheel. Additionally, it is recommended to wear loose cotton clothing and to avoid irritant-containing products. (Lynch, 2004; Torales et al., 2016)

The preceding description demonstrated how difficult it is to manage neurodermatitis, owing to the disease's complicated pathogenesis. As a result, various formulations or drug combinations, particularly topical ones, are required to treat neurodermatitis. The purpose of this journal is to compare the therapeutic efficacy of combination drugs containing 0.05 percent clobetasol, 3 percent liquor carbonis detergent, and 2% salicylic acid to standard therapy, which contains 0.05 percent clobetasol, for the treatment of neurodermatitis or chronic lichen simplex.

2. METHOD AND MATERIAL

This was a retrospective cohort study in which we compared two different treatment formulations. The population for this study was comprised of all patients with chronic lichen simplex on the skin seen at Indra's clinic between 2016 and 2017. The research sample is composed of individuals who meet the study's inclusion criteria. The study's inclusion criteria were a minimum age of 12 years and a dermatologist diagnosis of chronic lichen simplex. Incomplete medical record data or a history of allergy to drug content were used as exclusion criteria in this study. A minimum sample size of twenty samples is required for each treatment formulation group (type 1 error is 5 percent and type 2 error is 20 percent). Non-random purposive sampling was used to collect data. The purpose of this study is to examine all patient medical record data from 2016 to 2017 for information on the diagnosis and treatment of chronic lichen simplex. The study's independent variable was a treatment formulation for chronic lichen simplex in the skin consisting of 0.05 percent clobetasol or a combination of 0.05 percent clobetasol, 3% liquor carbonis detergent,

and 2% salicylic acid applied topically. In this study, the dependent variables were treatment success (improved or not), adverse events during treatment, and post-treatment symptoms. The two types of data analysis are descriptive data analysis and analytic data analysis. The proportion (percent) for the type of qualitative data and the distribution of centralized data are included in descriptive data analysis (mean, SD, median, minimum, maximum). Analytical data analysis employed a comparative test for unpaired categorical data in the form of the Pearson Chi Square test, the Chi Square with Yates Correction test, or the Fisher Exact test, as appropriate for each statistical test.

3. RESULT

This study included 237 respondents with neurodermatitis of the skin. 126 respondents received clobetasol formulation therapy (Clobetasol 0.05% with 3% liquor carbonis detergent and 2% salicylic acid) and 111 respondents received standard therapy in the form of 0.05% Clobetasol. Patient demographic characteristics are presented in full in Table 1 for each group.

Table 1. Demographic Characteristics of Respondents

Variable	Treatment		p-value
	Clobetasol Formulation N : 126 responden	Clobetasol 0,05% N : 111 responden	
Age	34,51 (15,8)	42,02 (18,86)	> 0,05
Sex			
• Male	76 (60,3%)	65 (58,6%)	> 0,05
• Female	50 (39,7%)	46	

The therapy was given for 2 weeks and was re-examined at the next visit. Of the 126 respondents who received a combination formulation containing a combination of 0.05% Clobetasol with 3% liquor carbonis detergent and 2% salicylic acid, a cure rate of 88.9% was obtained, while 111 respondents received standard therapy containing 0.05% Clobetasol. obtained a cure rate of 77.5%. According to the Chi Square with Yates Correction statistical test, it was found that there was a difference in the level of clinical improvement from neurodermatitis to the formulation therapy when compared with standard therapy (p-value: 0.029).

Table 2. Therapeutic Effectiveness between 2 Treatment Regimens

Parametric	Clinically after 2 week		p-value
	Remission in <2 week	Remission in > 2 week	
Combination of 0.05% clobetasol with 3% liquor carbonis detergent and 2% salicylic acid	112 (88,9%)	14 (11,1%)	0,029
The standard regimen of 0.05% Clobetasol	86 (77,5%)	25 (22,5%)	

Assessment of side effects was carried out on the use of 2 drug formulations. It was found that the symptoms of side effects were only persistent itching and redness during drug use. The Fisher Exact statistical test revealed that there was no significant difference in side effects between the 2 intervention groups.

