Original Article

Retrospective evaluation of the patterns of clinical use of anti-parasitic agents on animals presented for veterinary care at an animal hospital in Nigeria

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Abstract

Patterns of use of anti-parasitic agents (APAs) on animals presented for veterinary care at the Veterinary Teaching Hospital, Nsukka, Nigeria, from January 2013 to December 2017 were surveyed. Animals presented were predominantly dogs (84.0%) and goats (8.1%). A total of 4851 cases were evaluated, out of which 3196 (65.9%) were treated with APAs. There was a significant variation (p=0.002) in the annual frequency of use of APAs across the study period, but the effect size of the variation was small (ϕ_c=0.06). Ivermectin was the most frequently used APA (1479 out of the 3196 = 46.3%); followed by praziquantel-pyrantel-fenbendazole combined formulation (PPFCF) (1231 out of the 3196 = 38.5%), pyrantel pamoate (848 out of the 3196 = 26.5%) and benzimidazoles (477 out of the 3196 = 14.9%). The frequencies of use of others were below 10%. There were significant variations (p<0.01) in the frequency of use of all the APAs across the study period, but the effect size of the variations ranged from small for amitraz (ϕ_c=0.08; p=0.001), amprolium-sulphaquinoxaline combination (ASC) [ϕ_c=0.07; p=0.006] and fipronil (ϕ_c=0.09; p=0.000), to moderate for benzimidazoles (ϕ_c=0.12; p=0.000), diminazene aceturate (ϕ_c=0.11; p=0.000), ivermectin (ϕ_c=0.11; p=0.000) and pyrantel pamoate (ϕ_c=0.10; p=0.000), and large for cypermethrin (ϕ_c=0.15; p=0.000), levamisole (ϕ_c=0.15; p=0.000), metronidazole (ϕ_c=0.24; p=0.000), PPCFC (ϕ_c=0.18; p=0.000) and pyrethrin powder (ϕ_c=0.27; p=0.000). Out of the 3196 cases in which APAs were used, there were inappropriate use in 8.9% of cases, non-compliance in 44.0%, use of APAs without definitive diagnosis in 46.8%, and wrong combinations in 8.8%. The frequencies of misuse of the APAs varied significantly (p=0.000) across the study period, and the effect size was moderate for inappropriate use (ϕ_c=0.13; p=0.000), non-compliance (ϕ_c=0.14; p=0.000) and wrong combinations (ϕ_c=0.10; p=0.000), but large for the use of APAs without definitive diagnosis (ϕ_c=0.23; p=0.000). It was concluded that the overall frequency of use of APAs in the study population was high during the study period, with significant variations in the frequency and effect size of the specific APAs, and their misuse.

Keywords: Anti-parasitic agents, Use on Animals, Veterinary Hospital, Nigeria, Retrospective Survey

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Introduction

Parasite infections/infestations and parasitic diseases are globally recognised as important causes of morbidity and mortality in both animals and humans (Liu and Weller, 1996; Fairlamb *et al*., 2003; Hotez *et al*., 2008; Kappagoda *et al*., 2011; Rist *et al*., 2015). Parasites may induce pathophysiological alterations and cause damage in infected/infested hosts, which may range from mild discomfort, poor growth and loss in productivity to death (Hotez *et al*., 2008; FDA, 2012; Rist *et al*., 2015; Smith *et al*., 2015). Treatment and control of parasite infections/infestations and parasitic diseases rely heavily on the use of anti-parasitic agents administered to the host or applied against the parasite on the host (WHO, 1987, 2013; Watkins, 2003; Kappagoda *et al*., 2011; Bahk *et al*., 2018).

