The perspective of the owners on the 30-day lasting treatment with meglumine antimoniate injections and the quality of the dog's life

Demy van Eijk (Solis-ID: 4278585) | University of Utrecht | Faculty of Veterinary Medicine | July 2021
Supervised by dr. C. J. Piek

Key words: Canine, Leishmaniosis, meglumine antimoniate, glucantime, perspective, quality of life, QoL, questionnaire

Abstract

Canine leishmaniosis (CanL) is a global zoonotic disease, fatal for both humans and dogs. There are already endemics in over 70 countries in the world. The current first-choice therapy of CanL is chemotherapy with Pentavalent antimonials (SbV), used as monotherapy or in combination with other drugs (allopurinol® most of the time) to prevent relapses. The treatment is long, cumbersome, unpleasant for dogs and owners and renal disorders are frequently diagnosed. Besides that, the therapy is very costly. The perception of the owners on this therapy and the quality of life (QoL) of the dogs during the treatment is so far unknown. This work has investigated this by using a questionnaire.

A questionnaire was composed, which was done by comparing different literature studies and books about questionnaires. The questions investigated the perception of the owners on the 30-day treatment with meglumine antimoniate injections and the quality of the dog's life. 60 of the 87 owners filled in the questionnaire, which gives the questionnaire a 69 percent response rate.

The majority of the owners did think applying the medication was easy, the dogs did not seem to be bothered that much and they reported that when they had problems or questions, they could always ask their veterinarians. Also, the owner's QoL scored high. A small increase of dog QoL is seen during the treatment and an even bigger increase of dog QoL one month after the treatment. There is not one standard trajectory in which the treatment will occur. Every dog has got its own trajectory.

When looking at the positive outcomes, it can be concluded that a great majority of 95 percent of the dogs improved their QoL due to the treatment. Therefore, it can be concluded, together with the owner's conclusions, that the therapy is worthwhile.

Introduction

Canine leishmaniosis (CanL) is a global zoonotic disease, fatal for both humans and dogs. There are already endemics in over 70 countries in the world. It is found in regions like southern Europe, Asia, Africa and South and Central America, whereby the transmission occurs by dipters (Solano-Gallego, Miró et al. 2011a). In 2001 the prevalence of Leishmaniosis was studied in a region suffering an endemic, which showed a high prevalence of Leishmaniosis, between 63%-80% of that particular population (Solano-Gallego, Morell et al. 2001a). Different clinical signs can be seen, whereby a cutaneous and a visceral form can be distinguished. In general, pyogranulomatous inflammatory reactions are seen and the most prevalent clinical signs are peripheral lymphadenopathy, weight loss, muscular atrophy, decreased appetite, and lethargy. Different dermatological signs like alopecia, papular and nodular dermatitis, renal diseases and eye lesions occur. Mostly, the disease starts with the cutaneous form and evolves into the visceral form (Reguera, Moran et al. 2016,

Baneth, Koutinas et al. 2008). This information shows the impact of CanL and the importance of prevention and managing the symptoms. The current first-choice therapy of CanL is chemotherapy with Pentavalent antimonials (SbV), used as monotherapy or in combination with other drugs (allopurinol® most of the time) to prevent relapses. One of the available drugs is meglumine antimoniate (glucantime®). This is a parenteral medicine and must be administered by slow injections once a day for a period of four weeks. The effect of the medicine depends on the quantity of medicine that has reached the target organs, which are the spleen, liver and bone marrow. The chemical nature of the injection causes pain in the injection site, phlebotoxicity, thrombophlebitis, muscular fibrosis, or abscesses. The treatment is long, cumbersome, unpleasant for dogs and owners and renal disorders are frequently seen. Besides that, the therapy is costly (Reguera, Moran et al. 2016). The perception of the owners on this therapy and the quality of life (QoL) of the dogs during the treatment is as of yet unknown. This has been investigated by using a questionnaire. Expected was a raise in QoL of the dog after the treatment and a poor perspective of the owners on the treatment.

Material and Methods

A questionnaire was composed with questions which investigated the specifics of the treatment with meglumine antimoniate injections and the impact of the treatment on the quality of the dog's and owner's lives. This questionnaire was sent to a cohort of 87 owners who treated their dog at least one course of meglumine antimoniate. This cohort was selected from a list of owners who ordered meglumine antimoniate from the pharmacy at the University Clinic for companion animals in Utrecht (UKG). To receive as many responses as possible, a short film was made about the importance of the study and sent along with the questionnaire to the owners. For sending the questionnaire, the program Qualtrics[i] was used. This program makes sure the questionnaire is anonymous.

The questions were divided into five different categories. Firstly, the questions focused on the technical aspects of the treatment; whether or not the dog received a combination therapy, if glucantime® was administered once or multiple times a day, the time lapse between the last glucantime treatment and the moment of the questionnaire being documented, if the injections were given by medically trained persons or the owners and the time it took them daily to administer the treatment. The following set of questions examined therapy compliance. It was asked whether injections were missed, and if so, how often, and the reason why. Similarly, it asked the same if treatment was stopped prematurely.

In the second category, statements about the quality of the dog's life were presented and the owners could score them; not at all, mild, moderate, severe. These questions were divided into three sections; one during the period of illness whereby al the symptoms of Leishmaniosis were scored, one during the treatment period whereby side effects were scored and questions about the wellbeing of the dog; did the dog sleep more, was he less active, less playful and did the dog show stress. Lastly the same statements as before starting the treatment were given after finishing the treatment to measure the progress of the illness.

In the third category the owners were asked to give an indication on a progressive scale of the ease of giving the subcutaneous injections and their perspective on the treatment; if the dog was bothered by the injections, if they were able to contact their veterinarians with problems, if they wished for more support, if, in hindsight, the owners rather would have let their dogs be injected by their veterinarians every day, if the treatment was too intensive, if they would recommend it, and if it was worth it.