Table 3. Side effects between the 2 Treatment Regimens

Variable	Drug Formulation		p-value
	Clobetasol Formulation N : 126 responden	Clobetasol 0,05% N : 111 responden	
Side effects			
• Persistent itching	26 (20,63%)	38 (34,23%)	> 0,05
• Redness	14 (11,11%)	17 (15,32%)	> 0,05
• Skuama	-	-	-
• Hyperpigmentation	33 (26,19%)	36 (32,43%)	> 0,05
• Hypopigmentation	5 (3,97%)	3 (2,7%)	> 0,05

4. DISCUSSION

Neurodermatitis or Chronic Lichen Simplex is a chronic skin disease characterized by lichenified plaques that form as a result of constant scratching or rubbing on the skin. Itching is the main symptom affecting the course of neurodermatitis. Itching of the skin is mediated by atopy and psychological conditions. Due to repeated scratching and friction on the skin, epidermal hyperplasia and hyperkeratosis occurs so that the skin will become thickened and scaly known as lichenification. Generally itching is felt suddenly and gets worse at night. The most common triggers of this itching are mechanical irritation, heat, sweat, stress and anxiety. The clinical features of neurodermatitis are clearly defined itchy lichenified plaques with scale,

excoriation and pigmentation changes.(Fölster-Holst, 2017; Lynch, 2004; Voicu et al., 2017)

Neurodermatitis is difficult to treat and has a high recurrence rate. Preventing repetitive scratching is critical. Additionally, reducing stress and anxiety is critical for itching relief. Topical steroids, intralesional steroid injection, keratolytic agents, capsaicin, tacrolimus, pimecrolimus, cryotherapy, doxepin, and botulinum toxin are all available as topical treatments for neurodermatitis. Antihistamines, antidepressants, and psychotherapy are all examples of systemic therapy modalities. The primary treatment option for neurodermatitis is topical steroids. Menthol, camphora, and Liquor Carbonis Detergent can be combined to enhance the therapeutic effect of topical steroids.(Evers et al., 2016; HUBLER, 1949; Kägi, 1998; Manolache, 2013)

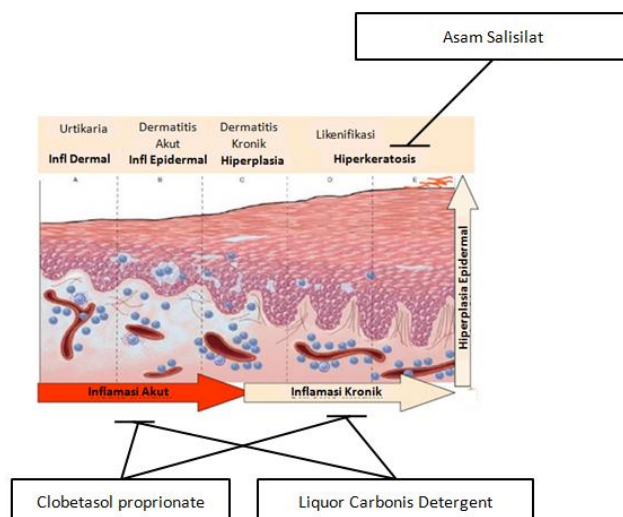


Figure 1. Mechanism of keratolytic and anti-inflammatory action in neurodermatitis.