Rational use of anti-parasitic agents (APAs) in animals will entail their use in a way appropriate to the clinical needs of the patient, given/applied at specified doses for an adequate time duration/interval and at the lowest cost (WHO, 2012; Beyene and Tesega, 2014; Teshome, 2018). The misuse/irrational use of drugs in general (including APAs) has been associated with increased occurrence of adverse drug reactions/toxicities, development and maintenance of drug resistance and unnecessary higher costs to the clients (Cupic *et al*., 2011; Brahma *et al*., 2012; Teshome, 2018; Zekaria and Toka, 2019). Adverse drug reactions following misuse/irrational drug use may be dose-related (due to overdose), allergic, idiosyncratic and/or due to drug interactions (Boothe, 2014; Coleman and Pontefract, 2016; Mouiche *et al*., 2019). Drug resistance is a global public health problem (WHO, 2014; Michael *et al*., 2014). Specifically, resistance to APAs used on animals, which is a big threat to animal health and production worldwide, is reported to be on the increase (Fairlamb *et al*.. 2003; Edmonds *et al*., 2010; FDA, 2012; Gasbarre, 2014; Smith *et al*., 2015, FMAEH, 2017; Pena-Espinoza, 2018). The additional cost of irrationally prescribed animal medicines to the clients constitutes part of the economic dimension of the demerits of misuse of medicines (Brahma *et al*., 2012; WHO, 2012; Mao *et al*., 2015; Islam, 2017).

Information in available literature on the use and misuse of antimicrobial agents in animals in general is very limited (OIE, 2016). Though there are some information on the use and misuse of antibiotics on animals in Nigeria (FMAEH, 2017; Ihedioha *et al*., 2020), there are no data/information in available literature on the patterns of use and misuse of APAs in animals. Knowledge of this is basically necessary as a basis for advocacy on rational use and recommendation of correctional measures for the appropriate use of APAs on animals. The present study evaluated the patterns of use and misuse of APAs on animals presented for veterinary care at the Veterinary Teaching Hospital Nsukka, Nigeria.

Materials and Methods

The design of the study was a quantitative longitudinal retrospective survey. Hospital records of all animals presented for veterinary care at the Veterinary Teaching Hospital Nsukka from 1st January 2013 to 31st December 2017 were used for the study. The Veterinary Teaching Hospital Nsukka renders veterinary clinical services to animals and animal owners in Enugu, Anambra, Kogi and Benue States of Nigeria, and also serves as a training facility (teaching hospital) for undergraduate/postgraduate veterinary students of the University of Nigeria.

The investigators applied for and received approval to use the hospital records for the study, and clients to the veterinary hospital consent to 'the medical records of their animals being used for research/studies that will benefit animal and human health'. Number coding was used to protect the confidentiality of patients and clients' personal data during the study.

A total of 4851 cases, involving ten different animal species (Table 1), were surveyed during the study. Information collected from each case file included: data on species, age and sex of each animal, primary compliant, case diagnosis (definitive or tentative), whether or not confirmatory laboratory diagnosis was done, whether or not anti-parasitic agents were prescribed and administered, and compliance to the treatment regimen. Instances of inappropriate use and use of wrong combinations were also documented, in addition to non-compliance and use of anti-parasitic agents without definitive diagnosis.

Table 1 The study population and animal species distribution of cases presented at the animal hospital, January 2013 – December 2017.

Animal Species	*Number of each of the animal species presented for veterinary care for the years studied.*						*Percentages*
	2013	*2014*	*2015*	*2016*	*2017*	*Totals*	
Cats	3	7	12	17	15	54	**1.1%**
Cattle herds	1	3	2	3	2	11	**0.2%**
Dogs	604	646	877	935	1012	4074	**84.0%**
Goats	36	114	105	81	59	395	**8.1%**
Horses	2	2	3	3	2	12	**0.3%**
Pigs	8	6	9	14	19	56	**1.2%**
Poultry	15	12	14	9	17	67	**1.4%**
Rabbits	12	10	7	9	14	52	**1.1%**
Sheep	28	39	12	18	21	118	**2.4%**
Zoo Primates	2	1	3	2	4	12	**0.3%**
Total no. of cases	711	840	1044	1091	1165	**4851**	

Data obtained were collated for each year of the study period (2013 – 2017) and for each of the anti-parasitic agents recorded to have been used during the study period, and subjected to descriptive statistics. Annual total frequencies and specific frequencies for each anti-parasitic agent and each form of misuse were compared using Chi square and Fisher's exact test. Effect size (Cramer's V) were also computed and interpreted for the frequencies (Fritz *et al*, 2012; Akoglu, 2018). Summary of the results were presented as tables and bar charts. The statistical analysis was done using Version 16.0 of the statistical package for social sciences (SPSS) software.

Results

The study population was predominantly dogs (84.0%), followed by goats (8.1%) and sheep (2.4%) (Table 1). Cats, pigs, poultry and rabbits each constituted between 1 and 2%, while the frequency of presentation of other animals (cattle, horses and zoo primates) were each less than 1% (Table 1).