The fourth category consisted of statements about the owners' wellbeing; if the treatment affected the bond between them and their dogs negatively, if it affected their mood, physical health, spare time, social life, and daily expenses negatively.

The fifth and last category asked some general questions about the owners age, gender, the period of time they were their dog's owners, the origin of their dogs, the dog's age during the first treatment, the dog's gender and weight, and if the dogs were still alive and, if not, why did they die. The questions about the QoL were asked negatively, to prevent a positive bias. When the questionnaire was finished, a pilot was performed based on which the questionnaire was finetuned. The complete questionnaire can be found in appendix 1.

For data analysis SPSS (version 25) [ii] was used.
Data analysis 1: a histogram was made to show the scatter between the different perspectives.
Data analysis 2: to gain comparable answers, positive asked questions were recoded into the opposite outcome. A boxplot was made to show the difference between each measured QoL of the dog, a mixed linear model was made to show the variance between the three moments per dog and the positive outcomes were counted to show how many dogs improved during the treatment period.
Data analysis 3: to measure the correlation between different outcomes, a Spearman test was used. A spearman was used because of the ordinal data (Baarda, Dijkum 2019, Petrie, Watson 2013).

Results

Population

Sixty owners responded to the questionnaire, which gives the questionnaire a 69 percent response rate. The population which filled in the questionnaire, consisted out of 60 owners; 9 males, and 51 females. Their age varied from 30 years old to 60 years old and older. Most of the dogs hailed from Spain (n=37), others came from Greece (n=12), Portugal (n=3), Italy (n=1), Romania (n=1), Turkey (n=1) and a few from the Netherlands (n=5), which had been abroad. The histogram in figure 1 displays the age range of the dogs during the first treatment period with glucantime®. Fourteen dogs were between the age of 1-2 years old during the first treatment with glucantime®. The other dogs ranged from 2-3 years old (n=9), 4-5 years old (n=9), 3-4 years old (n=7), 5-6 years old (n=6), 7-8 years old (n=5), 8-9 years old (n=3), 6-7 years old (n=1) and over 10 years old (n=1). The median age was 4 years old with a range of 10 years. Fifty-two dogs were castrated, there were 28 bitches and 32 male dogs.

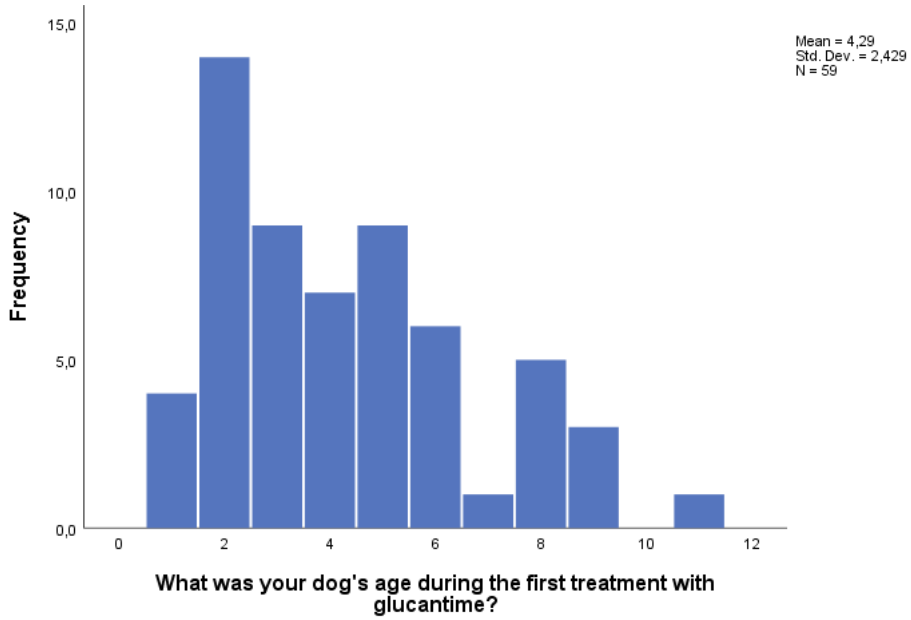

Figure 1: Histogram showing the dog's age during the first treatment with glucantime®. The X-axis shows the dog's age, the Y-axis the frequency.

Forty-two dogs used the meglumine antimoniate treatment in combination with allopurinol®, only 11 used it in combination with milteforan®. Thirty-four owners applied the injections for only one course, 14 owners for two courses, 6 owners for 3 courses and 3 owners for 4 courses. Forty-two owners injected the medication on their own, 12 owners did this together with somebody from their family, 6 owners made their veterinarian do it.
The explanation about applying the medication was done by their own veterinarian in 39 cases, in 11 cases by the University of Utrecht and some by a combination. Everyone did think the explanation was clear or absolutely clear. Most of the time, giving the subcutaneous injection only took 5 minutes a day or less.

Data analysis 1: Perspective of the owner on the treatment (question 13) and the QoL of the owner (question 14) during the treatment
Table 1 shows the mean of the owner's perspective per question, the median and the standard deviation. The best possible score is 5, the worst possible score is 1.

Statements question 13	*Mean*	*Median*	*Standard deviation*
1. I think it was easy to give my dog the treatment	3,5	4,0	1,3
2. My dog did not seem to be bothered by being injected every day	3,2	3,0	1,3
3. If there were problems or questions, I could always ask my veterinarian	4,5	5,0	0,8
4. During this month I wished for more support by a professional	2,1	2,0	0,9
5. In hindsight, I would have rather let my dog be injected by my veterinarian every day	2,2	2,0	1,2
6. I think this treatment is too intensive and not worth it	1,9	1,0	1,2
7. I think this treatment is worth it	4,2	5,0	1,2
8. I would recommend this treatment to other owners in the same situation as me and my dog	4,1	5,0	1,2

Table 1: Mean, median and standard deviation of the perspective of the owner per question.

