

COMUNICACIÓN

Analysis of 24 cases of Transmissible Venereal Tumour (TVT) in two veterinary clinics in Florencia, Colombia

Análisis de 24 casos de Tumor Venéreo Transmisible (TVT) en dos clínicas veterinarias de Florencia, Colombia

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ABSTRACT

The present study analyses the results of 24 complete clinical records of canine transmissible venereal tumour (TVT) obtained in two veterinary clinics in Florencia, Caquetá during 2014 and 2018. The effectiveness of treatments using vincristine sulphate on a weekly basis was greater than 65% after four sessions. Those that used only vincristine sulphate had 50% effectiveness, while those who implemented some type of adjuvant achieved 70% of effectiveness. However, the use of Yatrén (Chiniofon) as immunostimulant was not effective in 3/5 cases. Results showed treatment sessions should continue until after there is no visual evidence of the lesions to eliminate all tumour cells.

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Key words: venereal tumour, canine, Sticker's tumour, neoplasm

RESUMEN

El presente estudio analiza los resultados de 24 historias clínicas completas de tumor venéreo transmisible canino (TVT) obtenidas en dos clínicas veterinarias de Florencia, Caquetá entre 2014 y 2018. La efectividad de los tratamientos con sulfato de vincristina en forma semanal fue superior al 65% después de cuatro sesiones. Los que utilizaron solo el sulfato de vincristina tuvieron 50% de efectividad, mientras que quienes implementaron algún tipo de adyuvante lograron el 70% de efectividad. Sin embargo, el uso de Yatrén (Chiniofon) como inmunoestimulante no fue efectivo en 3/5 casos. Los resultados mostraron que las sesiones de tratamiento deben continuar hasta que no haya evidencia visual de las lesiones a fin de eliminar todas las células tumorales.

Palabras clave: tumor venéreo, canino, tumor de Sticker, neoplasia

INTRODUCTION

Transmissible venereal tumour (TVT), also known as Sticker's Tumour or Transmissible Venereal Sarcoma is a contagious neoplasm, which is transmitted naturally between canines by allogeneic implants of tumour cells mainly in the genital mucosa during intercourse (Mukaratirwa & Gruys, 2003; Grandez *et al.*, 2011), observed also in other species of canids such as foxes, coyotes and jackals (Fassati, 2018).

Physically the transmissible venereal tumour is characterized by having an appearance like cauliflower. It can also be pedunculated, nodular, papillary or multilobed; solitary or as multiple formations (Crossley & Ramírez, 2017). Lima (2013) affirms that the form that the tumour acquires varies for males and females, appearing in papules, nodular or multilobular forms. The location of the tumour is related to the mode of transmission. It is almost always in the genital area, due to transmission through mating, but these lesions can be evidenced in other parts of the body such as the adjacent skin,

as well as genital, oral and conjunctival mucosa, caused by transmission during social behaviours such as licking and sniffing (Ganguly *et al.*, 2016; Ojeda *et al.*, 2016).

TVT is considered a neoplasm of worldwide distribution, it is endemic in at least 90 countries, with an incidence of 6 to 30 cases per 100 000 dogs, being more common in tropical and subtropical countries among the stray dog population (Strakova & Murchison, 2014; Sabogal, 2019). In Colombia, the estimated prevalence of TVT is 7.5%, with a higher prevalence in the Andean region with 75.9%, while in the Amazon region is 7%, but probably this figure would be higher as the lack of case reports is the reason why such a low figure is represented for this tropical zone (Arcila-Villa *et al.*, 2018).

The treatments used such as surgery, radiotherapy, immunotherapy and chemotherapy have shown effectiveness against canine TVT and vincristine sulphate has proven to be the treatment of choice due to the results presented, either as a single therapy or as an adjunct to surgery (Komnenou *et al.*, 2015).

Vincristine exerts its cytotoxic mechanism by interfering in the tumour cell cycle. During metaphase, the action of vincristine in blocking and interrupting mitotic

metaphase is summarized. Some of the myelo-suppressive effects of this cytostatic agent are leukopenia as well as vomiting in 5-7% of cases. Besides, paresis has been described as a collateral effect. In the IV inoculation site, due to the extravasation during the application, skin lesions may occur and may lead to necrosis of the area (Quiroga *et al.*, 2020). According to Sousa *et al.* (2000), a white blood cell count is recommended prior to each treatment and if neutrophils are below 4000/ml the treatment should be delayed for 3-4 days. The dosage range is 0.5-0.75 mg/m² IV body surface area or 0.026 mg/kg weekly in cycles as part of a protocol for a chemotherapeutic combination (Jiménez & León, 2019).

In Caquetá, Colombia, the effectiveness of the procedures carried out in the treatment of TVT has not been evaluated, therefore a study was proposed to analyse the clinical histories of positive cases to TVT in two veterinary clinics in the city of Florencia, evaluating the procedural variants in medical protocols and their effectiveness.

