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Clinical Management of Acral Lick Dermatitis in Dogs with Comparison of Fluoxetine and Clomipramine Treatment

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ABSTRACT

Background: Acral lick dermatitis is defined as self inflicted skin disorder in dogs which induces localized alopecia and fibrotic lesion due to repetitive licking or chewing at the same 'site most commonly near carpus or hock areas.

Methods: The present study was carried out to investigate the approach to the management of various etiologies associated with ALD in dogs. A total of 30 dogs that were diagnosed with acral lick dermatitis (ALD) were rated on the day 0 of theirvisit to the hospital on the basis of three clinical scalesie; ALD severity scale, clinical global impression (CGI) and likert scale. Assessment and weekly rating of the ALD lesion was done during the entire treatment trial.

Result: Dogs positive for psychogenic primary triggers were randomly divided in Group 1 (n=9; 47.36%) and Group 2 (n=10; 52.63%). Dogs in group 1 were treated with fluoxetine and dogs in group 2 were treated with clomipramine. Whereas dogs diagnosed with organic triggers were treated empirically. Dogs treated under group 1 exhibited significant difference ($p<0.05$) in the licking and ALD score values at the end of the trial, however, CGI score values were found to be non significant ($p>0.05$) with mean recovery in 24±2 days and recurrence rate of 44.44% after mean 105±47 days of their treatment completion. 33.33% dogs were also reported with adverse effects of drug as drowsiness in group 1. Dogs treated under group 2 exhibited significant difference ($p<0.05$) in pre and post treatment values of all 3 scores (licking score, ALD score and CGI score) at the end of the trial with mean recovery in 41±5 days and 55.55% cases were reported with signs of reoccurrence after mean 37±21 days of their treatment completion. Total 2(20%) dogs out of ten were presented with adverse effects; 1(10%) with loss of appetite and 1(10%) was reported with vomiting. Both clomipramine and fluoxetine are effective in treating psychogenic triggers of ALD. However, fluoxetine helps in early recovery with lesser recurrence rates whereas clomipramine having better recovery rate with fewer side effects.

Key words: Acral lick dermatitis, Clomipramine, Dogs, Fluoxetine, Phsycogenic trigger.

INTRODUCTION

Dermatological disorders are among the most well-documented and difficult to treat of all the health symptoms, according to small animal medicine professionals. Amongst these, canine acral lick dermatitis (ALD) is one of the most frustrating dermatological disorders of dogs. The word Acral literally means "peripheral parts such as limbs" so the term acral licks dermatitis is defined as lesion of extremities occurreddue to repetitive licking. It is comparable to obsessive-compulsive disorder (OCD) of humans, well-known psychological disorder marked by repetitive obsessive thoughts and repetitive behaviour (overall *et al*. 2002). Most dogs with compulsive disorders exhibit signs such as tail chasing, spinning, pacing, or self-mutilation, which are persistentor recurring behaviours (Veith. 1986). Furthermore, due to the similarities of behaviours linked with human OCD and Canine ALD and similar responses to selective serotonin reuptake inhibitors (SSRIs), it was postulated that acral lick dermatitis could serve as an OCD neurobiological model in humans (Goldberger and Rapoport, 1991). The primary factors of ALD formation are the triggering factorsand propagating elements constitute a constant key drive to lick the areas affected. The primary organic factors are allergic disorders, bacterial infection, dermatophytosis, parasitic disorders (scabies, demodicosis), trauma, foreign body, neurological disorders, orthopaedic ailments, neoplasia and endocrine disorders. Stereotypic or obsessive-compulsive disorder (OCD), anxiety, boredom, attention seeking, or stresses are examples of primary psychogenic disorders. Secondary bacterial infections, keratin foreign bodies from licking and the establishment of a secondary compulsive behaviour or learned activity are all causes that reinforce each other (Shumakar *et al*. 2008). After the physical examinations are completed, a diagnostic strategy can be created to look into any underlying problems. Skin scraping, hair plucking, fine needle aspiration and impression smear collection are among the basic core tests

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which should be performed in each patient, additionally biopsy and tissue culture are needed to be done in required cases. ALD is infamous for being difficult to manage. Corticosteroids (intraregional or topical), surgical excision, proteolytic enzyme topical application, non-steroidal anti-inflammatory drugs, cobra venom, radiation therapy, restrictive and electronic collars, acupuncture and cryotherapy were all mentioned as ways to break the compulsive licking component of acral lick dermatitis. There hasn't been a single therapy that has been proven to cure lesions without recurrence. The present investigation was hence undertaken to study the therapeutic aspects of acral lick dermatitis in dogs.

