DOI : 10.4267/2042/69881

THE CONTRIBUTION OF THE VETERINARY HELMINTHOLOGY TO MEDICAL HELMINTHOLOGY

LA CONTRIBUTION DE L'HELMINTHOLOGIE VÉTÉRINAIRE À L'HELMINTHOLOGIE MÉDICALE

Par Jozef VERCRUYSSE[1]

(Communication présentée le 24 Janvier 2019
Manuscrit accepté le 11 Février 2019)

Abstract

Infections with helminths are very common in animals: all grazing animals can be considered to be infected. Over the last decades considerable progress has been made especially in: (1) the development of innovative diagnostic tools, (2) the development of new anthelmintics and large surveys to evaluate their efficacy and to assess the emergence of anthelmintic resistance and, (3) addressing the economic impact of helminth infections such as weight gain and milk yield. The technical and scientific advances developed in the veterinary helminthology contributed also in many ways to medical helminthology. Three examples are briefly presented and discussed: (1) the introduction of new diagnostic tools and the pooling of samples, (2) the initiation of studies to assess the efficacy of anthelmintics in children by the faecal egg count reduction test and making recommendations for monitoring drug efficacy in the field, and (3) studies to assess the impact of treatment at delivery to improve breastfeeding and optimize infant growth.

Key words: parasitic helminths, one health, anthelmintic, breastfeeding.

Résumé

Les infections avec les helminthes sont très fréquentes chez les animaux : tous les animaux qui broutent peuvent être considérés comme étant infectés. Au cours des dernières décennies des progrès considérables ont été faits spécialement dans : (1) le développement de techniques de diagnostic innovatrices, (2) le développement de nouveaux anthelminthiques et de vastes études pour évaluer leur efficacité et la présence de résistance aux anthelminthique et (3) l'initiation des études sur l'impact économique des helminthoses comme le gain de poids et la production de lait. Les développements techniques et scientifiques en helminthologie vétérinaire ont aussi contribué de plusieurs façons à l'helminthologie médicale. Trois exemples sont brièvement présentés et discutés: (1) l'introduction de nouvelles méthodes de diagnostic et la mise en commun des échantillons, (2) l'initiation d'études pour évaluer l'efficacité des anthelminthiques chez les enfants par le test du taux de réduction des œufs fécaux et faire des recommandations sur leur l'efficacité et l'interprétation des données recueillies, et (3) études pour évaluer l'impact d'un traitement à l'accouchement pour améliorer l'allaitement et optimiser la croissance de l'enfant.

Mots-clés : helminthes parasites, une seule santé, anthelminthiques, allaitement.

(1) Faculty of Veterinary Medicine, Ghent University, Salisburylaan 133, B9820 Merelbeke, Belgium.
Email : jozef.vercruysse@ugent.be

DOI : 10.4267/2042/69881

INTRODUCTION

In veterinary medicine the high prevalence of helminth infections - all grazing animals can be considered to be infected - resulted in the development of different diagnostic tools, the availability of more than 15 different anthelmintics (more than 18% of all veterinary drugs sold are anthelmintics) with large surveys to assess their efficacy, and the problems of anthelmintic resistance gave rise to new control approaches. In contrast helminth infections in people received less consideration ***(table 1)***. The technical and scientific advances developed in the veterinary helminthology contributed in many ways to medical helminthology. Three examples are briefly presented and discussed: (1) the introduction of new diagnostic tools including pooling of samples, (2) the initiation of studies to assess the efficacy of anthelmintics in children by the faecal egg count reduction test and making recommendations for monitoring drug efficacy in the field, and (3) studies to assess the impact of treatment at delivery to improve breastfeeding and optimize infant growth.