A total of 3196 cases out of the 4851 animals presented for veterinary care (65.9%) at the hospital during the five year study period (2013 – 2017) were treated with APAs (Table 2). The percentage of animals presented for veterinary care at the hospital which were treated with APAs across the five-year study period ranged from 62.2% to 68.8% (Figure 1).There were significant variations (p = 0.002) in the annual frequency of use of the APAs across the five year study period (Table 2), but the effect size of the variations was small (ϕ_c = 0.06).

The anti-parasitic agent with the highest overall frequency of use was ivermectin (1479 out of 3196 cases in which APAs were used = 46.3%), followed by praziquantel-pyrantel-fenbendazole combined formulation (PPFCF) [1231 out of the 3196 cases in which APAs were used = 38.5%], then pyrantel pamoate (848 out of the 3196 cases in which APAs were used = 26.5%) and benzimidazoles (477 out of the 3196 cases in which APAs were used = 14.9%) (Figure 2, Table 3). The frequencies of use of all others (diminazene aceturate, cypermethrin pour-on, metronidazole, pyrethrin powder, fipronil spray, levamisole, amitraz and amprolium-sulphaquinoxaline combination (ASC) were below 10%, with ASC being the least used (5 out of the 3196 cases in which APAs were used = 0.16%) (Figure 2, Table 3).

Table 2 The frequency of use of anti-parasitic agents on animals presented for veterinary care at the animal hospital from 2013 – 2017.

Specific period of study (year)	*Number of cases in which anti-parasitic agents were used in the year*	*Total number of cases presented in the hospital in the year*	*Percentage frequency of use of anti-parasitic agents in the year*
2013	446	712	62.6 %
2014	574	834	68.8 %
2015	642	1033	62.2 %
2016	749	1094	68.5 %
2017	785	1178	66.6 %
Total for the five-year study period (2013 – 2017).	**3196**	**4851**	**65.9** %

There were significant (p = 0.002) variations in the frequency of use of anti-parasitic agents across the study period (2013 – 2017), but the effect size of the variations was small (ϕ_c = 0.06).

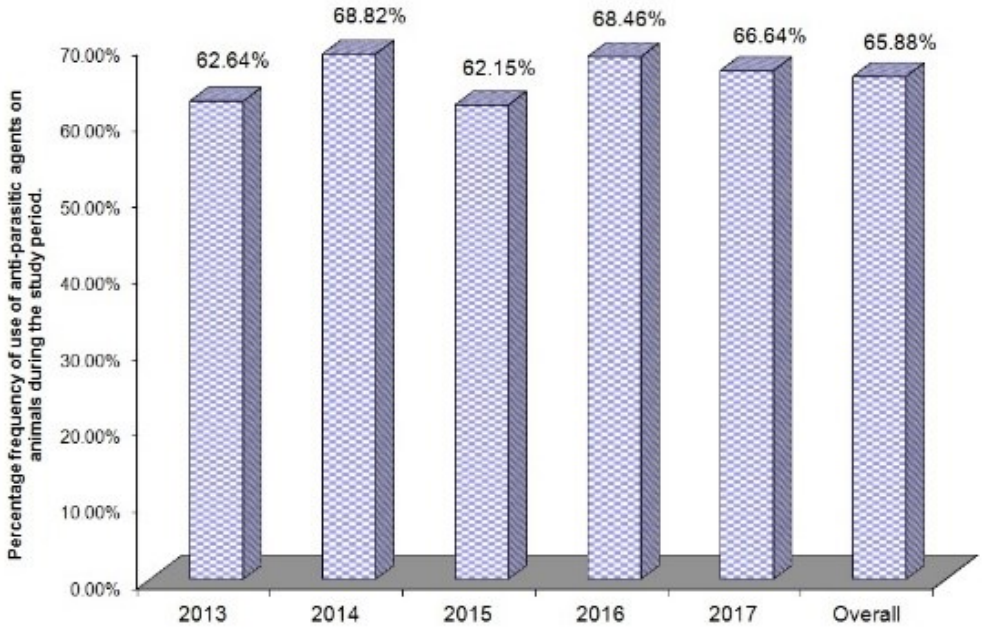

Figure 1 The annual and overall percentage frequency of use of anti-parasitic agents on animals presented for veterinary care in the animal hospital from 2013 to 2017.