MATERIALS AND METHODS

The study was carried out in Multi-Specialty Veterinary Hospital of GADVASU, Ludhiana (India). The study was conducted from September, 2019 to March, 2020 which included a total of 30 dogs diagnosed with acral lick dermatitis (ALD) out of 440 dogs affected with various dermatological conditions. ALD was approached in much the same way as other skin diseases. The schematic approach included signalment, medical history, initial presentation and location of lesion and detailed physical examination.

The information about the dog's lifestyle was also the part of history taking which included questions regarding exercise routine, confinement duration, feeding schedule, interaction with family members and other companion animals. A previous history of systemic, orthopedic or neurological illnesses as well as ongoing issues with these disorders, were questioned about. A thorough examination was carried out in order to rule out any dermatological, orthopedic or neurological stressors as key organic contributors in development of ALD. The basic essential tests which were performed in each case suspected for ALD were skin scrapings, trichography, fungal culture, impression smears and fine needle aspiration for cytological examination of the lesion. Dogs presented with more generalized skin diseasesunderwent additional investigation such as histopathological examination and those with generalized pruritic skin diseases were ruled out for atopic dermatitis using Favrots' criteria (Favrot *et al*. 2010) and flea allergy. The observation of dog's gait, balance and proprioceptive position were evaluated to rule out neurological stressor as primary cause of ALD. Surveys radiographs of the affected limbs were performed in the required cases to rule out any orthopedic stressor. To rule out primary psychogenic stressors like anxiety, obsessive compulsive disorder, attention seeking, boredom different questions were asked from owners regarding any other concurrent behavioral symptoms, change in environment, emotional stress *etc*.

Table 1: Scoring of ALD lesion using Acral Lick Scale, Stein *et al.* (1998).

Score	Severity
0	Normal
1-2	Minimal lesions, Subclinical
3-4	Mild clinical lesion, *e.g.,* Slight inflammation
5-6	Moderate lesion, *e.g.,* Inflammation obvious
7-8	Severe lesion, *e.g.,* Much inflammation
9-10	Very severe, *e.g.,* Purulent

Scales rating

Dogs were rated on the day they arrived hospitalon the basis of three clinical scales ALD severity scale Stein *et al*. (1998) (Table 1), Clinical Global Impression (CGI) (Table 2) and Likert scale (Table 2). ALD severity scale is 10-point scale using range of severity of lesion from 0 (normal) through 10 (very severe). The CGI is rated on a 7-point scale, with the severity of illness scale (Table 2) using a range of responses from 1 (normal) through to 7 (amongst the most severely ill patients). Post treatment CGI-C scores (Table 2) range from 1 (very much improved) through to 7 (very much worse). Likert scale is a 7-point scale using range of severity of licking from 1 (not rated) through 7 (Very severe excess licking).

Cases with organic stressors as primary cause of licking were treated with specific therapy and those with psychogenic stressors as primary cause were managed with behavioral modifier drugs such as fluoxetine and clomipramine. Nineteen dogs positive for psychogenic primary triggers were randomly assigned Group 1 (n=9; 47.36%) and Group 2 (n=10; 52.63%). Dogs in group 1 were treated with fluoxetine @ 1mg/kg body weight once a day for a period of at least 1 month to remission of clinical signs and dogs in group 2 were treated with clomipramine @ 1 mg/kg once a day initially and increased as tolerated further to 1-2 mg/kg twice a day for a period of at least one month to

Table 2: CGI- Measuring of severity of Illness, CGI C- Measuring of global improvement, recording of licking behaviour using likert scale.

Score	Degree of illness (CGI)	Degree of improvement (CGI-C)	Degree of licking (Likert scale)
0	Not assessed	Not assessed	-
1	Normal, not at all ill	Very much improved	Not rated
2	Borderline mentally ill	Much improved	No excess licking at all
3	Mildly ill	Minimally improved	Very mild excess licking
4	Moderately ill	No change	Mild excess licking
5	Markedly ill	Minimally worse	Moderate excess licking
6	Severely ill	Much worse	Severe excess licking
7	Among the most extremely ill patients	Very much worse	Very severe excess licking

remission of clinical signs. Dogs selected under this trial had no history of hepatic disease, renal disease, seizures, or diabetes mellitus and owners were willing to comply with the study procedures.Assessment and weekly rating of the ALD lesion was done during the entire trial. Owners were interviewed weekly through telephone for side effects and to ensure compliance for a period of 2 months.

