ASSESSMENT OF PRURITUS USING PRURITUS SCORE TEST IN DOGS WITH ATOPIC DERMATITIS TREATED WITH CYCLOSPORINE OR PREDNISONE

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Received for publication April 20, 2010

Abstract

The purpose of this study was to evaluate the suitability of pruritus score test in pruritus diagnosis in dogs. The test was used to assess the frequency and severity of pruritus in dogs between 1 and 3 years of age, suffering from atopic dermatitis. Skin pruritus was assessed: during the first visit (examination 0), after elimination of secondary dermatosis (examination 1), 2 weeks after the treatment with prednisone – group I-E or cyclosporine - group II-C (examination 2) as well as 6 weeks after treatment (examination 3). In examination 0, the skin pruritus in all dogs was scored at 26.75%. Reduction of pruritus was observed during the treatment in examination 3 in dogs of group I-E (by 80.46%) and in dogs of group II-C (by 86.12%) in comparison with examination 0. Localisation of pruritus in particular body parts was also examined, resulting in observation that in examination 0 it was mostly found in interdigital space of front paws, facial part of the muzzle, chin, ears but not always with the same intensity in symmetrically placed body parts. Mean values of the measurement were statistically significant (P ≤ 0.005) after 2, 4, and 6 weeks of the treatment in I-E and II-C groups. No statistically significant differences were observed between I-E and II-C groups in consecutive measurements.

Key words: dogs, canine atopic dermatitis, pruritus severity scale, pruritus score test.

Canine atopic dermatitis (CAD, AD) is a pruritic inflammatory skin disease resulting from genetic predisposition to development of IgE-dependent hypersensitivity for environmental allergens (6, 14, 18, 21, 30). It is chronic dermatosis with episodes of remission and exacerbations. Pruritus, observed by pet owners during disease, can occur seasonally (mostly in spring and summer) or it can persist all year and is mostly localised in predilectional body areas (6, 14, 19, 21, 30), where characteristics of bacterial and fungal infections, as well as disorders of sweat and sebaceous gland function, erythematous lesions, and signs of secondary dermatoses are observed. Skin lesions are mainly localised at facial part of the muzzle, chin, around eyes, auricle, external auditory canal, interdigital space even reaching to wrists and ankles, as well as axillae and groins (6, 14, 19, 21, 30). Generalised pruritus in the course of disease is observed infrequently.

Definition of pruritus as “… an unpleasant sensation with the urge of scratch” described 350 years ago by German physician Haffenreffer (according to 9) is also in use nowadays (4, 10, 22, 26, 27, 28). According to neuropathological classification proposed by Twycross et al. (29), pruritus occurring with AD is classified as neurogenic – caused by pruritogenic factors such as histamine, serotonin, tryptase, substance P, or IL-2 affecting the nervous system. According to IFSI clinical classification (22), pruritus occurring with AD is classified as type I (primary skin lesions) or type III (category I). Body reaction to noticeable pruritus is an action aiming at the reduction of this sensation by scratching, rubbing, licking, nibbling, or biting diseased various body parts.

In dogs affected by AD, symptomatic treatment is recommended (11, 13, 15, 17, 18, 21), including anti-inflammatory and anti-pruritic treatment and restoration of damaged skin to support its protective and defensive function against environmental allergens. In the treatment of canine AD, immunosuppressive, anti-inflammatory, and anti-pruritic medicines are used, such as cyclosporine A or glucocorticosteroids (prednisone, prednisolone, methylprednisolone), which inhibit the development of inflammatory reactions and the release of proinflammatory mediators inducing itching.

To assess pruritus, Pruritus Severity Scale (PSS) test was proposed in human medicine (3). Its purpose is to develop a mathematical model to assess the degree of pruritus noticeable by patient in time beyond appointments with a physician, when patient is exposed to environmental factors. This model was modified several times. Currently most often used test is 5-D-Itch.
Severity Scale (4). This test uses 5-point scale assessing five parameters: degree, duration, direction, disability, and distribution of pruritus.

In veterinary medicine to assess the pruritus in dogs affected by AD, several tests are used – PICAD-Pruritus Index in Canine Atopic Dermatitis (1), PS-Pruritus Score (1), PSS- Pruritus Severity Scale (8, 20), VAS- Visual Analogue Scale (12), OPS – Owner’s Pruritus Scores (23) – mostly based on two scales: 10-point scale proposed by Carlotti et al. (1), improved by Hill et al. (8) and Rybnicek et al. (20), as well as 5-point scale proposed by Burton et al. (1). This last scale allows assessing skin pruritus in dogs with AD and specifies frequency of the occurrence of pruritic episodes, their duration and localisation with provision of predilection sites.

