Topical TetraDecanol Complex in the Treatment of Periodontal Disease in Cats

Presented at EVDS May 25th, 2012 in Lisbon

Research conducted at the University of Saskatchewan by

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Periodontal diseases

- Are the most common oral diseases in cats and dogs of all ages though it is most common in older animals (*Lund 1999*)
- If left untreated, periodontal diseases often progress into more severe forms and results in loss of supporting tissues including periodontal attachment and bone.
- Similar to humans, its etiology is associated to bacteria found in the subgingival microbiota; being *Porphyromonas* sp. the most prevalent genus (*Pérez-Salcedo et al, 2011*).
- As a result, chronic inflammation, bad breath and pain/discomfort can be detected in cats with mild to moderate periodontal disease and as the disease progresses it becomes severe (*Malonee et al, 1988; Hennet 1995*).
Periodontal diseases

- Severe periodontal diseases can also result in release of bacteria into the blood stream that can accelerate a systemic inflammatory response and increase the risk of disease in distant organs such as heart, kidney, joints, and systemic conditions such as diabetes mellitus, osteoporosis and adverse pregnancy effects (Niemiec, 2008).

- Tooth resorption, the other most common dental condition in cats have been also found strongly associated with periodontal diseases (Girard et al, 2009).

- Home care including brushing and rinsing with antiseptics by their owners is the key to keep their oral cavities out of infection and to prevent and control the periodontal diseases including gingivitis and periodontitis (Ray and Eubanks, 2009).

- However, efficient home care is often found very difficult and stressful as some cats do not simply cooperate.
Treatment of periodontal diseases

- Oral hygiene and a healthy diet are crucial for the prevention and treatment of periodontal disease, however, is not sufficient when the disease is severe (Gawor et al., 2006).

- Most common treatment of periodontal disease in cats include scaling and debridement with hand and ultrasonic instruments, irrigations with antiseptics and further surgical operations and extractions of the hopeless teeth (Harvey, 2005).

- The use of anti-inflammatory medications were also found useful in conjunction with mechanical treatment (Lyon, 2005).
Increasing evidence is positive for the use of omega-3 fatty acids in cats and dogs in cardiac diseases and other inflammatory conditions (Freeman 2010).

Previously, the beneficial effects of dietary and topical application of fatty acids have been shown on experimental periodontitis in rats, mice and rabbits (Vardar et al, 2006, Kesavulu et al, 2008; Hasturk et al, 2007)
Monounsaturated fatty acids (MUFAs) have comparable capacity with omega-3 PUFA in suppressing pro-inflammatory cytokines and reducing expression of cell adhesion molecules in humans (De Caterina et al, 2000).

Evidence from epidemiological and controlled clinical studies have shown that MUFAs favorably affect a number of risk factors for CHD, including plasma lipids and lipoproteins, factors related to thrombogenesis, \textit{in vitro} LDL oxidative susceptibility, and insulin sensitivity in humans (McGee et al 1984; Kromhout et al 1995; Reaven et al 1994, 1995).
Tetradecanol Complex (1-TDC™)

- Recently, topical application of Tetradcanol complex was shown to restore the destructed periodontal tissues as a result of P. gingivalis induced periodontal disease in a rabbit model of experimental periodontitis (Hasturk et al. 2009).

- The fatty acid complex was not only able to stop the disease progression but also resulted in new tissue and bone reformation suggesting the potential novel therapeutic approaches for the treatment of periodontal diseases.
Hypothesis and Aim

- The hypothesis of this study is that topical application of Tetradecanol complex to the gingiva of the cats with severe periodontal disease will reduce inflammation and improve oral health.

- The aim of this study is to evaluate the outcome of the treatment of chronic periodontal disease with topical application of Tetradecanol complex (1-TDC™) in cats.
The study was performed at the Small Animal Clinical Sciences at the University of Saskatchewan, Canada.

The study protocol was reviewed and approved by the Saskatchewan University Animal Research Ethics Board (AREB) prior to study initiation.
Study Population

- 13 cats were selected among the teaching and research colony of the Animal Resources Centre with some degree of periodontal disease.
- All cats were already diagnosed with chronic periodontal disease and were on the waiting list for dental hygiene at the Veterinary Teaching Hospital.
- All cats were congenitally missing maxillary first premolar and both first and second premolars on the mandible.
- Free-housed and fed regular cat chow, canned food and tap water during the study period.
Study Design

Full mouth periodontal evaluations under general anesthesia*

Begin topical treatments**
1. Test: 1-TDC (525 mg per gel capsule/day)
2. Placebo: Olive oil (0.25 ml per gel capsule/day)

Daily treatment applications

Baseline

Six Weeks

*All measurements were performed by a single examiner blinded to treatment allocations.

**13 cats (9 1-TDC, 4 Olive Oil as placebo) were randomly assigned.
Clinical Periodontal Examination

- **Probing Pocket Depth (PPD)**
  - At six sites of each tooth

- **Gingival Index (GI-Löe & Silness)**
  - 0 = normal
  - 1 = mild inflammation, slight color change and edema, no bleeding
  - 2 = moderate inflammation, redness, edema, bleeding on probing
  - 3 = severe inflammation, marked redness and edema, ulceration, spontaneous bleeding

- **Clinical Attachment Level (CAL)**

- **Bleeding on Probing (1 or 0)**
  - * A recording of <1 mm was indicative of a healthy gingival sulcus.
  - ** Localization of gingival margin, measuring from the gingival margin to the cemento–enamel junction of the tooth, was measured to calculated.
  - *** William's periodontal probe with a Goldman Fox Flat / explorer combination was used.
Clinical Periodontal Examination

- **Mobility Index**

  **Stage 0** = Physiologic mobility up to 0.2 mm.

  **Stage 1** = The mobility is increased in any direction other than axial over a distance of more than 0.2 mm and up to 0.5 mm.