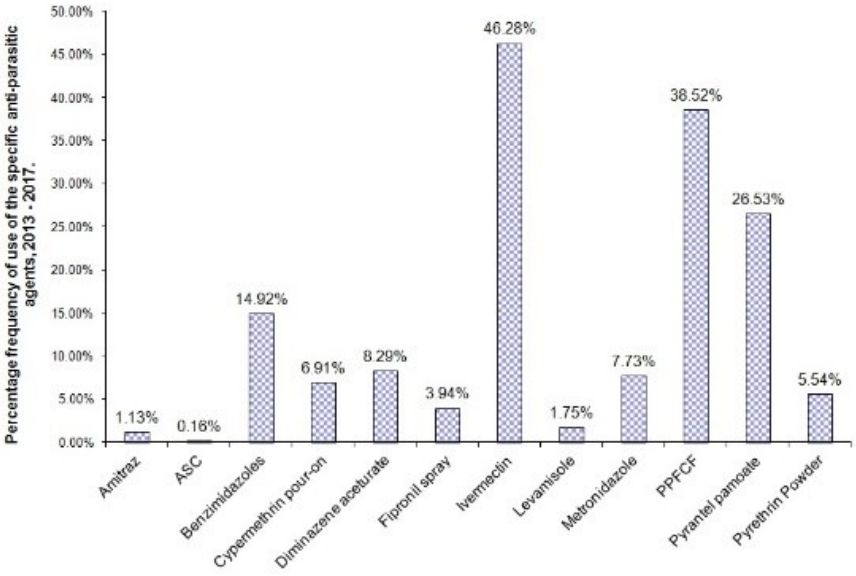

Figure 2 The percentage frequency of use of specific anti-parasitic agents on animals presented for veterinary care at the animal hospital from 2013 – 2017. [ASC – amprolium-sulphaquinoxaline combination; PPFCF – praziquantel-pyrantel-fenbendazole combined formulation].

Table 3 The frequency of use of specific anti-parasitic agents (APAs) on animals presented for veterinary care at the animal hospital from 2013 to 2017.

Specific Anti-parasitic agents	*Number of cases in which specific APAs were used across the years, with percentages in brackets.*							
	2013	***2014***	***2015***	***2016***	***2017***	***Totals***	***p***	ϕ_c
Amitraz	0 (0%)	14 (2.4%)	9 (1.4%)	2 (0.3%)	11 (1.4%)	36	0.001	0.08
ASC	0 (0%)	4 (0.7%)	1 (0.2%)	0 (0%)	0 (0%)	5	0.006	0.07
Benzimidazoles	46 (10.3%)	105 (18.3%)	74 (11.5%)	91 (12.2%)	161 (20.5%)	477	0.000	0.12
Cypermethrin Pour-on	24 (5.4%)	31 (5.4%)	92 (14.3%)	45 (6.0%)	29 (3.7%)	221	0.000	0.15
Diminazene aceturate	53 (11.9%)	32 (5.6%)	84 (13.1%)	46 (6.1%)	50 (6.4%)	265	0.000	0.11
Fipronil spray	19 (4.3%)	20 (3.5%)	46 (7.2%)	25 (3.3%)	16 (2.0%)	126	0.000	0.09
Ivermectin	168 (37.7%)	294 (51.2%)	338 (52.7%)	332 (44.3%)	347 (44.2%)	1479	0.000	0.11
Levamisole	29 (6.6%)	10 (1.7%)	2 (0.3%)	3 (0.4%)	12 (1.5%)	56	0.000	0.15
Metronidazole	14 (3.1%)	16 (2.8%)	15 (2.3%)	57 (7.6%)	145 (18.5%)	247	0.000	0.24
PPFCF	141 (31.6%)	152 (26.5%)	228 (35.5%)	391 (52.2%)	319 (40.6%)	1231	0.000	0.18
Pyrantel pamoate	89 (20.0%)	132 (23.0%)	160 (24.9%)	204 (27.2%)	263 (33.5%)	848	0.000	0.10
Pyrethrin Powder	15 (3.4%)	108 (18.8%)	16 (2.5%)	24 (3.2%)	14 (1.8%)	177	0.000	0.27
Number of cases in which APAs were used in the year	446	574	642	749	785	3196		

ASC – amprolium-sulphaquinoxaline combination ; PPFCF – praziquantel-pyrantel-fenbendazole combined formulation; p – probability value; ϕ_c – Cramer's V.