DIAGNOSTIC TOOLS

Advances in diagnostic tools are a very important issue to better guide the control of helminth infections. Until now the diagnosis of Soil Transmitted Helminths (STH) and *Schistosoma mansoni* in people is mainly based on the detection of eggs in faeces and the KatoKatz is the technique of reference (WHO). Recent applications of veterinary methods to diagnose infections with STH are the McMaster (Bekana *et al.* 2015), the Mini Flotac (Cringoli *et al.* 2017) and the FECPAKG2 (https://www.techion-group.com/FECPAKG2) techniques. The FECPAKG2 is a new complete remote-location parasite assessment tool for sheep/cattle farmers and their veterinarians to assess the intensity of helminth infections and efficacy of drugs. The platform accumulates helminth eggs into one microscopic view after which digital images are taken. A digital image of the sample is then captured by an ICD (image capture device) and attached to a submission form. Images are stored by the associated software and can be uploaded to a remote server when an Internet connection is available. Later, a web-based laboratory technician can count the eggs visible in the images, after which the results are returned to the user by e-mail. The FECPAKG2 platform thus potentially eliminates the need for skilled technicians on-site. FECPAKG2 generates results quickly and easily. Recently, Ayana *et al.* (2018) modified and optimized a FECPAKG2 protocol for the detection and quantification of human STH eggs in stool samples. With the development of the SERASCA®-test, a new and improved method is now available for the diagnosis of *Ascaris suum* infection pressure in fattening pigs (Vlaminck *et al.* 2012). The test is not only more sensitive compared to the detection of faecal eggs but, also a significant correlation between the serology and the average daily growth of pigs was observed. Presently, studies are initiated for the use of the SERASCA®-test in children infected with *Ascaris lumbricoides*. Traditionally, both the assessment of infection intensity and drug efficacy are based on the examination of individual stool samples. However, this strategy impedes the up-scale of epidemiological surveys that is required to support health care decision makers to further maximize the efficiency of preventive chemotherapy at nationwide level. In animal health it has been shown that pooling stool samples allows for a rapid assessment of infection intensity and drug efficacy. Pools of up to 10 animals provided estimates of intensity of helminth infections by means of faecal egg counts (FECs) comparable to those obtained by examination of individual stool samples. Mekonnem *et al.* (2013) highlights that pooling stool samples of children is a rapid procedure that holds promise as a cost-effective strategy for assessing the intensity of STH infection and for monitoring Preventive Chemotherapy programs. In their study they were able to reduce the faecal samples examined by a factor of 10 and 20 without a significant loss in accuracy of the FECs results. Examination of pooled urine and faecal samples applying urine filtration holds also promise for rapid assessment of intensity of *Schistosoma haematobium* and *S. mansoni* infections respectively, but may fail to detect presence of infections when endemicity is low (Degarege *et al.* 2015; Leta *et al.* 2018).

THE EFFICACY OF ANTHELMINTICS

Previously, most evaluations of the efficacy of anthelminthic drugs on STH and schistosomiasis were based on analysis of cure rate (CR) calculated as the percentage of infected individuals at baseline who are free from infection after treatment. CR is an efficient indicator of drug efficacy against bacterial diseases, and researchers in the field of helminthiasis adopted CR for analogy. Macroparasite infections differ from common bacterial and viral infections in that the parasites do not multiply within the

	Helminths of Animals	Helminths of Humans
Number of helminth species	>100	< 10
Importance	Temperate & tropical regions	Mainly tropical regions
Market of anthelmintics	>18% of all veterinary drugs Multiple (> 15) anthelmintics available	<1% of all medical drugs Only three anthelmintics (PZQ, ALB & MEB) available
Drug resistance	Major problem	No to limited problem
New drugs in pipeline	Yes	No (?)