MATERIAL AND METHODS

The present study was carried out in the municipality of Florencia, located in the department of Caquetá (Colombia). The area is within the equatorial climatic zone defined as hot and humid, with a well-defined dry season between the months of December and February. The average annual temperature is between 19 and 28 °C (Gobernación del Caquetá, 2017).

For the information gathering process, general guidelines of grounded theory were used, from which the medical records of canines between 2014 and 2018 from two veterinary clinics are related and analysed. From a total of 103 TVT cases, 24 histories were selected that had complete information on diagnosis, treatment, therapy, and effectiveness of the established protocols. In

the selection, it was anticipated that there would be information on drugs used in the treatments, number of sessions, effectiveness, among others (Kripka *et al.*, 2015). The data obtained were analysed using descriptive statistics, generating frequency tables and distribution graphs for their interpretation.

RESULTS AND DISCUSSION

Of the 24 cases of TVT selected, 19 corresponded to clinic A and 5 to clinic B. The treatments in all of them were made with vincristine sulphate on a weekly basis. The effectiveness of the treatments established was 57.7% (Clinic A: 57.9%; Clinic B: 60%). Treatments of vincristine sulphate in 4 to 5 sessions were more common (Figure 1). On this, Tomiyasu *et al.* (2010) indicates that it is usual to require between 4 and 7 applications of vincristine sulphate, according to the evolution of the patient.

It was evidenced that treatments with four or more sessions were more effective, showing that chemotherapy is more efficient when it is implemented for a longer time (Figure 1). Peña *et al.* (2017) said that treatment based on vincristine sulphate achieves total regression of the tumour on average between the fourth and sixth session. Similarly, other studies showed that the treatment is successful when it is applied between 5 to 10 weeks (Bonilla *et al.*, 2015; Ojeda *et al.*, 2016; Jiménez & León, 2019). The continuous activity of the established therapy allows a better immune response. The early involution of tumoral masses can even indicate a wrong concept of healing, since mutated cells may still exist in tissues, and therefore it is recommended to do two additional sessions to ensure the removal of this pathological tissue.

Chemotherapy gives the most promising results and a remission of up to 100% can be achieved. A variety of chemotherapeutic agents have been tested against TVT

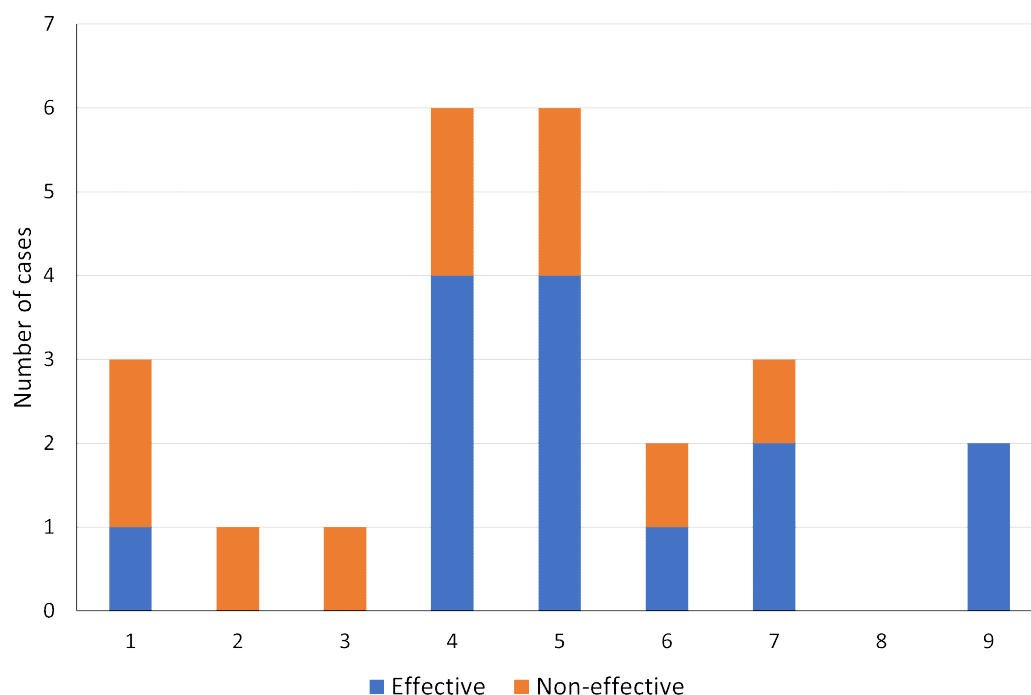


Figure 1. Effectiveness of vincristine sulphate treatment in the treatment of canine transmissible venereal tumour (TVT) by number of sessions