The frequency of use of the individual APAs significantly ($p < 0.01$) varied across the five year study period, but the effect size of the variations ranged from small to moderate and large (Table 3). The effect size of the variations was small for amitraz ($\phi_c = 0.08$; p = 0.001), ASC ($\phi_c = 0.07$; p = 0.006), and fipronil ($\phi_c = 0.09$; p = 0.000), but it was moderate for benzimidazoles ($\phi_c = 0.12$; p = 0.000), diminazene aceturate ($\phi_c = 0.11$; p = 0.000), ivermectin ($\phi_c = 0.11$; p = 0.000) and pyrantel pamoate ($\phi_c = 0.10$; p = 0.000) [Table 3]. The effect size of the variations in frequency of use was however large for cypermethrin pour-on ($\phi_c = 0.15$; p = 0.000), levamisole ($\phi_c = 0.15$; p = 0.000), metronidazole ($\phi_c = 0.24$; p = 0.000), PPFCF ($\phi_c = 0.18$; p = 0.000) and pyrethrin powder ($\phi_c = 0.27$; p = 0.000) [Table 3].

The forms of misuse/irrational use of APAs recorded during the study period were: inappropriate use, wrong combinations, non-compliance and use of anti-parasitic agents without definitive diagnosis (Table 4). The APAs were considered to have been inappropriately used when they are administered to animals that were neither presented with a complaint of nor diagnosed of any form of parasitic disease/infection/infestation (Table 4). Wrong combination was recorded in cases where varied APAs that are recommended individually for a particular parasitic disease/infestation are combined, e.g. a

combination of ivermectin with cypermethrin pour-on on the same animal for the treatment of tick infestation, or a combination of pyrantel pamoate, albendazole and PPFCF in the treatment of worm infection (Table 4). Non-compliance was recorded when clients did not re-present an animal for a repeat dose of APA that is usually repeated at a definite time after the first treatment (Table 4). Administration of APAs without definitive diagnosis was recorded in cases where laboratory confirmatory diagnosis was not done before APAs were administered, e. g. not examining blood for trypanosomes before administering diminazene aceturate or not doing faecal examination for worm eggs before administering a dewormer (Table 4).

The use of anti-parasitic agents without definitive diagnosis was the form of misuse recorded to have occurred with the highest frequency (1497 times out of the 3196 cases in which APAs were used = 46.8%), followed closely by non-compliance (1405 times out of the 3196 cases in which APAs were used = 43.9%) [Figure 3, Table 5]. Inappropriate use and wrong combinations had the recorded frequencies of 8.9% (284 out of the 3196 cases in which APAs were used) and 8.8% (280 out of the 3196 cases in which APAs were used), respectively (Figure 3, Table 5). Evaluation of the patterns of misuse across the five-year study period showed that there were significant ($p = 0.000$) variations in the frequencies of all the four categories of misuse, but the effect size of the variations ranged from moderate to large (Table 5). The effect size was moderate for inappropriate use ($\phi_c = 0.13$; $p = 0.000$), non-compliance ($\phi_c = 0.14$; $p = 0.000$) and use of wrong combinations ($\phi_c = 0.10$; $p = 0.000$), but it was large for the use of APAs without definitive diagnosis ($\phi_c = 0.23$; $p = 0.000$) [Table 5). The frequency of inappropriate use of APAs increased consistently across the study period, while the frequency of the use of APAs without definitive diagnosis consistently decreased (Table 5). The variations in the frequencies of non-complaince and use of wrong combinations did not follow a definite time related pattern (Table 5).

Table 4 Categories and instances of misuse/irrational use of anti-parasitic agents on animals presented for veterinary care at the animal hospital.