Table 1: *Differences between helminths of veterinary and human importance.*
PZQ: praziquantel; ALB: albendazole; MEB: mebendazole

DOI : 10.4267/2042/69881

host. Thus, the infection intensity (i.e. the number of infectious stages taken up and the size of the established parasite burden) is important, and not simply the state of the host as infected or uninfected. In veterinary control programs, reductions in FEC is used to direct treatment decisions. Vercruysse *et al.* (2011) evaluated the efficacy of albendazole (ABZ) by both the CR and the FECR, and compared statistically between seven trials which took place in geographically disparate parts of the world. They concluded that the CR is not the recommended parameter, as it is sensitive to variation in the intensity of infection before treatment. Also, Montresor (2011) concluded that the efficacy of helminth infections measurement of CR provides information of limited usefulness in the context of helminth (STH) control programs and reductions in FEC, as used for animals, are preferred. Many large-scale efficacy studies are available assessing the efficacy of anthelmintics for ruminants by the faecal egg count reduction test (FECRT). Keiser and Utzinger (2008) highlighted that there is a lack of high-quality trials to determine these reference values for STH infections. Studies that have generated a robust, reliable estimation of the FECR rate following treatment with albendazole (ABZ) and mebendazole (MEB), the only two anthelmintics available to treat infections with STH, were lacking. Moreover, most previous studies evaluating drug efficacy of benzimidazoles drugs against STHs have generally not summarized their efficacy results by means of the group-based FECR formula, using the arithmetic mean and its corresponding 95% confidence interval, which are now recognized as a suitable, indeed the most informative metric, for the outcome of such trials and are needed to enable a meta-analysis of drug efficacy against STHs. Vercruysse *et al.* (2011) and Levecke *et al.* (2014) performed ALB and MEB trials, respectively, that were standardized at a level unprecedented in the scientific medical literature. For both anthelmintics the efficacy against *Ascaris* was very high (> 95%) and against *Trichuris* low (< 65%). ABZ showed a higher efficacy against hookworms (> 95%) compared to MEB (80%). The findings also emphasized the need to revise the WHO recommended efficacy threshold for single dose of MEB and ALB treatments and to determine efficacy levels below which should raise concern about the possible emergence of drug resistance (Vercruysse *et al.* 2011; Vlaminck *et al.* 2018).

THE IMPACT OF TREATMENT AT DELIVERY TO IMPROVE BREASTFEEDING AND OPTIMIZE INFANT GROWTH

It is well known that deworming of lactating cows infected with gastro-intestinal nematodes will result in an increased milk production (Charlier *et al.* 2014). In worm-endemic areas, women of reproductive age are a high-risk group for infection because of their poor nutritional status and increased physiological needs during pre-pregnancy, pregnancy, and lactation. While maternal deworming will be of direct benefit to the infected woman (by curing or reducing her burden of STH infection), the unique interface between mother and child during lactation suggests that benefits may also accrue to the newborn infant.

To measure the effect of providing mothers with deworming treatment (ABZ) soon after delivery, a trial in was conducted in 1010 mother-infant pairs in Peru composed of both STH-infected and uninfected mothers (Mofid *et al.* 2017). Mothers were randomly assigned to receive either a single-dose ABZ or a placebo tablet. Mothers and their infants were visited in their homes at 1and 6 months following delivery. At the 6-month time point, among all mother-infant pairs, they could not detect an effect of deworming on infant growth or morbidity. However, among STH-infected mothers important improvements in infant length gain and length-for-age were observed. The benefits of maternal postpartum deworming should be further investigated in study populations having higher overall prevalence and intensity of STH infections and, in particular, where whipworm and hookworm infections are of public health concern.

CONCLUSIONS

Bringing human and animal health together is important and feasible. We have the responsibility to protect human health and well-being in all that we do. Veterinarians in all aspects of the profession—have the opportunity and responsibility to protect the health and well-being of people in all that they do, including protecting food security and safety; preventing and controlling infectious diseases and protecting environments and ecosystems. The above examples demonstrate how veterinary helminthologists have contributed in several ways to improve the control of STH in humans.

ACKNOWLEDGEMENTS

I thank Vaughan Southgate for reviewing the manuscript.

