THE EFFECT OF TARANTULA CUBENSIS EXTRACT APPLIED IN PRE AND POSTOPERATIVE PERIOD OF CANINE MAMMARY TUMOURS

Köpek Meme Tümörlerinde Pre ve Postoperatif Dönemde Uygulanan Tarantula Cubensis Extraktının Etkisi

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Summary

Background: The purpose of the research was to investigate the effects of Tarantula cubensis extract (Theranekron, 1:100 / D2, Richter Pharma, Austria) applied during pre and postoperative period on canine mammary tumours. **Methods : A** total of 30 bitches between the ages of 5-12 were used in the study. The breed distribution of the bitches was observed as 21 Terriers, two Pekinese, two St. Bernards, one Setter, one Danua, one German Shepherd, one Doberman and one Cocker. Group I consisted 20 bitches with mammary tumours and subcutaneus injections of Tarantula cubensis extract were performed preoperatively for three times at one week intervals with the dosage of 3 ml per 10 kg. Between the days of 7th and 10th following the third injection, complete unilateral mastectomy was performed and injections were repeated at the 1st and 5th month of postoperative period. Histopathologic results of this group revealed that 10 mammary tumours were malignant and 10 was benign. Group I was compared to Group II consisted of 10 bitches with malignant tumours which were treated by surgical

excision alone. **Results:** In group I, no change was observed with palpation or inspection after the first Tarantula cubensis extract injection. A week later the second injection there was 10% regression in 10 cases. Benign tumours (n=10) were observed to be hard and regressed 50% in the week following the 3rd Tarantula cubensis extract injenction performed preoperatively while malignant ones showed no regression but became hard. Reoccurence on the intact mammary chain was not observed for a year of postoperative period in Group I. In Group II reoccurence was observed in six bitches and pulmonary metastasis was determined in two. **Conclusion:** It was determined that Tarantula cubensis extract applications in the bitch resulted in regression and hardness of benign mammary tumours while only hardness was detected in malignant mammary tumours. Postoperative injections can be performed in order to prevent the reoccurence.

Key words: Canine mammary tumour, homeopathy, Tarantula cubensis extract.

Özet

Amaç: Bu çalışmada köpek meme tümörlerinde pre ve postoperatif dönemde uygulanan Tarantula cubensis extraktının (Theranekron, 1:100 / D2, Richter Pharma, Austria) etkisi araştırıldı.

Materyal ve Metot: Çalışmada meme bezinde kitle şikayetiyle getirilen yaşları 5-12 arasında değişen toplam 30 köpek kullanıldı. Irk dağılımı 21 terrier, iki pekinez, iki St. Bernard, bir stter, bir danua, bir alman çoban köpeği, bir doberman ve bir cocker şeklindeydi. Grup I'de tümör tipi postoperatif dönemde belli olan 10 benign ve 10 malign meme tümörü değerlendirildi. Bu grupta Tarantula cubensis ekstraktı preoperatif dönemde birer hafta arayla üç kez ve 10 kg için 3 ml dozda subkutan yolla uygulandı. Üçüncü enjeksiyondan 7-10 gün sonra komple unilateral mastektomi yapıldı.

Enjeksiyonlar postoperatif 1. ve 5. ayda tekrarlandı. Grup I'de elde edilen bulgular, sadece operasyon yapılan malign meme tümörlü kontrol köpekleriyle (Grup II, n=10) karşılaştırıldı.

Bulgular: Bu grupta birinci Tarantula cubensis ekstraktı enjeksiyonundan sonra tümörlerde palpasyon veya inspeksiyonla belirlenebilen bir değişiklik olmadı. İkinci enjeksiyondan 7 gün sonra yapılan muayenede, tümörlerin hepsinde hafif bir sertleşme olduğu belirlendi. Ayrıca 10 olguda % 10 oranında bir regresyon tespit edildi. Preoperatif üçüncü ilaç uygulamasından 7 gün sonra ise 10 olguda tümörlerin ortalama %50 oranında regrese olduğu ve sertleştiği, diğer 20 olguda ise tümörlerin sadece sertleştiği ve regresyon meydana gelmediği tespit edildi. Kitlelerin postoperatif histopatolojik muayenesinde, ilaç uygulaması sonrasında regrese olanların benign yapıda olduğu belirlendi. Grup I'deki köpeklerde postoperatif bir yıllık dönemde, uzaklaştırılmayan meme zincirinde yeni tümör oluşumuna rastlanmadı. Grup II'de ise 6 köpekte yeni tümör oluşumu ve iki köpekte de akciğer metastazı belirlendi.