This study evaluated the results of PS test assessing pruritus in dogs with AD treated with cyclosporine or prednisone.

### Material and Methods

Study was performed in two groups of 20 dogs. Each group comprised patients of Dermatology Consult Room of Veterinary Clinics in University of Life Sciences in Lublin in 2007-2009, with confirmed diagnosis of AD (19, 21, 30).

Group I-E included eight bitches and eleven dogs of various breeds: five American Staffordshire Terriers, three German Shepherds, two mongrels, two Boxers, two West Highland White Terriers and one up Chow-Chow, Rhodesian Ridgeback, English Bulldog, Beagle, Fox Terrier, and Shar-Pei breed.

Group II-C comprised seven bitches and 13 dogs of following breeds: six American Staffordshire Terriers, two mongrels, two French Bulldogs, two Labradors and one of each German Shepherd, Fox Terrier, Doberman, Central Asian Shepherd, Bernese Mountain Dog, Dalmatian, Cane Corso, and Dogo Argentino breed.

Age of the dogs varied between 1.3 and 3.2 years. Average age in group I-E was 2.4 years, and in group II-C – 2.6 years.

In treatment of secondary dermatoses, antibiotics and topical therapy (shampoos) were used according to generally accepted rules; then skin pruritus was assessed in examination 1. Anti-allergic, anti-inflammatory, and anti-pruritic treatment had been started after examination 1 and was continued for 6 weeks. Dogs qualified to group I-E were treated with oral prednisone (Encorton- Polfa, Poland) at dose of 0.5 mg/kg b.w. per day, while dogs qualified to group II-C – orally with cyclosporine A (Sandimun Neoral – Novartis Pharma) at dose of 5 mg/kg b.w. per day. Pruritus assessment was made at examination 2 and examination 3.

In PS test, 5-point scale was used according to Burton et al. (1) with author’s modifications. Pet owners were requested to assess the pruritus 4 times by filling a special questionnaire in appropriate day of therapy. This procedure allowed to monitor variability of scores given by owners during treatment i.e. on the day of first visit in consulting room (before treatment), in erythematous pruritic phase (after treatment of secondary dermatoses), 2 and 6 weeks after anti-inflammatory and antipruritic treatment with the use of prednisone (Encorton- Polfa, Poland) in group I-E or cyclosporine A (Sandimun Neoral – Novartis Pharma) in group II-C. The prepared questionnaire allowed assessing the frequency and severity of skin pruritus in their dogs according to pattern provided below.

#### A. Occurrence frequency of pruritus episodes:

- 0 – no pruritus.
- 1 – sporadic - dog scratches itself 2-3 times a day but more frequently than before the occurrence of skin problems.
- 2 – periodic - dog scratches itself 4-6 times a day, sleeps easy at night, does not scratch when eating, playing or working.
- 3 – frequent - a few times a day (>6) and sometimes at night, does not scratch when eating or playing.
- 4 – constant - dog scratches itself constantly during observation – much of day scratches itself, also when eating and playing, disturbs owners’ sleep at night.

#### B. Severity of pruritus:

- 0 – none.
- 1 – mild - few seconds, but no longer than 30.
- 2 – medium - dog concentrates on scratching, licking, nibbling particular body parts for short periods over 30 s.
- 3 – intensive - dog concentrates on scratching, licking, nibbling particular body parts for longer periods, which can be disturbed, signs can be observed – coat loss, excoriation and crusts.
- 4 – severe - dog scratches itself aggressively, bites itself to blood, scratching is hard to disturb.

Assessment of pruritus was performed in appointed day, during 24-h observation, recording pruritus episodes occurring in specified body parts. Pruritus observed in other body parts was also recorded by owners in “others” section of questionnaire. Selection of specified body parts was made on the basis of Willemse’s clinical criteria (30) and Prelaud’s (19) criteria used in diagnosis of canine atopic dermatitis. Conclusions resulting from analysis of Germain et al. (7), Steffan et al. (25), and Hill et al. (8) were also considered. Fifteen body areas were coherently specified in which assessment was made in scale 0 to 4. Assessment of pruritus was performed on appointed days, i.e.:

- Examination 0 – the day of first visit,
- Examination 1 – after treatment of secondary infections with the use of oral antibiotics, shampoos, creams, lotions not containing glucocorticosteroids or immunomodulating and antihistaminic compounds,
- Examination 2 – after two weeks of treatment with the use of prednisone (group I-E) or cyclosporine (group II-C),
- Examination 3 – the day after completion of the treatment.
The results of the survey enabled the quantitative assessment of pruritus by examination of two parameters: severity and frequency of pruritus episodes as well as the qualitative assessment by using 5-points scale (from 0 to 4) for both parameters, which made possible the estimation of pruritus severity.