Table 2 shows the mean, median and standard deviation of the QoL of the owners. A score of 1 is the best QoL, a score of 5 the worst.

Question 14: The treatment with glucantime®…	*Mean*	*Median*	*Standard deviation*
Negatively affected the bond between me and my dog	1,6	1,0	0,8
Negatively affected my mood	2,2	2,0	1,2
Negatively affected my physical health	1,6	1,0	0,7
Affected my spare time	2,1	2,0	1,2
Negatively affected maintaining of my social contacts	1,6	1,0	0,7
Negatively affected my daily expenses	2,6	2,0	1,4
Total	1,9	2,0	0,7

Table 2: Mean, median and standard deviation of the QoL of the owners per question.

Data analysis 2: Quality of life of the dogs
Appendix 2 shows the mean QoL of each dog at each point in time. The total mean QoL before the treatment was 2,19, the mean QoL during treatment was 2,0 and the mean QoL one month after the treatment was 1,5. The lower the QoL score, the better. The score ranges between 1 and 4. This table also shows the differences per time period. Between the moment before the treatment and during the treatment, the mean QoL increased with 0,16. Between the treatment and after the treatment the mean QoL increased with 0,55 and the total increase between the moment before the treatment

and after the treatment was 0,71.
The boxplots in figure 2 show the differences in QoL during the three different moments. Outliers number 15 and 29 are dogs with an extremely low QoL after the treatment. Outlier number 15 is the 75th percentile +3x IQR, outlier number 29 is the 75th percentile Q3 + 1,5xIQR.

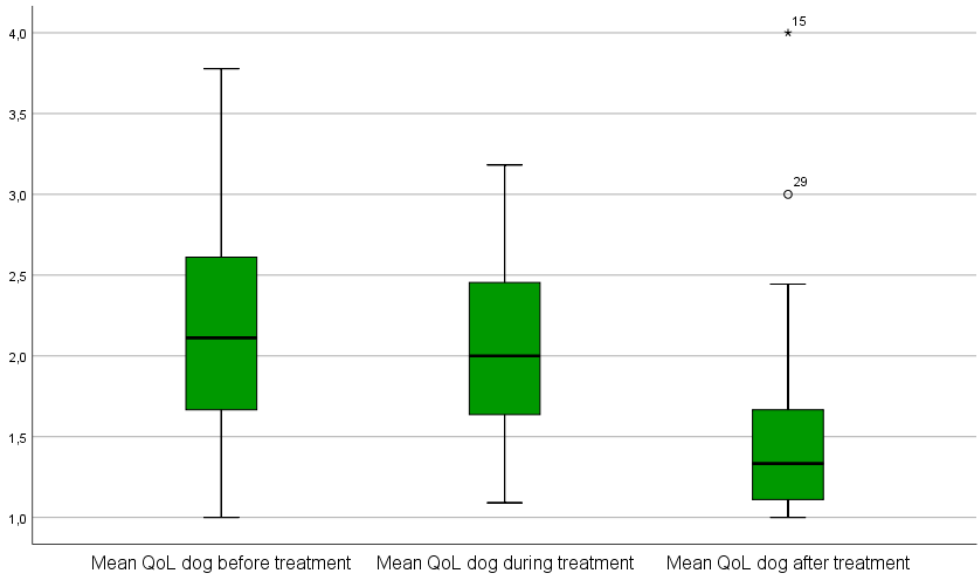

Figure 2: These boxplots show the mean QoL of the dogs before, during and after treatment. The X-axis shows the three moments, the Y-axis the mean QoL, scored between 1 (high) to 4 (low).

The graphs in figure 3 show the course of the QoL during the three moments per dog. Moment 1 is before the treatment, moment 2 during the treatment and moment 3 one month after the treatment. On the Y-axis the mean QoL is scored between 1 (high) to 4 (low). A green line shows an improved QoL over the three moments, yellow shows it stayed the same and red shows a decreased QoL. Each graph shows a different kind of course. Graph A: a linear improvement; graph B: an improved QoL during treatment; graph C: a decreased QoL during treatment; graph D: a linear decrease.