Table 1. Drugs used together as adjuncts to vincristine in the treatment of canine transmissible venereal tumour (TVT)

Drug used	Number of reports	Reference
Avermectin	2	Machiori (2010)
Corticoid	1	González <i>et al.</i> (2004)
Antibiotic	3	Fernández <i>et al.</i> (2018); Ramírez <i>et al.</i> (2015)
Multivitamin	2	Peña <i>et al.</i> (2017); Loyola (2014)
Haemostatic	2	Guerrero y Perez (2010)
Immunostimulant	5	Cohen (1980)
Nosode	1	Alvarado y Zea (2014)
Total	16	

cyclophosphamide with methotrexate (Amber *et al.*, 1990). Vincristine has become the drug of choice for therapy against TVT and it has been included in treatment protocols since the 1980s (Ganguly *et al.*, 2016).

Regarding the use of adjuvant medications, seven types of medications were found, both individually and in combination, among which are: avermectin (ivermectin), corticosteroid (dexamethasone), antibiotics (doxycyc-

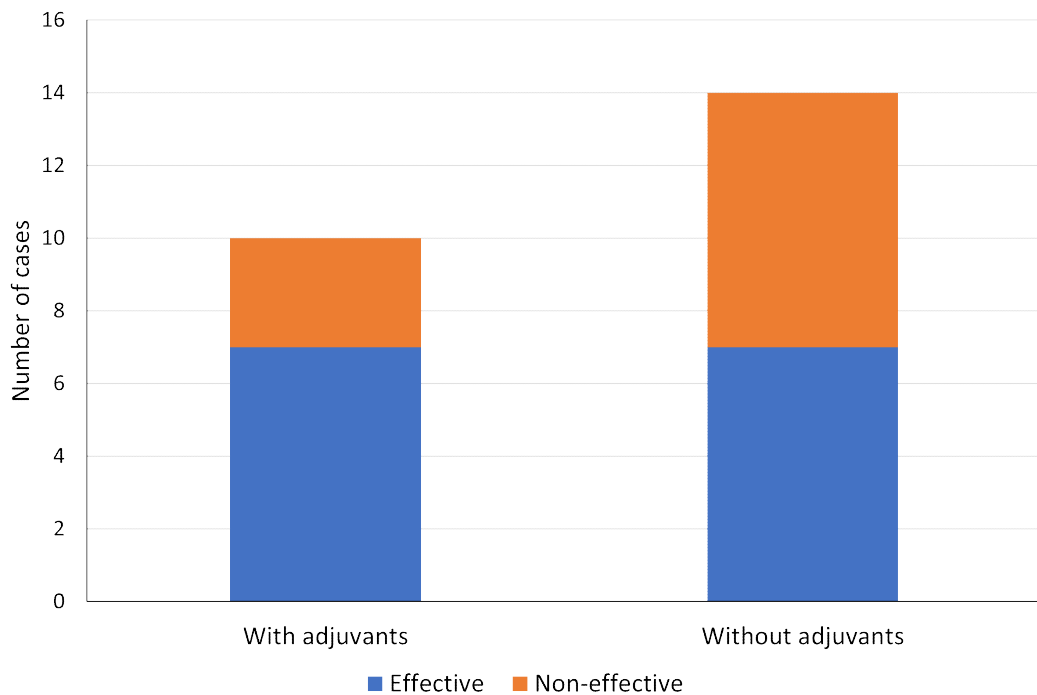


Figure 2. Effectiveness of cases with and without adjuvants in the treatment of canine transmissible venereal tumour (TVT)

line and benzathine cloxacillin, as curative or preventive of bacterial infections in lesions), multivitamins, haemostatic (etamsylate), immunostimulant (Yatrén) and nosode (Table 1). On the other hand, some studies have reported autohemotherapy as an adjunct in the treatment of TVT (Benavides Castro & Murcia Marroquin, 2017) and homeopathic serum (Galliumdib + Immunodib) (Rojas *et al.*, 2017) to stimulate the immune system. Furthermore, Sastre *et al.* (2019) have used chemotherapy with vincristine sulphate as an adjunct to surgery.

Of the cases in which adjuvants were used, 70% were considered effective, while 50% were effective when chemotherapy was done alone (Figure 2). According to Fernández *et al.* (2018) and Bonilla *et al.* (2015), this neoplasm is exposed to easy contamination by bacteria, which could complicate the clinical picture, therefore, the advantage of using antibiotics in some cases. Cohen (1980) also

including cyclophosphamide, methotrexate, cyclophosphamide with prednisone, vinblastine with cyclophosphamide or methotrexate, vincristine with doxorubicin, and indicated the importance of using an adjuvant immunotherapy in immunosuppressed patients, and González *et al.* (2004) indicates that dexamethasone significantly reduces angiogenic activity in canine TVT.