RESULTS AND DISCUSSION

The treatment strategy included addressing the underlying causes, infection and lesions, as well as addressing any behavioral issues that may exist. Identify any environmental changes that may be responsible and modify them to reduce anxiety.

A total of 30 cases out of 440 dermatological cases with prevalence of 6.81 per cent were diagnosed with ALD. It was found that there was maximum occurrence of psychogenic stressors with 19 cases (63.33%) followed by only organic stressors in 9 cases (30%) and combination cases which included primary organic stressors with secondary psychogenicstressors were 2 cases (6.66%). The maximum prevalence among organic stressors were reported with atopic dermatitis (16.66%) followed by demodicosis (6.66%), orthopaedic stressors (3.33%), hypothyroidism (3.33%), flea allergic dermatitis (3.33%) and lymphoma (3.33%). However, no relevant data was available on percent prevalence of etiology of ALD. The findings of present study correspond to the findings of Patel (2010) and Shumaker (2019) who found that creation of ALD lesion required multifactorial triggers and these might have both organic and behavioural causes.

Out of total 30 dogs, only 4 dogs had no history of prior treatment for ALD. Of the remaining 26 subjects, 8 had been on systemicantibiotic treatment (26.66%), 6 had history of bandages applied on the lesion (20%) and 12 were using local antibiotic ointments (40%).

The pre and post treatment values of three clinical scores in group 1 were compared using with Wilcoxon signed ranks test ($p<0.05$). The Mean±SE of licking score, ALD score and CGI score of the pre-treatment group were 4.9±0.454, 5.8±0.894 and3.9±0.423, respectively whereas the Mean±SE of licking score, ALD score and CGI score of the post-treatment group were 2.8±0.493, 2.2±0.741 and 2.6±0.647, respectively. Significant difference ($p<0.05$) was observed in the licking and ALD score values at the end of the trial, however, CGI score values were found to be non significant ($p>0.05$). The drug was found useful in controlling licking and inflammation associated with the disease but had poor recovery in some patients due to side effects which are discussed later. The findings of the present study are partially in agreement with the results of previous studies (Wynchank and Berk's 1998) who studied efficacy and tolerability of fluoxetine in the treatment of canine ALD and explained that the drug appeared to be a useful therapeutic modality for ALD disorder in dogs. In our study fluoxetinewas found to be efficient in the treatment of ALD but tolerability of drug was found less in dogs with ALD.

The pre treatment values of Group 2 (Mean±SE) of licking score, ALD score and CGI score were 4.9±0.378, 6.2±0.573, 3.8±0.359 respectively. The post treatment Mean±SE values of licking score, ALD score and CGI-C score in this group were 2.8±0.326, 2.5±0.601, 2.2±0.326, respectively.Significant difference ($p<0.05$) in pre and post treatment values of 3 scores (licking score, ALD score and CGI score) were recorded at the end of the trial. This study was in agreement with Overall (1994) who reported clomipramine was the drug that had been reported as most successful in the treatment of canine compulsive diseases. Another study reported that clomipramine was also more effective than the other tricyclics as a treatment for obsessive compulsive disorder (McTavish and Benfield 1990).

Post treatment score of Group 1 and Group 2 were compared using Mann-Whitney test ($p<0.05$). Dogs were compared for post treatment licking score, ALD score and CGI score with one assumption that all the dogs presented for the treatment of ALD were equally affected with disease. The mean±S.E. of licking score, ALD score, CGI-C score in post treatment group 1 were 2.8±0.493, 2.2±0.741, 2.6±0.647, respectively and the mean±S.E. of licking score, ALD score, CGI-C score in post treatment group 2 were 2.8±0.326, 2.5±0.601, 2.2±0.326, respectively. No significant difference ($p>0.05$) was observed in the post treatment score values between two groups suggesting both drugs were equally effective. However, on comparing pre and post treatment score values separately for two groups, clomipramine was found to be more effective than fluoxetine. This study was in line with (Pigott *et al.* 1990 and Yalcin 2010) who concluded that the two drugs were successful in the treatment of OCD and that they did not have superiority over each other. Although, Jenike *et al*. (1990) had suggested that clomipramine had larger effect than fluoxetine in reduction of scores on the Yale-Brown Obsessive-Compulsive Scale.