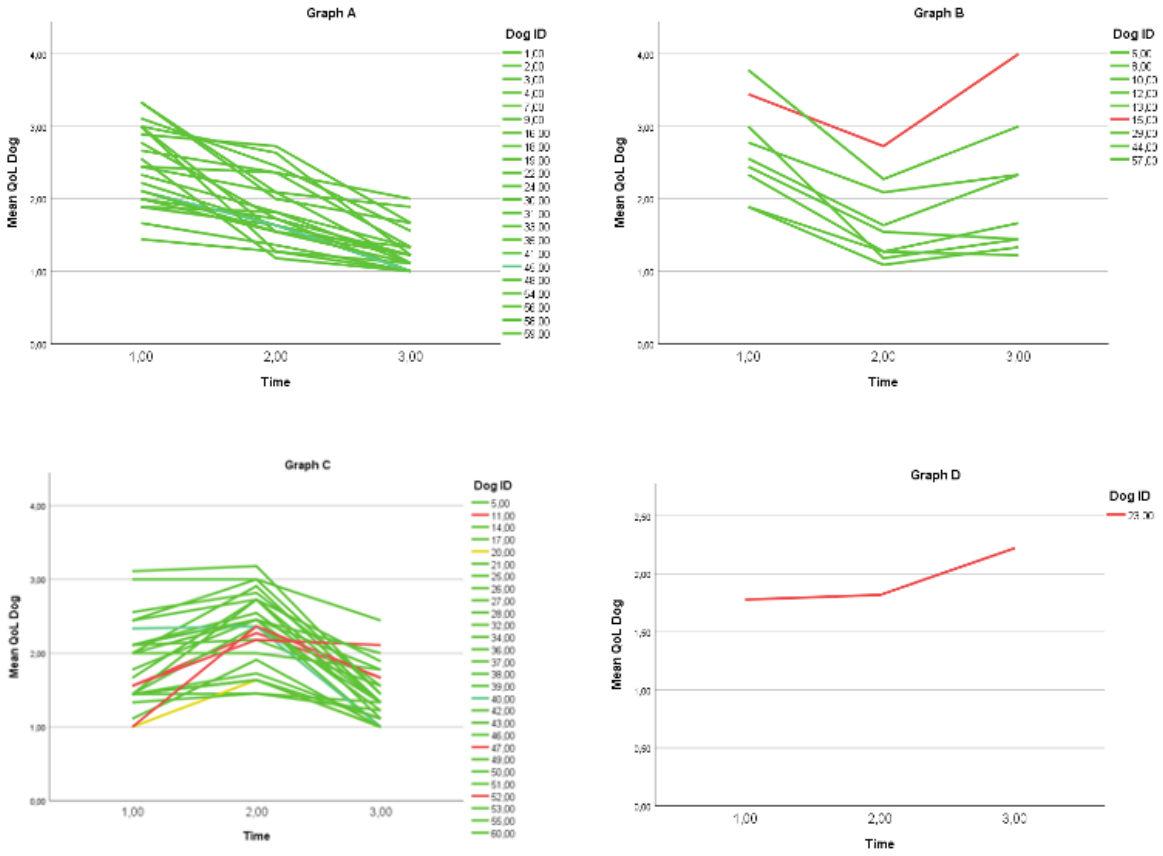

Figure 3: These graphs show the course of the QoL during the three moments per dog. On the X-axis moment 1 (before the treatment), moment 2 (during the treatment) and moment 3 (after the treatment). On the Y-axis the mean QoL, scored between 1 (high) to 4 (low). A green line shows an improved QoL over the three moments, yellow shows it stayed the same and red shows a decreased QoL. Each graph shows a different kind of course. Graph A: a linear improvement; graph B: an improved QoL during treatment; graph C: a decreased QoL during treatment; graph D: a linear decrease.

Table 3 shows, when counting the positive outcomes among the 60 dogs, 95 percent of the dog's QoL was improved one month after the treatment, 5 percent stayed the same or did not improve.

Positive Outcome

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	not improved	6	5,0	5,0	5,0
	improved	114	95,0	95,0	100,0
	Total	120	100,0	100,0	

Table 3: Positive outcome

Data analysis 3: Correlations between different parameters

Table 4 shows the correlation between the QoL of the dog and owner and the owner's perspective with the age and gender of the owners. This shows gender did not correlate with any of the moments. Age did correlate with the QoL of the dog during the treatment.

Correlations

			What is your gender?	What is your age?	Mean_QoL_dog_before_treatment	Mean_QoL_dog_during_treatment	Mean_QoL_dog_one_month_after_treatment	Mean_perspective_owner	Gem_QoL_eigenaar
Spearman's rho	What is your gender?	Correlation Coefficient	1,000	-,162	-,150	,254	-,085	,082	,239
		Sig. (2-tailed)	.	,221	,257	,052	,522	,538	,068
		N	59	59	59	59	59	59	59
	What is your age?	Correlation Coefficient	-,162	1,000	-,240	-,327*	-,231	,173	-,150
		Sig. (2-tailed)	,221	.	,065	,011	,076	,185	,252
		N	59	60	60	60	60	60	60
	Mean_QoL_dog_before_treatment	Correlation Coefficient	-,150	-,240	1,000	,237	,392**	-,001	,190
		Sig. (2-tailed)	,257	,065	.	,068	,002	,995	,147
		N	59	60	60	60	60	60	60
	Mean_QoL_dog_during_treatment	Correlation Coefficient	,254	-,327*	,237	1,000	,411**	-,436**	,469**
		Sig. (2-tailed)	,052	,011	,068	.	,001	,000	,000
		N	59	60	60	60	60	60	60
	Mean_QoL_dog_one_month_after_treatment	Correlation Coefficient	-,085	-,231	,392**	,411**	1,000	-,192	,077
		Sig. (2-tailed)	,522	,076	,002	,001	.	,141	,557
		N	59	60	60	60	60	60	60
	Mean_perspective_owner	Correlation Coefficient	,082	,173	-,001	-,436**	-,192	1,000	-,444**
		Sig. (2-tailed)	,538	,185	,995	,000	,141	.	,000
		N	59	60	60	60	60	60	60
	Mean_QoL_owner	Correlation Coefficient	,239	-,150	,190	,469**	,077	-,444**	1,000
		Sig. (2-tailed)	,068	,252	,147	,000	,557	,000	.
		N	59	60	60	60	60	60	60

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

Table 4: Correlations between the owners' gender or age

There was no correlation found between the QoL of the dog and his age, gender or the fact of whether the dog was still alive or not. Also, there was no correlation found between the owner's perspective and the owner's age.

Correlations were found between the perspective and QoL of the owners and the QoL of the dogs during the treatment. The graph in figure 4 shows the correlation between the owner's QoL and the dog's QoL during the treatment period. This shows the higher the dog's QoL, the higher the owner's QoL.