A. Inappropriate use:
i. Administration of ivermectin or other anti-parasitic agents to dogs that came for routine vaccination.
ii. Giving Prazquantel-Pyrantel-Febendazole combined formulation (PPFCF) and/or albendazole to animals with a confirmed diagnosis of trypanosomosis only.
B. Wrong Combinations (Combination misuse):
i. Co-administration of PPFCF, albendazole, ivermectin and cypermethrin pour-on on the same animal diagnosed of having ticks and helminthosis.
ii. Co-administration of pyrantel pamoate, albendazole and PPFCF (all combined) on an animal diagnosed of helminthosis.
iii. Co-administration of ivermectin, amitraz and cypermethrin pour-on an animal with tick infestation.
C. Non-Compliance:
i. Not returning for a repeat dose of diminazene aceturate (normally two weeks after the administration of the first dose).
ii. Not returning for a repeat dose of ivermectin (normally two weeks after the administration of the first dose).
iii. Not returning for a repeat dose of a de-wormer after the administration of the first dose.
D. Use of anti-parasitic agents without definitive diagnosis.
i. Use of de-wormers without faecal examination to confirm presence of worm eggs.
ii. Use of trypanocide (diminazene aceturate) without microscopic examination of the blood to confirm the presence of trypanosomes.

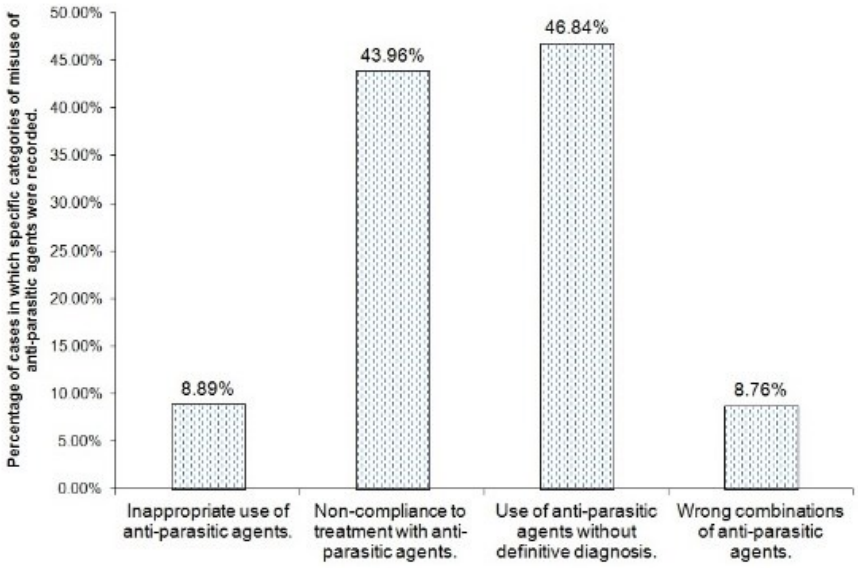

Figure 3 The percentage frequency of the various categories of misuse of anti-parasitic agents on animals presented for veterinary care at the animal hospital.

Table 5 The frequency of misuse/irrational use of anti-parasitic agents (APAs) on animals presented for veterinary care at the animal hospital from 2013 to 2017.

Categories of misuse of APAs	*No. of cases in which specified category of misuse of APAs was recorded across the years, with percentages in brackets.*							
	2013	***2014***	***2015***	***2016***	***2017***	***Totals***	***p***	ϕ_c
Inappropriate use	11 (2.5%)	28 (4.8%)	69 (10.8%)	84 (11.2%)	92 (11.7%)	284	0.000	0.13
Non- Compliance	172 (38.6%)	304 (53.6%)	221 (34.4%)	315 (42.1%)	393 (50.1%)	1405	0.000	0.14
Use of APAs without definitive diagnosis	283 (63.5%)	359 (62.5%)	270 (42.1%)	311 (41.5%)	274 (34.9%)	1497	0.000	0.23
Wrong combinations	16 (3.6%)	34 (5.9%)	57 (8.9%)	91 (12.2%)	82 (10.5%)	280	0.000	0.10
Number of cases in which APAs were used in the year	446	574	642	749	785	3196		

p – probability value; ϕ_c – Cramer's V.

Discussion

The predominance of cases involving dogs (84.0%) in the study population is characteristic of animal population distribution in urban/suburban areas in which pets and security/guard dogs (instead of farm animals) are the most commonly kept animals (Satterthwaite *et al*., 2010; Otolorin *et al*., 2014). Livestock keeping and farming is comparatively minimal in the study area, with small ruminants (goats and sheep) being the most predominant livestock in the area. The lower frequency of presentation of livestock at the veterinary hospital may also partly be due to the fact that most small-holder livestock farmers do not routinely utilize orthodox veterinary services (Lawal-Adebowale, 2012).