This disease is viewed as disease with combination of both primary and perpetuating factors.All dogs presented for acral lick dermatitis were treated initially with antibiotics, as infection is a major contributor to the lesion's persistence. The antimicrobial therapy was prescribed after culture and sensitivity test (CST) to control secondary bacterial infections for a period of 1 to 2 weeks along with the treatment of primary psychogenic triggers. Oral cephalexin was given at dose rate of 25 mg/kg body weight twice a day, oral clindamycin at the dose rate of 10 mg/kg body weight twice daily, enrofloxacin was given orally at the dose rate of 5 mg/kg body weight twice daily, (Amoxycillin + clauvulanic acid) orally at dose rate of 15 mg/kg body weight twice dailydepending upon the CST results.

Another crucial step in the treatment is to minimize access to the acral lick location. Even if the primary cause and underlying infection are properly managed, healing is unlikely if the dog is allowed to continue licking the wound. Physical restraint using Elizabethan collars was customised for dogs and was very effective.

Among the dogs treated under group 1, 6 (66.66%) dogs recovered completely with mean recovery in 24±2 (Table 3, Fig 1a and 1b) days and among dogs treated under group 2, 9 (90%) dogs showed recovery in mean 41±5 days (Table 3, Fig 2a and 2b).In the present study, it was seen that theanimals treated with fluoxetine (Group 1) recovered earlier than clomipramine (Group 2) which was contrary to the study of Pigott *et al*. (1990) who reported that responses to clomipramine drug took as long to occur as responses to the fluoxetine drug.

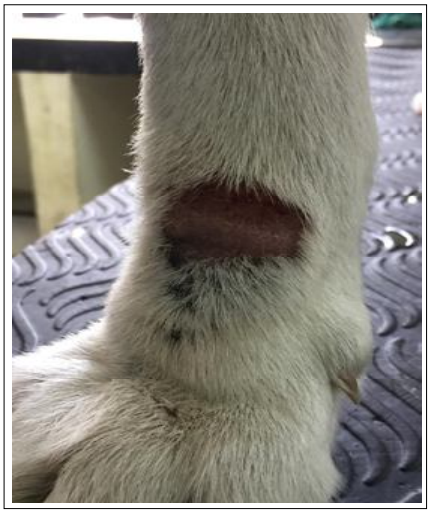

Fig 1a: ALD lesion in dog affected with psychogenic trigger.

Fig 1b: The same dog treated with fluoxetine for 4 weeks.

Four out of thenine dogs (44.44%) under group 1 were reported with reoccurrence of symptoms after mean 105±47 days of their treatment completion whereas under Group 2, five out of ten dogs (55.55%) were reported with signs of reoccurrence after mean 37±21 days of their treatment completion (Table 4). The present study was in agreement with Luescher (2003) and Virga (2003) who reported that there is no single therapy that had been successfully shown to fix lesions without reoccurrence.

In group 1, nine dogs were treated with fluoxetine and 3 (33.33%) dogs were reported with adverse effects of drug as drowsiness and in Group 2, ten dogs were treated with clomipramine and 2(20%) dogs were presented with adverse

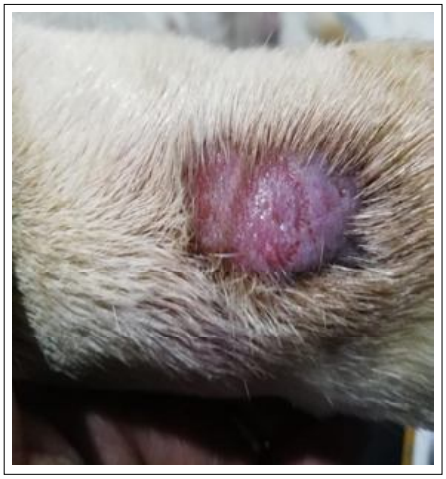

Fig 2a: Lick granuloma diagnosed with psychogenic trigger.