DOI : 10.4267/2042/69881

REFERENCES

- Ayana M, Vlaminck J, Cools P, Ame S, Albonico M, Dana D, *et al.* Modification and optimization of the FECPAKG2 protocol for the detection and quantification of soil-transmitted helminth eggs in human stool. PLOS Neglected Tropical diseases 2018; 12: e0006655.
- Bekana T, Mekonnen Z, Zeynudin A, Ayana M, Getachew M, Vercruysse J.et al. Comparison of Kato-Katz thick-smear and McMaster egg counting method for the assessment of drug efficacy against soil-transmitted helminthiasis in school children in Jimma Town, Ethiopia. Transactions of the Royal Society of tropical Medicine and Hygiene 2015; 109: 669 – 671.
- Charlier J., van der Voort M., Kenyon F. and Vercruysse J. Chasing the helminth and its economic importance in ruminants. Trends in Parasitology 2014; 30: 361 – 367.
- Cringoli G, Maurelli MP, Levecke B, Vercruysse J, Utzinger J & Rinaldi L. The Mini-FLOTAC techniques for the diagnosis of helminths and protozoa in humans and animals. Nature Protocol 2017; 12: 1723 – 1732.
- Degarege A., Erko B., Mekonnen Z., Legesse M., Negash Y., Vercruysse J. et al Comparison of individual and pooled urine samples for estimating the presence and intensity of *Schistosoma haematobium* infections at the population level. Parasites and Vectors 2015; 8: Article number 593.
- Keiser J and Utzinger J. Efficacy of current drugs against soil transmitted helminth infections. Journal of the American Medical Association 2008; 299: 1937–1948.
- Leta GT, French, Dorny P, Vercruysse J and Levecke B. Comparison of individual and pooled diagnostic examination strategies during the national mapping of soil-transmitted helminths and *Schistosoma mansoni* in Ethiopia. PLOS Neglected Tropical Diseases 2018; 12: Article number: e0006723.
- Levecke B, Montresor A, Albonico M, Ame SM, Behnke JM, Bethony JM *et al.* Assessment of anthelmintic efficacy of mebendazole in school children in six countries where soil-transmitted helminths are endemic. Plos Neglected tropical Diseases 2014; 8: Article number e3204.
- Mekonnen Z, Meka S, Ayana M, Bogers J, Vercruysse J & Levecke B. Comparison of individual and pooled stool samples for the assessment of soil-transmitted helminth infection intensity and drug efficacy. PLOS Neglected Tropical Diseases, 2013; 7: e2189.
- Mofid LS, Casapia M, Aguillar E, Silva H, Montresor A, Rahme E, et al A Double-blind Randomized Controlled Trial of Maternal Postpartum Deworming to Improve Infant Weight Gain in the Peruvian Amazon. PLOS Neglected Tropical Diseases, 2017; 11: Article number e0005098.
- Montresor A. Cure rate is not a valid indicator for assessing drug efficacy and impact of preventive chemotherapy interventions against schistosomiasis and soil-transmitted helminthiasis. Transactions of the Royal Society of Tropical Medicine and Hygiene 2011; 105: 361– 363.
- Vercruysse J., Albonico M., Behnke J., Kotze C.K., Prichard R., et al. Is anthelmintic resistance a concern for the control of human soil-transmitted helminths? International Journal for Parasitology: Drugs and Drug Resistance, 2011; 1: 14-27.
- Vercruysse J., Behnke J.M., Albonico M., Shaali Makame A., Angebault C., Bethony J.F., et al Assessment of the anthelmintic efficacy of Albendazole in school children in seven countries where Soil-Transmitted Helminths are Endemic. PLOS Neglected Tropical Diseases 2011; 5: Article number e948.
- Vlaminck J, Cools P, Albonico M, Ame S, Ayana M, et al. Comprehensive evaluation of both stool-based diagnostic methods to assess drug efficacy and benzimidazole resistance markers to assess the emergence of anthelmintic resistance: a Starworms study protocol» PLOS Neglected Tropical Diseases, 2018; 12: Article number e0006912
- Vlaminck J, Nejsum P, Vangroenweghe F, Thamsborg S, Vercruysse J, Geldhof P. Evaluation of a serodiagnostic test using *Ascaris suum* haemoglobin for the detection of roundworm infestation in pigs. Veterinary Parasitology 2012; 189: 267 -273.