  **Stage 2** = The mobility is increased in any direction other than axial over a distance of more than 0.5 mm and up to 1.0 mm.

  **Stage 3** = The mobility is increased in any direction than axial over a distance exceeding 1.0 mm or any axial movement.

- **Missing teeth**
The unit of measurement was tooth present in the mouth.

Each tooth was represented by a score obtained by the measurement of PPD, GI, and CAL.

BOP was recorded for each tooth as an overall bleeding as bleeding present or not 15 second upon probing.

The mean and standard deviations were calculated for each cat and used for comparison within group and between groups before and after treatment.

Statistical analysis were performed using paired t-test for within group analysis and Student t test for group comparisons using SPSS statistical software package.

Significance set at alpha=0.05
# Results - Baseline parameters

<table>
<thead>
<tr>
<th>Group</th>
<th>1-TDC group (test)</th>
<th>Olive Oil (placebo)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>9</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td># of teeth present</td>
<td>23.1± 8.1</td>
<td>25 ± 1.8</td>
<td>0.5</td>
</tr>
<tr>
<td>(Mean± SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PPD (mm) (Mean± SD)</td>
<td>1.0±1.0</td>
<td>1.3±1.1</td>
<td>0.7</td>
</tr>
<tr>
<td>CAL (mm) (Mean± SD)</td>
<td>1.1±0.9</td>
<td>1.7±0.7</td>
<td>0.3</td>
</tr>
<tr>
<td>GI (Mean± SD)</td>
<td>2.4±0.4</td>
<td>2.4±0.9</td>
<td>1.0</td>
</tr>
<tr>
<td>BOP % (Mean± SD)</td>
<td>85.8±15.9</td>
<td>89.8±20.4</td>
<td>0.8</td>
</tr>
</tbody>
</table>

March 25th, 2012
21st European Congress of Veterinary Dentistry
Results- Clinical Observations

- No complications/adverse events have occurred during the study period.
- All cats continued their regular daily life with no obvious discomfort.
- Daily applications were easy, quick and had no negative impact on oral tissues or in general on cats.
- Cats were very cooperative and willing to get the daily applications suggesting that the acceptance of the topical 1-TDC and olive oil was high.
Results - Impact of treatment within group and between groups - PPD

![Graph showing the comparison of Probing Pocket Depth (mm) between Baseline 1-TDC, 6 weeks 1-TDC, Baseline Placebo, and 6 weeks Placebo. The graph indicates a statistically significant difference (P=0.03) between Baseline 1-TDC and 6 weeks 1-TDC, marked with an asterisk (*). The difference between Baseline Placebo and 6 weeks Placebo is not statistically significant (p=0.12), marked with a hashtag (#).]
Results - Impact of treatment within group and between groups-CAL

![Graph showing clinical attachment level (mm) for different groups at baseline and after 6 weeks, with statistical significance indicated by * and # symbols.]

* $P=0.05$

# Not statistically significant ($p=0.06$)
Results - Impact of treatment within group and between groups-GI

[Graph showing comparison of Gingival Index across different time points and treatment groups.}

- Baseline 1-TDC: Significant difference with *P=0.0001
- 6 weeks 1-TDC: No significant difference
- Baseline Placebo: Significant difference with #P=0.05
- 6 weeks Placebo: No significant difference
Results - Impact of treatment within group and between groups-GI

- Baseline 1-TDC
- 6 weeks 1-TDC
- Baseline Placebo
- 6 weeks Placebo

* P=0.00003
# P=0.03
Results- Impact of treatment within group and between groups-Mobility

![Bar chart showing Tooth Mobility levels at different time points: Baseline 1-TDC, 6 weeks 1-TDC, Baseline Placebo, and 6 weeks Placebo. The chart indicates a comparison of mobility levels across these conditions.](image-url)
Summary

- No significant difference was found between groups at baseline with any parameters tested.
- All patients presented moderate to severe periodontal disease at baseline with varying degrees of PPD, CAL, GI, BOP and mobility.
- Although the placebo group showed slightly more disease at baseline with respect to PPD, CAL and BOP, the difference was not statistically significant.
- 1-TDC group exhibited statistically significant reduction in pocket depth, clinical attachment loss, gingival index and bleeding on probing after treatment at 6 weeks, while placebo group did not show any significant change.
- Compared to placebo group, 1-TDC group demonstrated significant reductions in clinical attachment loss, gingival index and bleeding on probing at six weeks.
- Mobility was dramatically reduced after treatment with topical 1-TDC, however due to high variation between patients the difference did not reach to statistical significance.
Conclusions

- Topical treatment with Tetradecanol complex resulted in significant reductions in all parameters of clinical periodontal disease at 6 weeks.

- Olive oil application on gingiva did not improve the periodontal health, yet no obvious disease progression was seen during the test period suggesting a potential but weak anti-inflammatory effect of olive oil (oleic acid) on periodontal tissues, especially on gingiva (slight reduction in GI and BOP was seen).

- Tetradecanol complex provides significant improvement in gingival and periodontal health and can be an alternative, safe and non-invasive therapeutic approach in cats suffering from destructive periodontal diseases.
Acknowledgements

- Colette Wheler, Co-investigator
- Colleen Zielke
- Wanda Warren
- Carla Hudy

Thank you!