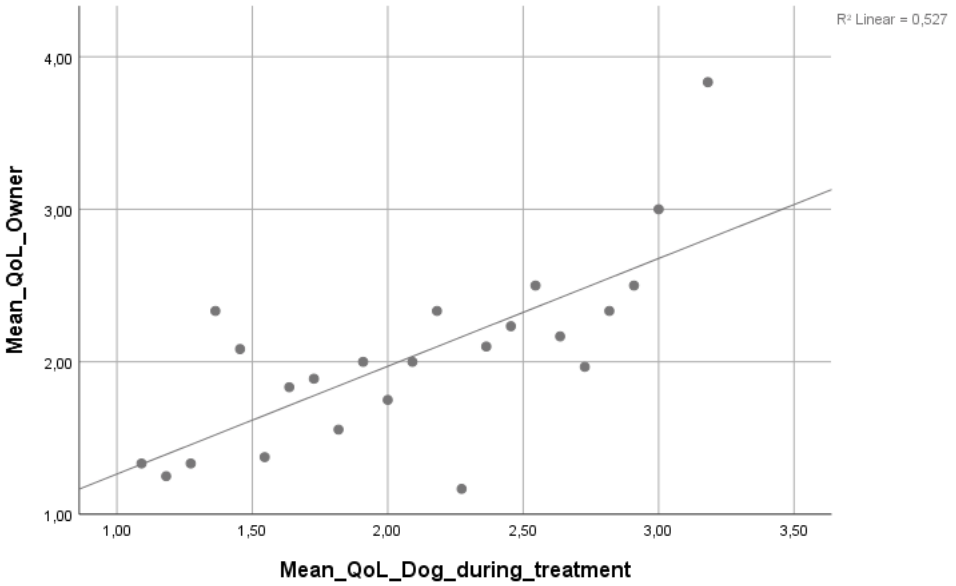

Figure 4: Correlation between the owner's QoL and the dog's QoL during the treatment period. The X-axis shows the dog's QoL during the treatment and the Y-axis shows the mean QoL of the owner during the treatment period. The line shows the total mean.

Also, correlations were found between the mean dog's QoL after the treatment period and before and during the treatment period, which is showed in figures 5 and 6. When the QoL is higher during or before the treatment period, it also was higher one month after the treatment period. When watching the line, the dots are not always as close to this line. This means the increase in QoL during the different periods is not the same

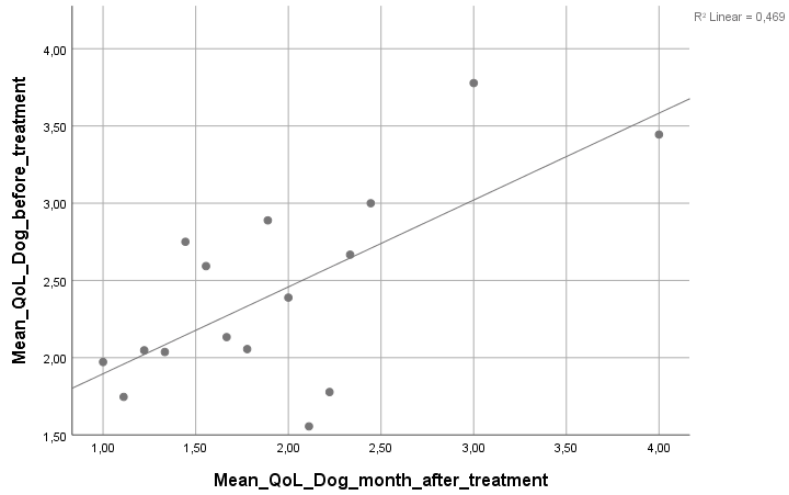

Figure 5: Correlation between the dog's QoL a month after treatment and the dog's QoL before the treatment period. The X-axis shows the dog's QoL a month after the treatment and the Y-axis shows the mean QoL of the dogs before the treatment period. The line shows the total mean.

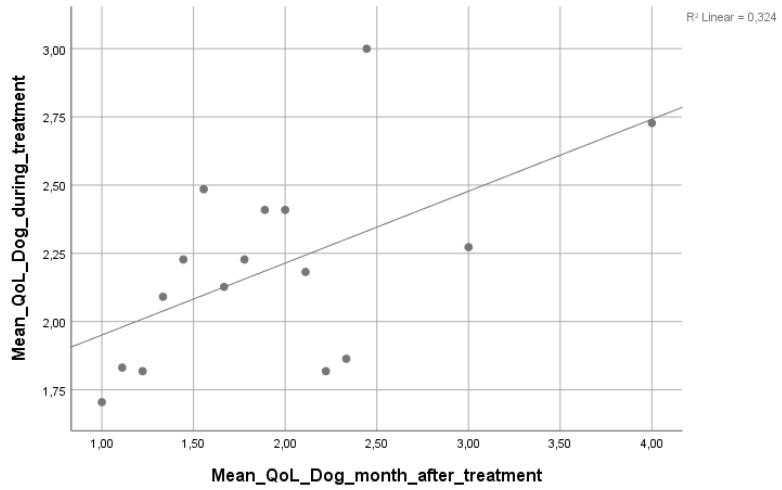

Figure 6: Correlation between the dog's QoL a month after treatment and the dog's QoL during the treatment period. The X-axis shows the dog's QoL a month after the treatment and the Y-axis shows the mean QoL of the dogs during the treatment period. The line shows the total mean.

When looking at the correlation coefficients, the correlations between the dog's QoL mutually are the greatest. Those correlations are significant at the 0,01 level. The other correlations do have a 0,05 significance.

Further noteworthy correlations were not found.

Discussion

The aim of this study was to get to know the perception of the owners on the therapy with Pentavalent antimonials injections and the quality of life (QoL) of the dogs during the treatment, which was investigated by using a questionnaire. A questionnaire was composed, which was done by comparing different literature studies and books about questionnaires (Baneth, Shaw 2002a, Nieto, Alvar et al. 2003, Slappendel, Teske 1997a, Freeman, Rush et al. 2005, Lynch, Savary-Bataille et al. 2011, Rattray, Jones 2007). Expected was an increase in QoL of the dog after the treatment and a poor perspective of the owners on the treatment.