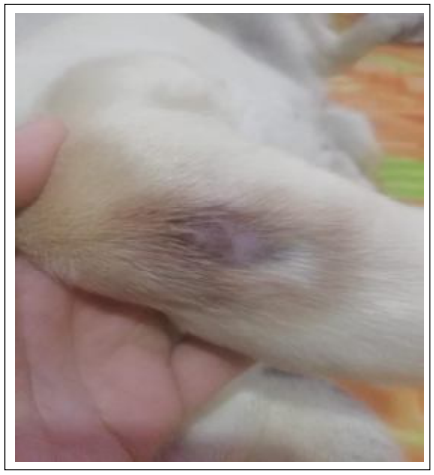

Fig 2b: The same dog after treatment with clomipramine for 5 weeks.

Table 3: Recovery in dogs treated under Group 1 and 2.

Group	No. of cases	Number of cases recovered						Percent recovery
		Days post treatment					Total no. of dogs recovered	
		15	30	45	60	>60		
1	9	2	4	-	-	-	6	66.66%
2	10	-	4	3	2	-	9	90%

effects; 1(10%) with loss of appetite and 1(10%) was reported with vomiting. The study was in agreement with Irimajiri *et al.* (2009) who studied that the most commonly reported adverse effects with fluoxetine were lethargy 12(39%)and decreased appetite 7(23%). Another study reported lethargy, loss of appetite, diarrhoea and growling as the common side effects of clomipramine treatment Rapoport *et al*. (1992). The present study was contradictory to Pigott *et al*. (1990) findings who reported that there were significantly fewer total side effects reported with fluoxetine than with clomipramine treatment.

Therapeutic management of organic stressors; atopic dermatitis (n=5), demodicosis (n=2), orthopaedic stressors (n=1), hypothyroidism (n=1), flea allergic dermatitis (n=1) and lymphoma (n=1)creating pseudo lick wounds were carried out along with comparison of pre and post treatment scores of three scales used in the study (Table 5). Cases diagnosed with atopic dermatitis (n=5) stressorwere treated with prednisolone at anti- inflammatory dose 0.5 mg/kg twice a day for one week and tapered to dose 0.5 mg/kg once a day on alternative days in a period of 4 weeks. All the cases responded completelyto the primary treatment and no behavioural modification was required in any of the case (Fig 3a and 3b). Dogs diagnosed with demodicosis stressor (n=2) were treated with ivermectin at the dose of 400 mcg/kg subcutaneously weekly shots for four weeks. Recovery was seen in both the cases with no need of behavioural management. Orthopaedic stressors (n=1) were treated with carprophen 4 mg/kg bwt. orally once a day for a period of 5 days. Complete resolution in limping was seen with no improvement in lick wound, considering the licking as a learned way of acting, behavioural modification was done with serotonin reuptake blockers. Improvement in the wound afterwards noticed within a period of 1 month. Only one dog was diagnosed with hypothyroidism (n=1) and later treated with levothyroxine 20 µg/kg once a day for period of one month. Complete recovery in the lesion was seen with no need of behavioural modification. This study was in agreement with (Jöchle. 1998) who used thyroxine for management of disturbed abnormal behaviour in dogs suffering from hypothyroidism. One dog with ALD was also diagnosed with flea allergic dermatitis primary treatment was done with fipronil (9.8% w/w)/ (s)-methoprene (8.89%w/w) spot on. Animal did not show complete recovery from licking. Behavioural modification was done afterwards.One case with lick wound diagnosed with lymphoma animal was treated with Doxorubicin 30 mg/m^2, iv in NSS and repeated after a period of 21 days for 3 times. Animal showed complete recovery from wound after the treatment. Denerolle *et al*. (2007) also mentioned in their study a case of lymphoma mimicked with canine acral lick dermatitis.

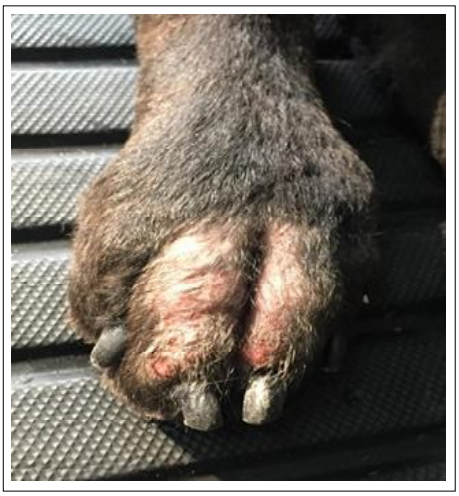

Fig 3a: ALD affected dog with atopic dermatitis trigger.