Sonuç : Tarantula cubensis ekstraktının preoperatif uygulamalarının benign tümörlerde regresyon ve sertleşme, malign tümörlerde ise sadece sertleşme oluşturduğu gözlendi. Ayrıca ilacın postoperatif dönemde kullanımının yeni tümör oluşumlarını önleyebileceği sonucuna varıldı.

Anahtar kelimeler: Köpek meme tümörleri, homeopati, Tarantula cubensis ekstraktı

Introduction

Mammary tumours are originated mainly from secretoric epitelium, myoepitelium or mesenchymal tissue of the mammary gland (Morgan, 1997). The incidence of mammary tumours in the bitch is 25 – 42 % (Brearley, 1989) . The most

frequent observed tumours of the bitch is mammary tumour second to skin neoplasia (Brearley, 1989). The incidence of the mammary tumour is 4% for the dog of 3-4 years, 29% for the dog of 4-8 years, while bitches over 8 years of age accounts for 67% (Zaninovic and Simcic, 1991). Mammary tumours are classified as benign or malign and 41-50 % of them are malignant types (Macewen, 1990).

Main treatment ways of mammary tumours are surgery, radiotherapy, chemotherapy or combined therapy of all. Succesful treatment depends on tumor staging and early diagnosis (Novosad, 2003) It is thought that only tumours seem malignant should be extirpated but early clinical approach is recommended for all types of tumours because of the reason that benign tumours can be diverted into malign types (Ciekot, 1995).

Homeopathy is a complementary treatment which is introduced by Dr. Samuel Hahnemann in the end of 18th century. It was based on the opinion that “like cures like = similia similibus curantur”. Homeopathy is the selection of a substance to cure a disease by knowing that same substance could cause the symptoms seen in the patient (Pingel, 1992). It was determined that as a homeopathic medicine, Tarrantula cubensis extract stops tumour growth in canine mammary tumours by forming demarcation (Koch and Stein, 1980).

In the present study, morphologic effects of preoperative application of Tarrantula cubensis extract (Theranekron, 1:100 / D2, Richter Pharma, Austria) on canine mammary tumours and its protective effect on new mass formation during the postoperative period was investigated.

Material and methods

A total of 30 cases of mammary tumours from different ages and breeds, presented to University of Ankara, Faculty of Veterinary Medicine, Department of Obstetrics and Gynaecology were used in this study. Treatment procedure was performed on the bitches presented with mammary masses without the knowledge of tumour type.

The mean age of 30 bitches was 8.8 ranging from 5 -12 . The breed distribution of the bitches was observed as 21 Terriers, 2 Pekinese's 2 St. Bernards, 1 Setter, 1 Danua, 1 German Shepherd, 1 Doberman and 1 Cocker.

Clinical Identification of Tumours

On the initial examination of the dogs, clinical identification of tumours were carried out according to Tumour – Nodule - Metastasis (TNM) classification system which was advised by World Health Organization (Owen, 1980). The clinical staging of each primary tumour can be seen in Table 1. In case of multiple tumours in a dog, the tumour which had the biggest diameter was accepted as primary tumour. The diameter of primary tumour was determined by measuring the distance between two farest points using a ruler. Lymph node enlargements were determined by palpation. Lateral and dorsoventral radiographs of the chest were taken in pretreatment of dogs to determine lung metastasis. None of the bitches used in this study had lung metastasis on the initial examination.

Treatment Protocol

The bitches of Group I (n=20) were treated with Tarrantula cubensis extract (Theranekron, 1:100 / D2, 1.0 mg/ml, Richter Pharma, Austria) which is a homeopathic medicine. Subcutaneus injections of Tarantula poison was applied preoperatively three times a week at one week intervals with a dosage of 3 ml per 10 kg of body weight.