Population

When looking at the population, it can be concluded that most of the dogs in this study were originally from the South of Europe. This corresponds with the prevalence studies, where the endemic regions are throughout the Mediterranean basis, with the highest prevalence found in Spain (Solano-Gallego, Morell et al. 2001b). Also looking at the population, most of the treated dogs were young, between 1-5 years old. The following research, completed in 2016, researched the distribution of the Leishmaniosis between different breeds and ages. This research showed that there is a primary peak among young dogs, from 1-4 years old and a secondary peak among older dogs, over 7 years old. The primary peak of 1-4 years old matches our treatment peak of 1-5 years old dogs (Miranda, Roura et al. 2008). Besides that, Leishmaniosis medication tends to cause kidney failures and shows different side effects like vomiting and diarrhoea (Solano-Gallego, Miró et al. 2011b, Reguera, Morán et al. 2016). A possible reason of why the treated dogs were very young, could be due to the benefit and costs of the medication. Because of the high costs, owners may easier lean towards abstaining from the treatment with older dogs (Reguera, Morán et al. 2016).

The perspective of the owner on the treatment

When looking at the owner's perspective, the majority of the owners did think applying the medication was easy, the dogs did not seem to be bothered that much and with problems or questions, they could always ask their veterinarians. Expected was a poor perspective of the owners on the treatment. To my best knowledge a questionnaire investigating owner satisfaction has not been performed, but our study suggest that the majority of the owners did think the treatment is worth it and they would recommend it to other owners in that same situation.

QoL of the owner during the treatment

The owner's QoL scored a mean of 1,9 out of 5. This shows a high QoL, whereby the bond between the owner and the dog, their mood, physical health, spare time, maintenance of their social contacts and daily expenses did not get affected too negatively by the treatment. This intensive treatment showed some bad side effects, like vomiting, diarrhoea and pain, but still the owners were satisfied. The treatment is long and intensive, but still, this does not seem to affect the owner's QoL too much. This period could be compared with diabetes mellitus, whereby the owners have to inject their dogs with insulin. Questionnaires about the perspective of the owner with diabetic pets, mostly show a good outcome, as long as their veterinarians provided sufficient information. Owners even reported feeling more attached to their pet during this period of treatment (Aptekmann, et al. 2014). From this outcome it can be concluded that outsourcing of the treatment to the owners is a good solution.

QoL of the dogs

The boxplot in figure 2 shows a small rise of dog QoL during the treatment and an even bigger rise of dog QoL one month after the treatment. This is in line with a variety of previous studies, where the efficacy of the therapy with meglumine antimoniate is followed up (Denerolle, Bourdoiseau 1999, Slappendel, Teske 1997b, MirÃ³, Oliva et al. 2009, Torres, Bardagí et al. 2011).
Graph 3 shows there is not one standard course in which the recovery will occur. Every dog has its own course. For example, it is not found that with minimal symptoms before treatment the QoL will

rise less afterwards. A reason for this effect could be the variation in immune systems, which is different within every individual dog. The characteristic of different immune systems is the genetic background (Santos, Alexandre-Pires et al. 2019). This corresponds with the following research, which shows higher occurence of Leishmaniosis in different breeds, like German shepherds, Rottweilers and Boxers (Miranda, Roura et al. 2008). Unfortunately, this questionnaire did not ask for the breed, only for the weight of the dogs.
When looking at the positive outcomes, it can be concluded that a great majority of 95 percent of the dogs improved their QoL due to the treatment.

Just like different studies show, Leishmaniosis is a disease known for its relapses (Baneth, Shaw 2002b, Santos, Alexandre-Pires et al. 2019, Miranda, Roura et al. 2008). In this study 34 owners applied the injections for only one course, the other 26 owners for two, three or four courses. From this could be concluded 26 dogs suffered from relapses.
The following research observed 23 dogs in Leishmaniosis clinical stage II for 2-9 years. These dogs all got a combined therapy with meglumine antimoniate and allopurinol®. This research shows only few relapses, which are easily controlled with allopurinol® (Torres, Bardagí et al. 2011). The following up on the dogs' wellbeing was beyond the scope of this study.

Correlations
In this research, no correlation is found between the gender of the owner and the QoL of the dogs or the owners themselves. In research based on humans it is often found that females score a lower QoL (Holm, E. A., Wulf et al. 2006, Holm, Elisabeth A., Esmann et al. 2004, Mulder, Sigurdsson et al. 2001, Stangier, Ehlers et al. 2003, Whalley, McKenna et al. 2004). (Santos, Alexandre-Pires et al. 2019). On the contrary, in two different pieces of research on dogs, no correlation was found between the owner's gender and the dog's QoL (Noli 2019, Yazbek, Fantoni 2005). One of the reasons for the lack of correlation in this study could be the low number of men who filled in the questionnaire. There were only 9 males relative to 51 females.

There was no correlation found between the QoL of the dog and his age, gender, or whether the dog was still alive or not. The owners did not score a lower QoL when their dog did die from Leishmaniosis.

Correlations were found between the perspective and QoL of the owners and the QoL of the dogs during the treatment. Also, correlations were found between the mean dog's QoL after the treatment period and before and during the treatment period, which is showed in figures 4, 5 and 6. When the QoL is higher during or before the treatment period, it also was higher one month after the treatment period. This is likely due to the positive approach taken by the owners, which translates to a more positive reporting of the impact of the treatment on the dogs.

Further noteworthy correlations were not found.

Conclusion
When considering starting up a dog with a meglumine antimoniate therapy against Leishmaniosis on a dog, the perspective of the owner must be taken into account. The results of this research show the majority of the owners have a positive perspective and their QoL is not altered too much. Despite the clinical stage of the dogs, 95 percent of the dogs did improve during and one month after the treatment. This, paired with the owner's own conclusions, indicates that the therapy is worthwhile.

Acknowledgment
I would like to thank dr. C. J. Piek from Utrecht University, The Netherlands, for the valuable help and comments of this thesis.

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Appendix

Appendix 1: The Questionnaire

First, you will get some introductory questions to gain some more information about the treatment period you and your dog have gone through.