The overall high frequency of use of APAs recorded in this study (65.9%) is in agreement with reports in available literature that parasitic diseases are the most frequently occurring diseases in veterinary hospitals in Nigeria (Ebbo *et al*., 2003; Garba *et al*., 2011; Shima *et al*., 2015) and some other tropical countries (Sarker *et al*., 2015; Islam *et al*., 2019). This overall 65.9% frequency of use of APAs recorded in this study is comparable to the 64.7% frequency reported by Beyene *et al*. (2016) in their two-year survey at Adama District Veterinary Clinic, Central Ethiopia; the 65.9% is however higher than the 38.3% reported by Beyene *et al*. (2015) and 35.2% reported by Mojo *et al*. (2019) for the frequency of use of anthelmintics in other veterinary clinics in Ethiopia. The lower frequencies reported by these two studies (Beyene *et al*., 2015 and Mojo *et al*., 2019) are believed to be due to the fact that these studies were focused on the frequency of use of anthelmintics only; anti-protozoal and anti-ectoparasitic agents were not included in their studies.

The small effect size of the variations in the annual frequency of use of APAs across the study period suggests that the annual variations in the frequency of occurrence of parasitic diseases in animals presented at the veterinary hospital may not be of practical significance, since APAs are specific in their clinical application - they, in contrast to antibiotics, are not used to manage other diseases. APAs are used only specifically for the treatment of parasitic diseases/infestations, but in contrast, in addition to the use of antibiotics to treat bacterial diseases/infections, they (antibiotics) are also used to manage viral diseases (prevention/control of possible secondary bacterial infections) and in surgery to prevent infection of surgical wounds (Condon and Wittmann, 1991; Beading and Slifka, 2004, Hendaus *et al*., 2015; Yang *et al*., 2018). The finding of small effect size in the variations of the overall frequency of use of anti-parasitic agents across the five year study period contrasts with the reports of Ihedioha *et al*. (2020) of significant increase in the use of antibiotics in the same hospital (VTH Nsukka) during the same study period.

Ivermectin, followed closely by PPFCF, are the APAs that recorded the highest frequency of use (46.3% and 38.5%, respectively) in the present study. The relatively high frequency of use of these two is thought to be due to their well known broad spectrum anti-parasitic activity – ivermectin is a trusted endo-ectocide (Bennett *et al*., 1988; Chhaiya *et al*., 2012; Campbell, 2016), while PPFCF effectively covers the spectrum of anthelmintic activity required to tackle almost all helminth infections of animals (Taweethavonsawat *et al*., 2010; Lloyd *et al*., 2014). It is believed that this trust on ivermectin may have accounted for its consistently high frequency of use all through the study period. The finding in the present study that ivermectin is the most commonly used anti-parasitic agent concurs with the reports of a two-year (2012 – 2013) survey by Beyene *et al*. (2016) at Adama District Veterinary Clinic in Ethiopia and that of Mojo *et al*. (2019) in their 6-year survey (2012 – 2017) at Modjo Veterinary clinic in Ethiopia, both of which showed that ivermectin was the most commonly used anthelmintic. However, in contrast, reports from a five-year (2009 – 2013) survey by Beyene *et al*. (2015) and that of a two-year study (2014 – 2016) by Kassahun *et al*. (2016), both from animal hospitals in Ethiopia, showed that benzimidazoles were the most frequently used anthelmintics followed by ivermectin.

In the present study, the recorded consistent increase in the frequency of use of PPFCF from 2013 to 2016 may have compensated for the significant decline in use of levamisole during this period, as the effect size of the variations in the combined frequency of use of all APAs was small. This recorded decline in the frequency of use of levamisole may not be unassociated with the adverse reactions that commonly occur in many animal species when it is used (Hsu, 1980; Siroka and Suobodova, 2013; Junquera, 2017). The relatively low frequency of use of amitraz, cypermethrin pour-on, fipronil spray and pyrethrin powder is believed to be due to the availability of ivermectin which is a more effective and convenient alternative treatment for ectoparasites.