The results were analysed statistically used Excel 2007 and STATISTICA9 PL software. Arithmetical mean (x) and standard deviation (+SD) were determined. To perform variance analysis (quotient of variation) Student’s t-test was used to assess the differences between means of two groups and between successive examinations. Significance level was set at \( P=0.05 \).

Results

On the day of the first visit (examination 0), all dogs, which were qualified to further investigations received in PS test 1,284 points of 4,800 possible i.e. 26.75%, while in assessment of pruritus frequency – 622 points, and pruritus severity – 662 (Table 1).

During the study, the sum of points, assessing severity and frequency of pruritic episodes was decreasing. In examination 3, in group I-E, according to owners’ assessment, pruritus was reduced from 614 points to 120 points, i.e. – by 80.46%, while in group II-C – by 86.12% in comparison to examination 0.

The survey data enabled the qualitative assessment of pruritus, informing about pruritus nuisance for patient and owner. Overall sum of the analysed marks in each moment of survey was 30 points for each dog and 600 points for each group. The results are presented in Table 2.

On the basis of the obtained data, it can be concluded that in young dogs (1 to 3 years old) suffering from AD, pruritus assessed by owners as “4” points, i.e. persistent and constant, is occurring rarely and constitutes not more than 1.33% of all episodes. Generally, owners assessed pruritus in their dogs at “2” points i.e. dog scratches itself few times a day, though it sleeps easy at night, does not scratch when eating, playing or working, as well as concentrates on scratching, licking, nibbling particular body parts for short period over 30 s, which can be disturbed.

Analysis of localisation of pruritus assessed by overall sum of points obtained in PS test, indicates that, according to owners’ assessment, on the day of the first visit (examination 0), pruritus was observed on the chin (154 points), interdigital space of front paws (159 points and more), facial part of the muzzle (124 points), ear auricles (119 points each), and eyelids area (93 - right and 91 - left). Pruritus observed by owners was found in few locations recognised as typical for clinical lesions in AD, but was not present in all locations simultaneously. In 38.67%-47.83% of specified body parts, dogs’ owners did not observe pruritus. The pruritus of the interdigital space of rear paws, according to owners’ assessment, was spread irregularly, and overall sum of points obtained in PS test for right limb was 96, whereas 70 for left limb. Definitely owners noticed less intense pruritus in axillae and groins (41 to 62 points). In examination 0, the pruritus was observed in other than specified in PS form body parts, which were labelled as “others” (totally 55 points). These were body sides, neck, and region of the anus. In examination 3, in group I-E, the reduction of pruritus was noticed in all observed body parts, whereas in group II-C, pruritus was eliminated in axillary region, groins, eyes, and eyelids area.

**Table 1**

<table>
<thead>
<tr>
<th>Examination</th>
<th>Total obtained points in group I-E</th>
<th>Total obtained points in group II-C</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pruritus frequency</td>
<td>Pruritus severity</td>
</tr>
<tr>
<td>Maximum points’ number</td>
<td>1,200 (100%)</td>
<td>1,200 (100%)</td>
</tr>
<tr>
<td>Examination 0</td>
<td>298 (24.83%)</td>
<td>316 (26.33%)</td>
</tr>
<tr>
<td>Examination 1</td>
<td>252 (21%)</td>
<td>282 (23.5%)</td>
</tr>
<tr>
<td>Examination 2</td>
<td>135 (12.75%)</td>
<td>112 (9.33%)</td>
</tr>
<tr>
<td>Examination 3</td>
<td>51 (4.25%)</td>
<td>69 (5.75%)</td>
</tr>
</tbody>
</table>