Resistance to chemotherapy is a multifactorial phenomenon that can be conferred by various cellular mechanisms related to defects in the regulation of apoptosis, increased intracellular detoxification, alterations in DNA repair systems, and activation or overexpression of molecules such as glycoprotein P. This element is part of a family of cellular transporters that function of eject a series of drugs to the outside of the cell, thus reducing their intracellular concentrations to low lethality levels (Gaspar *et al.*, 2011). The cytomorphological types of TVT have

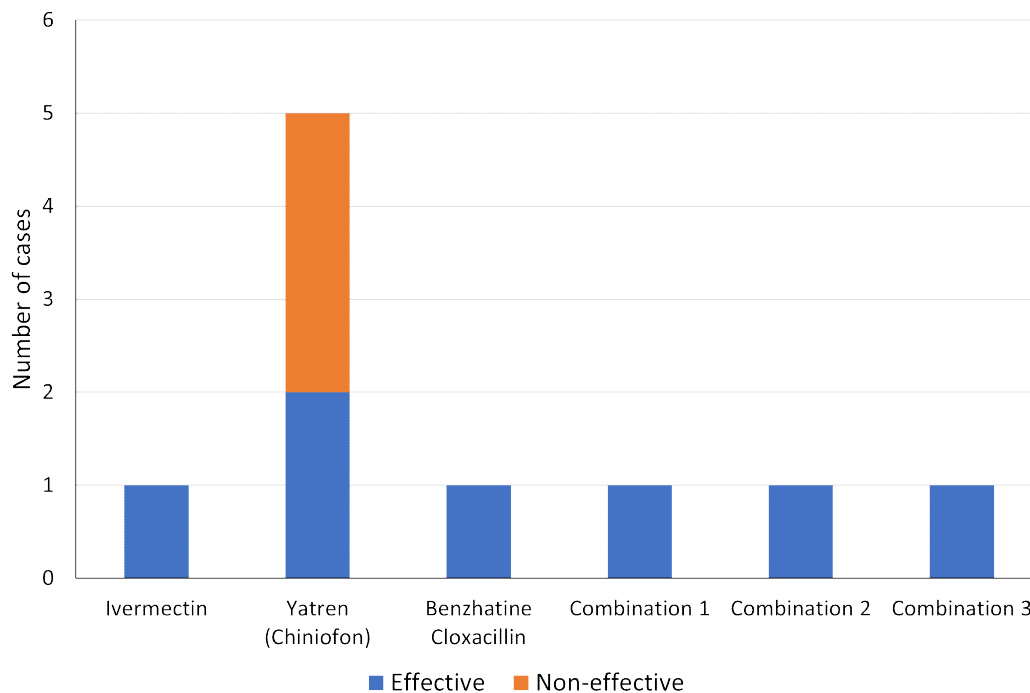


Figure 3. Effectiveness of the treatments according to drugs used in the treatment of canine transmissible venereal tumour (TVT)

been related to biological behaviour, being the plasmacytoid type the highest degree of aggressiveness and less sensitivity to conventional chemotherapy. Some studies have verified the relationship between the expression of the glycoprotein and the plasmacytoid type and a direct relationship of the partial response to chemotherapy was observed with a strong expression of p-glycoprotein (Montoya Floréz *et al.*, 2014).

Ivermectin is a possible alternative drug for the treatment of TVT due to its ability to inhibit the low toxicity P-glycoprotein. Ivermectin associated with vincristine in the treatment of TVT has shown to cause a reduction in tumour mass in a shorter time ((Baldrich *et al.*, 2021). Therefore, ivermectin may decrease the number of chemotherapy applications, minimizing its undesirable effects (Carvalho, 2010).

Yatren (Chiniofon, Ark Pharm, Sigma-Aldrich) was used in 5 out of 10 cases in which a treatment accompanied by adjuvants

was instituted. Ivermectin and benzathine cloxacillin (ophthalmic ointment for ocular TVT) were used on one case each, and ivermectin and dexamethasone (combination 1), doxycycline, ethamsylate and multivitamin (combination 2) and doxycycline, ethamsylate, multivitamin and nosode (combination 3) were used in one case each. Yatren used in three cases was not effective as adjuvant (Figure 3), despite it was used in 3, 4 and 5 sessions. This compound is used for its immunostimulant function, however, Alzamora (2018) showed no evidence of effectiveness in the treatment for TVT where no positive leukocyte effect was obtained.

CONCLUSIONS

- Treatment of canine transmissible venereal tumour (TVT) based on vincristine sulphate administered weekly has proven to be effective when implemented over a long period of time (4 to 9 sessions), depending on how the tumour regresses, so that the treatment

is concluded only when the total regression of the tumour is observed.

- It's important to complement chemotherapy treatment with the use of adjuvant drugs. However, Yatrén had no clinical effectiveness in its immunostimulant role.

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