However, the low frequency of use of ASC and diminazene aceturate is thought to reflect the low frequency of occurrence of coccidiosis and trypanosomosis in the study population. Earlier studies on the frequency of occurrence of coccidiosis and trypanosomosis in veterinary hospitals in Nigeria reported low frequencies that concur with this (Ebbo *et al*., 2003; Garba *et al*., 2011; Shima *et al*., 2015).

Among the categories of misuse of anti-parasitic agents, the frequency of use of anti-parasitic agents without definitive diagnosis (46.8%) and the frequency of non-compliance (44.0%) were higher than the frequency of inappropriate use (8.9%) and wrong combinations (8.8%). Though high, the frequency of use of anti-parasitic agents without definitive diagnosis (46.8%) recorded in the present study is about half of the frequency of use of antibiotics without definitive diagnosis (88.1%) reported by Ihedioha *et al*. (2020) in the same veterinary hospital during the same study period. The comparatively lower frequency of use of anti-parasitic agents without definitive diagnosis when compared to antibiotics usage without definitive diagnosis may be attributed to the relative ease with which most parasitic diseases could be definitively diagnosed when compared to bacterial diseases – parasite identification and definitive diagnosis of most parasitic diseases can be done on the instant and results delivered within 15 minutes, while bacterial culture and identification takes comparatively longer time, several days in most cases; animal health personnel and animal owners may not wait patiently for these number of days before instituting treatments. In contrast to the 46.8% overall frequency of use of anti-parasitic agents without definitive diagnosis recorded in this study, reports of surveys from animal hospitals in Ethiopia (Beyene *et al*., 2015, 2016; Kassahun *et al*., 2016; Mojo *et al*., 2019) reported far higher frequencies (92.1% – 98.2%) of use of anti-parasitic agents without definitive diagnosis.

The high frequency of non-compliance to use of anti-parasitic agents recorded in this study may be blamed on lack of knowledge on the part of animal owners and inefficiency of animal health workers who should enlighten and prevail on animal owners to complete scheduled treatment regimens for their animals. Enlightenment and sensitization of animal health workers and animal owners on the negative consequences of non-compliance (Zekarias and Toka, 2019) are needed to tackle this problem. The 8.9% frequency of inappropriate use of anti-parasitic agents recorded in the present study is relatively lower than the 21.6% – 44.3% reported for animal hospitals in Ethiopia (Beyene *et al*., 2015; Kassahun *et al*., 2016; Mojo et *et al*., 2019). The 8.8% frequency of wrong combinations of anti-parasitic agents recorded in this study, though low, is a cause for concern because of the possible attendant adverse reactions and toxicities usually associated with such combinations (Gautam and Aditya, 2006; Dunn *et al*., 2011; Brahma *et al*.,, 2012; Siroka and Suobodova, 2013), and a conscious enlightenment of clinicians on these is necessary.

The findings in the present study of increases across the study period (2013 – 2017) in the frequency of inappropriate use, non-compliance and the use of wrong combinations are a cause for concern, and need to be addressed by enlightenment and sensitization of animal health workers, trainee clinical students and animal owners on the consequences of such misuse (Gautam and Aditya, 2006; Brahma *et al*., 2012). However, the progressive decline across the study period (2013 – 2017) in the frequency of use of anti-parasitic agents without definitive diagnosis is commendable and should be sustained by enlightenment of clinicians and laboratory staff, maintenance of laboratory equipment, reagents supplies and manpower (laboratory personnel).

Based on the results of this study, it was concluded that there was an overall high frequency of use of APAs on animals in the study population, with significant variations in frequencies and effect sizes of the annual overall use and individual use of the specific APAs. Ivermectin was the most commonly used APA, followed by PPFCF. The frequencies of use of APAs without definitive diagnosis and non-compliance to treatment were high. The frequency of inappropriate use of APAs consistently increased, while the frequency of use of APAs without definitive diagnosis consistently declined. Enlightenment of animal health workers, trainee clinical students and animal owners is advocated to minimize misuse.

Statement of Animal Rights: Animals were not used for the study. Only medical records of animals presented for veterinary care at the hospital were used for the study, and the use of the medical records was approved by the Director of the veterinary hospital.

Conflict of Interest: The authors declare no conflict of interest.

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