**Table 2**

<table>
<thead>
<tr>
<th>Examination</th>
<th>Group</th>
<th>4</th>
<th>3</th>
<th>2</th>
<th>1</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 I-E</td>
<td>8 (1.33%)</td>
<td>56 (9.33%)</td>
<td>159 (26.5%)</td>
<td>90 (15%)</td>
<td>287 (47.83%)</td>
<td></td>
</tr>
<tr>
<td>II-C</td>
<td>1 (0.17%)</td>
<td>60 (10%)</td>
<td>179 (29.83%)</td>
<td>128 (21.33%)</td>
<td>232 (38.67%)</td>
<td></td>
</tr>
<tr>
<td>1 I-E</td>
<td>1 (0.17%)</td>
<td>19 (3.17%)</td>
<td>136 (22.67%)</td>
<td>130 (21.67%)</td>
<td>314 (52.33%)</td>
<td></td>
</tr>
<tr>
<td>II-C</td>
<td>1 (0.17%)</td>
<td>24 (4%)</td>
<td>164 (27.33%)</td>
<td>210 (35%)</td>
<td>201 (33.5%)</td>
<td></td>
</tr>
<tr>
<td>2 I-E</td>
<td>0</td>
<td>0</td>
<td>42 (7%)</td>
<td>157 (26.17%)</td>
<td>401 (66.83%)</td>
<td></td>
</tr>
<tr>
<td>II-C</td>
<td>0</td>
<td>0</td>
<td>33 (5.5%)</td>
<td>119 (19.83%)</td>
<td>440 (73.33%)</td>
<td></td>
</tr>
<tr>
<td>3 I-E</td>
<td>0</td>
<td>2 (0.33%)</td>
<td>22 (3.67%)</td>
<td>163 (27.17%)</td>
<td>413 (68.83%)</td>
<td></td>
</tr>
<tr>
<td>II-C</td>
<td>0</td>
<td>0</td>
<td>15 (2.5%)</td>
<td>63 (10.5%)</td>
<td>522 (87%)</td>
<td></td>
</tr>
</tbody>
</table>
Table 3
Statistical analysis (Student’s t-test) of differences between group I-E and group II-C

<table>
<thead>
<tr>
<th>Examination</th>
<th>Group I-E x ±SD</th>
<th>Group II-C x ±SD</th>
<th>Significance level P≤0.05</th>
<th>Quotient of variation (F)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>30.7±8.82</td>
<td>33.5±11.8</td>
<td>0.4007 (No)</td>
<td>0.2133</td>
</tr>
<tr>
<td>1</td>
<td>26.7±6.19</td>
<td>27.15±10.22</td>
<td>0.8672 (No)</td>
<td>0.0348</td>
</tr>
<tr>
<td>2</td>
<td>9.2±5.84</td>
<td>12.35±6.04</td>
<td>0.0938 (No)</td>
<td>0.6033</td>
</tr>
<tr>
<td>3</td>
<td>6±4.96</td>
<td>4.65±4.63</td>
<td>0.3971 (No)</td>
<td>0.7622</td>
</tr>
</tbody>
</table>

x - arithmetical mean values; ± standard deviation.

Table 4
Results of statistical analysis (Student’s t-test) of differences between successive examinations

<table>
<thead>
<tr>
<th>Examination</th>
<th>Group I-E F  t</th>
<th>Group II-C F  t</th>
</tr>
</thead>
<tbody>
<tr>
<td>0/1</td>
<td>0.506 1.229 0.673</td>
<td>0.2535 1.259 1.165</td>
</tr>
<tr>
<td>0/2</td>
<td>0.000209* 3.287 4.258</td>
<td>0.000089* 3.415 4.574</td>
</tr>
<tr>
<td>0/3</td>
<td>0.00092* 2.735 3.706</td>
<td>0.000021* 2.49 5.099</td>
</tr>
<tr>
<td>1/2</td>
<td>0.000834* 2.673 3.743</td>
<td>0.001614* 2.712 3.491</td>
</tr>
<tr>
<td>1/3</td>
<td>0.003832* 2.223 3.153</td>
<td>0.000327* 1.977 4.093</td>
</tr>
<tr>
<td>2/3</td>
<td>0.5203 1.202 0.651</td>
<td>0.324268 1.371 1.003</td>
</tr>
</tbody>
</table>

* - P≤0.05; F - quotient of variation; t – variation.

Statistical analysis of the results received in groups I-E and II-C in examination 0 (Table 3) shows that means of both groups are statistically equal to significance level P≤0.05 (P=0.400747, t=0.849821). In further examinations, no statistically significant differences between means in groups I-E and II-C were found.

No statistically significant differences between measurements 0 and 1 were observed in group I-E (Table 4). However, statistically significant differences between means were found between examinations 0 and 2, 0 and 3, 1 and 2, and 1 and 3. No statistically significant differences in pruritus assessment between examinations 0 and 1, and 2 and 3 were observed in group II-C. The remaining results of statistical analysis of data from group II-C were similar to those of group I-E (Table 4).