Regression rates of primary tumours were determined by measuring the diameter. Surgical removal by complete unilateral mastectomy was performed between the days of 7th and 10th following the third injection.

In Group II (n=10) complete unilateral mastectomy was performed in the following week of initial examination. No other treatment was applied. This group was evaluated as the control group.

Postoperative histopathologic examinations of the tumours were performed in University of Ankara, Faculty of Veterinary Medicine, Department of Pathology. Tumours were fixed in formaldehid, waxed in parafine and stanied in hemotoxilen and eosine. Tumours were classified according to Hampe and Misdorp (1974) classification system.

Paired T-Test was used for statistical analysis ($p<0.001$).

Follow up

Tarantula cubensis extract injections of dogs were repeated at 1st and 5th months of postoperative period.

During the first year after the treatment all the bitches were evaluated once a month for reoccurence on the other mammary chain. They were controlled by radiographic examinations performed laterolateral and ventrodorsal positions at 2nd and 12th months of postoperation for possible lung metastasis.

Results

It was observed that 11 primary tumours of 30 cases were located on caudal abdominal gland, 10 on inguinal gland, four on cranial abdominal gland, three on cranial toracal gland and two on caudal toracal gland.

In group I, no morphological change that could be determined by inspection or palpation was observed in the masses after the first Theranekron injections. There was no change of the masses that could be determined by palpation or inspection after the 1st Theranekron injection done preoperatively. On the 7th day following the second injection, it was determined that all the tumours became slightly firm. Also there was 10 % regression in 10 cases. Expected effect of Theranekron was observed in the week following the 3rd injection and all primary tumours were evaluated as very hard by palpation. Morover, significant regression was observed in 10 tumours which were determined to be benign. Since there were only three cases of adenoma among the benign tumours it was not possible to conclude that there was a correlation between tumour type and regression rate. has not been come to the conclusion that there is no correlation between tumour type and regression rate. Regression rates are given in Table 2. Malignant tumours were firm but no regression was determined. Regression rates of benign tumours were statistical significance ($p<0.001$).

In Group I, there was also no recurrence during the year of postoperative period. Additionally, no side effects such as vomiting or diarrhea were determined, however, only morphological changes were observed in the tumours of tumours were observed.

Axillar or inguinal lymph node enlargement of six bitches determined in the initial examination became firm and smaller and in the postoperative period no growth of lymph nodes were detected. During the study, lung metastasis was not seen on the radiographs of the bitches.

In group II the bitches only had complete unilateral mastectomy. Six of these dogs had recurrence on the other mammary chain in the year of postoperative period.

The regional lymph node enlargements of three dogs which were examined preoperatively were stable. New lymph node enlargements were not observed in other dogs of this group during the year of postoperation. But two dogs had lung metastasis determined by the radiograph.

Discussion

In this study, morphological effects of Tarantula cubensis extract on canine mammary tumours and the postoperative observations for one year were presented..

The study by Koch and Stein (1980), which is the only work investigated the effectiveness of tarantula cubensis extract on canine mammary tumours determined that as a homeopathic medicine, Tarrantula cubensis extract stopped tumour growth by forming demarcation area when used preoperatively a week for three times with the dosage of 3-6 ml depending on the body weight. In the same study (Koch and Stein, 1980), it was observed that tumours became smaller, no reoccurence was determined for years and life quality got better in some cases. Tarantula cubensis extract ceased tumour growth, improved wellfare, decreased the lymph enlargement, made tumour center harder and capsule thicker and created a demarcation ares on the surrounding tissue of tumour (Koch and Stein, 1980). In our study, the results were similar with those found in the study of Koch and Stein (1980).

It was reported that lymph nodes are biological barrier of the body and extirpation of normal or contaminated lymph nodes has some disadvantages (Gilson, 1995). It was also pointed out that extirpation of lymph nodes during mastectomy may improve the treatment; but expanding the incision line up to lymph nodes may increase surgical

morbidity. Besides, and extirpation of normal or contaminated lymph nodes has some disadvantages such as distribution of residual tumour cells (Gilson, 1995).