Different topical steroid formulations have varying degrees of potency. Its effectiveness is proportional to the extent to which the steroid

molecule penetrates the skin, which is determined by the chemical structure of the steroid used. Additionally, the dosage form and the state of the

skin affect the drug's absorption. Low-potency steroids should be used in children. Steroids should be of low to moderate potency in adults. Clobetasol is an extremely potent anabolic steroid. It is typically used in the treatment of skin diseases at a concentration of 0.05 percent. Clobetasol is an anti-inflammatory medication that is used to treat a number of different skin conditions.(Feldman & Yentzer, 2009; Gottlieb et al., 2003; Olsen & Cornell, 1986; Pels et al., 2008; Warino et al., 2006)

The primary condensation of coal results in the formation of Liquor Carbonis Detergent. This preparation is thought to work by inhibiting DNA synthesis and proliferation of keratinocytes. Liquor Carbonis is a topical detergent that has keratolytic, antiacanthotic, photosensitizing, vasoconstrictor, antipruritic, and antimicrobial properties. In comparison to corticosteroids, this medication is more effective at managing mild to moderate psoriasis over the long term, with fewer side effects and a decreased risk of recurrence.(KANZLER & GORSULOWSKY, 1993; MERK et al., 1984; Thawornchaisit & Harncharoen, 2007)

In neurodermatitis, keratolytics are recommended as adjuvant therapy. Keratolytics are primarily used to hydrate the stratum corneum, desquamate the skin, alleviate itching, and increase the penetration of topical drugs and phototherapy. Salicylic Acid (also known as 2- Hydroxybenzoic Acid / Orthohydrobenzoic Acid) is a hydroxy acid. Salicylic Acid can be obtained naturally or chemically synthesized. Salicylic acid acts as a keratolytic, comedilytic, sebolytic, antihyperplastic, desmolytic, antimicrobial, and anesthetic on the skin. Salicylic acid has been extensively studied and used as a keratolytic. This preparation has a rapid and deep keratolytic effect that results in desquamation at concentrations of 5% and greater. Salicylic acid works by dissolving intercellular material and lowering the pH of the stratum corneum, resulting in increased hydration and softening.(Arif, 2015; de Mare et al., 1988; Jacobi et al., 2015; Lebwohl, 1999; Torsekar & Gautam, 2017)

Combination of clobetasol, Liquor Carbonis Detergent, and Salicylic Acid Effects on neurodermatitis based on: (A) Urticaria is a hypersensitivity reaction to acute inflammation that begins with dermal inflammation. (B) In acute dermatitis, the epidermal layer remains inflamed. (C) If the dermatitis is chronic, the epidermal layer will undergo hyperplasia. (D) Over time,

hyperkeratosis occurs, resulting in the appearance of scales (E) on the skin, as seen with lichenification. Clobetasol propionate and Liquor Carbonis Detergent act on the skin by inhibiting inflammation, thereby controlling the progression of the disease that results in hyperplasia and hyperkeratosis. Salicylic Acid acts as a keratolytic, removing the excess scales associated with hyperkeratosis. The combination of the three will gradually eliminate the thickening and scales on the skin's surface.(Carrera et al., 2018; Hugh & Weinberg, 2018; Ogawa et al., 2018; Pascoe et al., 2015; Talamonti et al., 2018)

Ointments and serums are prepared according to the dermatological drug preparation standard. A combined psoriasis ointment is prepared by combining 500 grams of Vaseline Album with 0.05–1.5 percent Clobetasol, 3-5 percent Liquor Carbonis Detergent, and 2–5% Salicylic Acid. The serum contains 20% Natrosol, 0.05–1.5% Clobetasol, 3-5% Liquor Carbonis Detergent, and 2–5% Salicylic Acid. The mixture is diluted to a 100 percent aqua concentration. The ointment and serum preparations are combined in a specially designed container. The container includes instructions for use, indications, contraindications, and adverse effects.

5. CONCLUSION

The innovative therapy of a 0.05% clobetasol mixture formulation with 3% liquor carbonis detergent and 2% salicylic acid has been shown to provide a better clinical improvement rate in patients with neurodermatitis compared to standard therapy which is only 0.05% clobetasol. The cure rate in the group of 0.05% Clobetasol mixed formulation therapy innovation with 3% liquor carbonis detergent and 2% salicylic acid was 88.9%, while the group receiving standard therapy containing 0.05% Clobetasol had a cure rate of 77.5%. There were significant differences between the 2 therapy groups, and no significant differences in side effects were found between the 2 groups.

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