Discussion

In clinical veterinary practice, in dogs with AD, oral doses of cyclosporine of 5 mg/kg/d and prednisone or prednisolone 0.5-1 mg/kg/d were recommended (15, 16, 17, 24). All dogs in this study were treated with 5 mg/kg/d of cyclosporine or 0.5 mg/kg/d of prednisone. The obtained results show that using prednisone or cyclosporine in young dogs with AD reduces pruritus in 80.46% (prednisone) and 86.12% (cyclosporine) of treated dogs, but there is no statistically significant difference in reducing pruritus between these drugs. Results published by authors of other studies also rate highly the efficacy of both drugs, but there are differences between authors. According to Steffan et al. (24, 25), efficacy of cyclosporine, used 4 weeks in oral dose of 5 mg/kg/d for in treating dogs with AD, in pruritus reduction was assessed for 36%, whereas of methylprednisolone in dose of 0.5-1 mg/kg/d, for 45%; however, after the application of the drugs for 8-16 weeks, their efficacy was about 43%. On the other hand, Olivry et al. (13, 17) assessed efficacy of cyclosporine, in pruritus reduction in AD dogs after 2 week treatment, for 60%-100%. In both publications, the studies were conducted on dogs older than 4 years of age. Data published by Burton et al. (1), are the closest to our results. They showed 83% of efficacy of cyclosporine in pruritus reduction after 6 weeks of treatment, however, in most dogs the clinical effect was observed just after 3-4 weeks. The average age of the dogs was 3.7 years.

The comparison of the efficacy of both drugs made by Olivry et al. (16) and Steffan et al. (23) revealed no statistically significant difference in pruritus reduction after 6 week treatment, which is consistent with author’s results.

Statistical analysis of literature data published in years 2001-2005, concerning the efficacy of cyclosporine in treatment of CAD, was conducted by Steffan et al. (25). It included 627 dogs treated only with cyclosporine, 206 dogs – with cyclosporine and glucocorticosteroids (prednisolone or methylprednisolone) and 74 dogs treated only with glucocorticosteroids. According to the analysis, reduction of lesions was usually 30%-52% after 2 weeks of the application of cyclosporine; however in some
dogs, 60% reduction of lesions was observed after this therapy. After 6 weeks of treatment, the efficacy of cyclosporine was assessed at 53%-84%. Owners assessed the reduction of pruritus at 27%-34% after 4 weeks and at 45%-78% after 6 weeks of treatment. Longer application of cyclosporine (12-16 weeks) did not improve the reduction of skin lesions and pruritus, and induced the development of secondary dermatoses. In dogs treated with glucocorticosteroids for 4-6 weeks, the reduction of skin lesions was by 53% and pruritus by 49%. The application of both drugs in dogs with AD was maintained on level 2 in 0-4-point PICAD score scale. Results obtained in this study confirmed these observations. In young dogs with AD, in measurement 0, pruritus was assessed for 2 and 1 points, rarely for 3 points, sporadically for 4 points, and usually, if pruritus was present, for 1 point.

Assessment of clinical efficacy of drugs used to reduce erythematous pruritic lesions in dogs with AD in the age of 1.2-11 years, reviewed by Olivry et al. (18) in 2010 indicates, that cyclosporine in a dose of 5 mg/kg/d administered orally for 4-6 weeks reduces skin pruritus and clinical symptoms of the disease by over 50% in half of described cases, and by 90% in 13%-27% of the cases of CAD. However, glucocorticosteroids (prednisone, prednisolone, or methylprednisolone), administered orally in a dose of 0.5-1mg/kg/d, reduced cases of CAD. However, glucocorticosteroids (prednisone, prednisolone, or methylprednisolone), administered orally in a dose of 0.5-1mg/kg/d, reduced skin pruritus and clinical symptoms by 50% in 69% of the examined dogs just after one week.

The heterogeneity of results can be caused by lack of objective, standardised criteria of pruritus assessment, which makes the interpretation of scientific results difficult.

The analysis of clinical criteria of AD in dogs, lately presented by Favrot et al. (5), indicates that skin lesions localised in interdigital space of front and rear paws, on elbows, ear auricles, flies, in axillae and groins, on skin folds and chest, and abdomen sides are statistically significant for this disease. The analysis performed by Favrot et al. (5) is in accordance with author’s study, in which dogs revealed pruritus of the interdigital space of front paws, ears, muzzle, chin, and around eyes. In our study, pruritus of the axillae, groins, body sides, neck, and anus was also observed.

The analysis of the obtained data proves to be useful for the assessment of treatment efficacy in dogs with AD and allows assessing the pruritus severity in affected dogs.

Acknowledgments: I thank sincerely Professor Zbigniew Pomerolski for his significant support during the study and all participants for devoted time. Study was funded by the research project N 30801632/1409 “Assessment of selected parameters of immunological response in the course of canine atopic dermatitis”.

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