1. Which medicine(s) or medicine combination(s) did your dog receive? U can choose more than one option.
    a. Allopurinol
    b. Glucantime
    c. Allopurinol in combination with glucantime
    d. Milteforan
    e. Milteforan in combination with glucantime
    f. Something else, namely:

2. How many times did you and your dog follow the treatment with glucantime injections?
    a. One time
    b. Two times
    c. Three times
    d. Something else, namely:

3. How long ago did you stop the last treatment with glucantime?
    a. Less than a week ago
    b. 1 weak to 1 month ago
    c. 1 to 3 months ago
    d. 3 to 6 months ago
    e. 6 to 12 months ago
    f. 1 to 2 years ago
    g. More than 2 years ago

4. Who injected the medicine during this month?
    a. I did it myself
    b. I did this together with someone, namely:
    c. My veterinarian
    d. Someone else, namely:

5. Who explained you how to administer the medication?
    a. The University of Utrecht
    b. My own veterinarian
    c. Someone else, namely:

6. I think the explanation about administering the treatment was clear. (You may explain you answer)
    a. Absolutely not
    b. Not
    c. Partly correct/not correct
    d. Correct

e. Absolutely correct

7. I practised the administering together with my veterinarian.
   a. Yes
   b. No

8. How long did administering the treatment take you per day?
   a. 5 minutes
   b. 10 minutes
   c. 15 minutes
   d. 20 minutes
   e. Something else, namely:

9. Normally the treatment occurs by one subcutaneous injection once a day for a period of four weeks. Is this how you or your veterinarian did it?
   a. Yes, I did not miss more than three injections (proceed to question 9, skip question 7 and 8)
   b. No, I missed more than three injections (proceed to question 7)
   c. No, I quit the treatment prematurely (proceed to question 8, skip question 7)
   d. My veterinarian composed a different treatment plan, namely: (proceed to question 9, skip question 7 and 8)
10. Why did you miss more than three injections?

11. You quit the treatment prematurely, what was the reason for this?
   a. The Leishmania symptoms in my dog worsened.
   b. My dog got more ill, probably because of the injections
   c. We were not able to give our dog the injections, it was too painful for my dog
   d. We were not able to give our dog the injections, my dog developed an inflammation at the injection site
   e. We were not able to give our dog the injections, because of another reason, namely:

12. Below you will find a few statements about the Leishmania symptoms of your dog **before** starting the treatment with glucantime. To what extent did your dog express them? You can choose between: not – mild – moderate – severe.

Symptoms	*Not*	*Mild*	*Moderate*	*Severe*
Lethargy	O	O	O	O
Exercise intolerance	O	O	O	O
Loss of weight	O	O	O	O
Skin disorders	O	O	O	O
Stiffness	O	O	O	O
Lameness	O	O	O	O
Decreased appetite	O	O	O	O
Vomiting	O	O	O	O
Eye disorders	O	O	O	O

13. Next, you will find a few statements **about applying the injections** with glucantime. You can choose to what extent you agree with these statements. You can choose between:

absolutely not – not – partly correct/not correct – correct – totally correct.

Statements	*Absolutely not*	*Not*	*Partly correct/not correct*	*Correct*	*Totally correct*
I think it was easy to give my dog the treatment	O	O	O	O	O
My dog did not seem to be bothered by being injected every day	O	O	O	O	O
If there were problems or questions, I could always ask my veterinarian	O	O	O	O	O
During this month I wished for more support by a professional	O	O	O	O	O
In hindsight, I rather would have let my dog be injected by my veterinarian every day	O	O	O	O	O
I think this treatment is too intensive and not worth it	O	O	O	O	O
I think this treatment is worth it	O	O	O	O	O
I would recommend this treatment to other owners in the same situation as me and my dog	O	O	O	O	O

14. The following statements relate to the impact of the treatment **on your own wellbeing**. With every statement, you can indicate to what extent this is true for you. You can choose between: absolutely not – not – partly correct/not correct – correct – totally correct.
The treatment with glucantime:…

Statements	*Absolutely not*	*Not*	*Partly correct/not correct*	*Correct*	*Totally correct*
Negatively affected the bond between me and my dog	O	O	O	O	O
Negatively affected my mood	O	O	O	O	O
Negatively affected my physical health	O	O	O	O	O
Affected my spare time	O	O	O	O	O
Negatively affected the maintaining of my social contacts	O	O	O	O	O
Negatively affected my daily expenses	O	O	O	O	O

15. Indicate to what extent your dog showed the following signs **during the treatment** with glucantime. You can choose between: not – mild – moderate – severe.

Signs	*Not*	*Mild*	*Moderate*	*Severe*
My dog seemed painful on the injection site	O	O	O	O
My dog gained a bump/inflammation on the injection site	O	O	O	O
My dog's appetite reduced	O	O	O	O
My dog seemed ill and/or threw up	O	O	O	O
My dog drank more than usual	O	O	O	O
My dog urinated more than usual	O	O	O	O
My dog had diarrhoea	O	O	O	O
My dog slept more than usual	O	O	O	O
My dog was less active	O	O	O	O
My dog was less playful	O	O	O	O
The treatment seemed to cause stress in my dog	O	O	O	O

16. Below you will find a few statements about the Leishmania symptoms of your dog **one month after** the treatment with glucantime. To what extent did your dog express them? You can choose between: not – mild – moderate – severe.