In the present study lymph nodes were not removed. Ceasing of lymph node growths was observed in Group I and no new tumour formation was seen, so this points out that Tarantula cubensis extract might be effective on lymph nodes.

In the present study, cases were only evaluated clinically and a detailed pathologic investigation was not performed about why Tarantula cubensis extract causes regression of benign mammary tumours. Therefore, it has been concluded that this study can be a source of inspiration for future studies on pathologic effects of Tarantula cubensis extract. Additionally, the fact that Tarantula toxin causes regression of benign tumours but not malign ones may give an idea about histopathologic type before surgery. But detailed study is necessary to come that conclusion.

Table 1. Classification of primary tumours

Case	Group I		Group I		Group II	
	Clinical staging	**Histopathologic type**	**Clinical staging**	**Histopathologic type**	**Clinical staging**	**Histopathologic type**
1	T1bN0M0	Malign mixed tumour	T1aN0M0	Simple adenoma	T1aN0M0	Papillary adenocarsinom
2	T2aN0M0	Tubular adenocarcinom	T1aN0M0	Fibroadenoma	T1bN0M0	Malign mixed tumour
3	T2bN0M0	Malign mixed tumour	T2aN0M0	Benign mixed tumour	T1aN0M0	Malign mixed tumour
4	T2cN1bM0	Malign mixed tumour	T2aN0M0	Benign mixed tumour	T1aN0M0	Malign mixed tumour
5	T2cN1bM0	Malign mixed tumour	T2aN0M0	Benign mixed tumour	T2cN1bM0	Malign mixed tumour
6	T3aN1bM0	Malign mixed tumour	T2aN0M0	Benign mixed tumour	T2aN0M0	Papillary adenocarsinom
7	T3cN1aM0	Malign mixed tumour	T3aN0M0	Simple adenoma	T2cN0M0	Tubular adenocarcinom
8	T3bN0M0	Malign mixed tumour	T3bN0M0	Benign mixed tumour	T2aN0M0	Papillary adenocarsinom
9	T3cN0M0	Tubular adenocarsinom	T3aN1aM0	Benign mixed tumour	T3aN1bM0	Papillary adenocarsinom
10	T3bN0M0	Papillary adenocarsinom	T3cN1bM0	Benign mixed tumour	T3cN1bM0	Malign mixed tumour

M0 = No metastasis; N0 = No regional lymph node (RLN) involvement; N1 = Ipsilateral RLN inolvement; N1a = Not fixed; N1b = Fixed; T1 = Tumour <3 cm maximum diameter; T1a = Not fixed; T1b = Fixed to skin; T2 = Tumour 3-5 cm maximum diameter; T2a = Not fixed; T2b = Fixed to skin; T2c = Fixed to muscle; T3 = Tumour >5 cm maximum diameter; T3a = Not fixed; T3b = Fixed to skin; T3c = Fixed to muscle

Table 2. TNM classification, tumour types and regression rates of primary tumours

Case	Classification	Tumour type	Regression rate
1	T1a N0 M0	Simple adenoma	++
2	T1a N0 M0	Fibroadenoma	++
3	T2a N0 M0	Benign mixed tumour	+
4	T2a N0 M0	Benign mixed tumour	+++
5	T2a N0 M0	Benign mixed tumour	++
6	T2a N0 M0	Benign mixed tumour	++
7	T3a N0 M0	Simple adenoma	++
8	T3b N0 M0	Benign mixed tumour	++
9	T3a N1a M0	Benign mixed tumour	++
10	T3c N1b M0	Benign mixed tumour	++

M0 = No metastasis; N0 = No regional lymph node involvement; N1 = Ipsilateral RLN metastasis; N1a = Not fixed; N1b = Fixed; T1 = Tumour <3 cm maximum diameter; T1a = Not fixed; T2 = Tumour 3-5 cm maximum diameter; T2a = Not fixed; T3 = Tumour >5 cm maximum diameter; T3a = Not fixed; T3b = Fixed to skin; T3c = Fixed to muscle; + = 1-25%; ++ = 25-50%; +++ = 50-100% regression

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