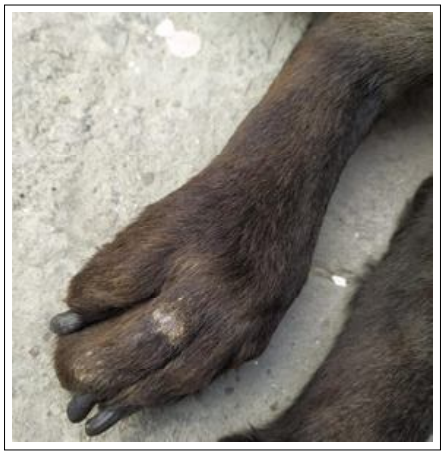

Fig 3b: Same dog after treatment with prednisolone

Dogs with ALD have been shown to have changes in their serotonergic and dopaminergic neurotransmission systems. Serotonin is a neurotransmitter that governs several physiological activities, including sleeping, eating, aggressiveness and self-grooming (Vermeire *et al*. 2012). In dogs, antidepressants known as selective serotonin reuptake inhibitors (SSRIs) have shown considerable improvement in fluoxetine groups (Wynchank and Berk 1998). Other pharmaco-therapeutic medications have also been demonstrated to be beneficial in combating ALD with varying responses, indicating that more than one transmitter or variables apart from serotonin are responsiblefor ALD.

Table 4: Reoccurrence reported in dogs treated under Group 1 and 2.

Groups	<1 month	1-2 months	2-5 months	>5 months	Reoccurrence %
Group 1	1	1	1	1	4
(n=9)	(11.11%)	(11.11%)	(11.11%)	(11.11%)	(44.44%)
Group 2	4	-	1	-	5
(n=10)	(40%)		(10%)		(55.55%)

Table 5: Therapeutic management of organic triggers (n=11).

Organic trigger	treatment	Regimen	Pre treatment			Post treatment			Recovery (yes/No)	Treatment2 (behavioural modification)
			Licking score	ALD score	CGI score	Licking score	ALD score	CGI-C score		
Atopic (n=5)	Prednisolone 0.5 mg/kg bwt	1 week bid, followed by 2 weeks days od and further for 2 weeks on alternate day, p.o	4	3	2	1	0	1	Yes	Not required
			5	3	3	1	0	1	Yes	Not required
			4	3	2	2	1	1	Yes	Not required
			6	6	4	3	2	2	Yes	Not required
Demodicosis (n=2)	Ivermectine 400 mcg/kg	once a week for 4 weeks, sc	5	5	4	2	1	1	Yes	Not required
			5	8	4	4	3	2	Yes	Not required
Orthopaedic (n=1)	Carprophen 4 mg/kg bwt	4 mg/kg p.o once a day for a period of 2 weeks	5	5	3	2	2	2	Yes	Not required
			5	2	4	4	2	3	No	Done
Hypothyroidism (n=1)	Levothyroxine 20 µg/kg	Once a day for period of 1 month, p.o	3	4	2	1	0	1	Yes	Not required
Flea allergic dermatitis (n=1)	Fipronil (9.8% w/w)/ (s)-methoprene (8.89% w/w) spot on	Once, local application	4	4	3	4	4	4	No	Done
Lymphoma (n=1)	Doxorubicin 30mg/m^2, iv in NSS	Repeated after a period of 21 days × 3 times	5	6	4	5	6	4	No	Done

Clomipramine, a tricyclic antidepressant (TCA), was found to be beneficial for treatment of ALD in dogs. TCAs block both serotonin and norepinephrine reuptake, but SSRIs are more selective, blocking just serotonin reuptake; as a result, SSRIs are associated with less adverse side effects.

Thus ALD is known to be more complicated, with numerous potential underlying primary and perpetuating factors. As a result, a thorough diagnostic work-up is required to identify the primary trigger, whether organic, psychogenic, or a combination of both and to tailor the appropriate treatment plan. A multimodal treatment approach is required for a successful outcome, including identifying and treating any secondary infections and interrupting the itch-lick cycle.

CONCLUSION

ALD is a multifactorial ailment and accurate diagnosis of underlying stressor is important for its management. Clomipramine and Fluoxetine both are effective in treating psychogenic stressors of ALD with fluoxetine helps in early recovery from the lesions with lesser recurrence rate whereasclomipramine is having better recovery rate and fewer side effects.

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Conflict of interest: None.

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