Symptoms	*Not*	*Mild*	*Moderate*	*Severe*
Lethargy	O	O	O	O
Exercise intolerance	O	O	O	O
Loss of weight	O	O	O	O
Skin disorders	O	O	O	O
Stiffness	O	O	O	O
Lameness	O	O	O	O
Decreased appetite	O	O	O	O
Vomiting	O	O	O	O
Eye disorders	O	O	O	O

Finally, you will get some general questions on yourself and your situation

17. What is your age?
    a. 17 years old or younger
    b. 18-20 years old
    c. 21-29 years old
    d. 30-39 years old

e. 40-49 years old
f. 50-59 years old
g. 60 years old or older

18. What is your gender?
    a. Male
    b. Female
    c. Different

19. How long are or were you the dog's owner before you started the treatment with glucantime?
    a. Less than a week
    b. 1 week to 1 month
    c. 1 to 3 months
    d. 3 to 6 months
    e. 6 to 12 months
    f. Over 1 year

20. What is your dog's country of origin?
    a. The Netherlands
    b. Spain
    c. France
    d. Portugal
    e. Greece
    f. Different, namely:

21. What was your dog's age during the first treatment with glucantime?
    a. Less than 1 year old
    b. 1-2 years old
    c. 2-3 years old
    d. 3-4 years old
    e. 4-5 years old
    f. 5-6 years old
    g. 6-7 years old
    h. 7-8 years old
    i. 8-9 years old
    j. 9-10 years old
    k. Older than 10 years old

22. What is your dog's gender?
    a. Intact male
    b. Castrated male
    c. Intact female
    d. Castrated female

23. What is your dog's weight?

24. Is your dog still alive?

a. Yes (proceed to question 24)
b. No (proceed to question 22)

25. When did your dog die?
    a. Less than a week ago
    b. About 1 month ago
    c. 1-3 months ago
    d. 3-6 months ago
    e. 6-12 months ago
    f. 1-3 years ago
    g. Over 3 years ago

26. What was the reason for your dog's death?
    a. Leishmania
    b. Something else, namely:

27. When you want to be informed about the results, leave your e-mail below:
28. Do you have any remarks on this questionnaire?

Thank you so much for your time and effort to fill in this questionnaire!

Appendix 2: Table mean QoL per dog

N	QoL before (Q12)	QoL during (Q15)	QoL after (Q16)	QoL_before minus QoL_during (Q12-Q15)	QoL_during minus QoL_after (Q15-Q16)	QoL_before minus QoL_after (Q12-Q16)
1	2,44	2,1	1,1	0,35	0,98	1,33
2	1,89	1,6	1,2	0,25	0,42	0,67
3	2,44	2,4	1,3	0,08	1,03	1,11
4	2,89	2,7	1,7	0,16	1,06	1,22
5	1,44	1,6	1	-0,2	0,64	0,44
6	2,33	1,3	1,2	1,06	0,05	1,11
7	2,22	1,6	1	0,58	0,64	1,22
8	2,56	1,6	2,3	0,92	-0,69	0,23
9	2,67	2,4	2	0,31	0,36	0,67
10	3	1,2	1,4	1,82	-0,26	1,56
11	1,56	2,3	1,7	-0,7	0,6	-0,1
12	2,78	2,1	2,3	0,69	-0,24	0,45
13	1,89	1,3	1,7	0,62	-0,4	0,22
14	2,11	2,6	1,3	-0,4	1,22	0,78
15	3,44	2,7	4	0,71	-1,27	-0,6
16	1,44	1,3	1,1	0,17	0,16	0,33
17	1,44	1,5	1,3	-0	0,12	0,11
18	3,33	2,1	1,9	1,24	0,2	1,44
19	1,89	1,8	1,1	0,07	0,71	0,78
20	1	1,6	1	-0,6	0,64	0
21	1,44	2,4	1,3	-0,9	1,03	0,11
22	2	1,6	1,2	0,45	0,33	0,78

23	1,78	1,8	2,2	-0	-0,4	-0,4
24	3,11	2,5	1,6	0,66	0,89	1,55
25	2	2,5	1	-0,5	1,45	1
26	3	3	2,4	0	0,56	0,56
27	1,44	1,6	1,1	-0,2	0,53	0,33
28	1,78	2,5	1,2	-0,7	1,23	0,56
29	3,78	2,3	3	1,51	-0,73	0,78
30	3	1,6	1,3	1,45	0,22	1,67
31	2	1,7	1,2	0,27	0,51	0,78
32	1,44	2,7	1,1	-1,3	1,62	0,33
33	2,78	1,7	1	1,05	0,73	1,78
34	1,44	1,6	1	-0,2	0,64	0,44
35	3	2,6	1,2	0,36	1,42	1,78
36	2,56	2,8	1,6	-0,3	1,26	1
37	2,11	2,2	1,6	-0,1	0,62	0,55
38	2	2,9	1,3	-0,9	1,58	0,67
39	2,44	3	1,4	-0,6	1,56	1
40	2,33	2,4	1	-0	1,36	1,33
41	1,67	1,4	1	0,31	0,36	0,67
42	1,11	1,9	1	-0,8	0,91	0,11
43	1,33	1,5	1,2	-0,1	0,23	0,11
44	2,44	1,6	1,4	0,89	0,11	1
45	2,11	1,6	1	0,47	0,64	1,11
46	2,11	2,5	1,8	-0,3	0,67	0,33
47	1,56	2,2	2,1	-0,6	0,07	-0,6
48	3	1,3	1	1,73	0,27	2
49	1,44	1,7	1,1	-0,3	0,62	0,33
50	2,44	2,7	1,9	-0,3	0,84	0,55
51	2	2	1,8	0	0,22	0,22
52	1	2,4	1,7	-1,4	0,69	-0,7
53	1,67	2,7	1,3	-1,1	1,4	0,34
54	2,56	1,2	1	1,38	0,18	1,56
55	3,11	3,2	1,4	-0,1	1,74	1,67
56	2,11	1,6	1,1	0,56	0,44	1
57	1,89	1,1	1,3	0,8	-0,24	0,56
58	3,33	2	1,7	1,33	0,33	1,66
59	2,33	1,8	1,3	0,51	0,49	1
60	2,11	2,5	2	-0,3	0,45	0,11
Mean	2,19	2	1,5	0,16	0,547	0,71

[i] Qualtircs: www.qualtrics.com

[ii] SPSS Version 25: www.surfspot.nl