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Research Article

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A Comparative Study of the Treatment of Giardiasis with Commercially Marketed Medicine, Metronidazol with Compounding Medicine at a Rural Hospital in Ethiopia

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Abstract

Synopsis: The objective of this study was to evaluate the treatment of giardiasis condition with metronidazole, comparing commercially marketed medicine metronidazole, with in-house metronidazole compounding medication, in a rural hospital situated in the south of Ethiopia.

Material and Methods: A cross-sectional observational study was carried out at Gambo Rural Hospital in Ethiopia. From 1st to 18th July 2014 the treatment used was by administration of commercially marketed metronidazole and, thereafter, from19th July to 6th August 2014 by administration of in-house metronidazole compounding medicine, produced at the Pharmacy of the Gambo Hospital Pharmacy.

Results: The final study sample consisted of 37 patients: 12 patients were treated with commercially produced medicine and 25 with compound medicine. Three out of the 12 patients treated with commercial medicine were unsuccessful (25%), whilst zero out of the 25 patients treated with the compound medicine were unsuccessful, (0%) (p=0.03) (A difference of 25%; Confidence interval of 95%: 0.3% - 57.1%).

Conclusions: Metronidazole compounding medicine was a better alternative against commercial marketed metronidazole for the treatment of giardiasis condition in a country with limited/ low resources.

Keywords

Giardiasis; Compounding medicine; Commercial medicine

Introduction

Intestinal parasites represent a serious health problem in those countries with few or low resources. As a consequence these parasites can cause different conditions and symptoms such as malnutrition, chronic diarrhoea or anaemia: it also leads to a deterioration of the intellectual and physical capacities in young people [1-3]. Amongst the category of intestinal parasites, *Giardia intestinalis* is the most frequently protozoan associated with diarrhoea [4,5] in children and young adults (adolescents) who attend health centres in these countries. The most common choice to treat this condition is metronidazole. Metronidazole treat is fairly cheap, although inexpensive medicines may eventually be unsuccessful due to a poor quality of the medicine used in low resource countries. Existence of counterfeit medicines (false, fake, or falsely-labelled) might be one reason. Those falsified medicines can be either fake labelled products, unstable intermediate products during poor manufacturing processes, untracked transport, inadequate storage – storage conditions, poor quality control during manufacturing and also untracked importation [6-8]. These medicines may show a low overall pharmaceutical quality, which leads to a failure in the therapeutic treatment due to lack of efficacy. Recently, Sueliman [9] have analysed the quality of commercially produced –azole antifungals (metronidazole, albendazole and tinidazole) for treatment of intestinal parasites and noted that, only 43% achieved maximum quality, whilst the other 57% were associated with therapeutic failure. Another problem in those countries with few resources is medicine's availability on the marked and the prescription schemes [8]. Compounding medicines can be considered as another route to produce individual medicines for patients but also as collective medicine produced by a hospital pharmacist or under his/her supervision in low resource countries. The objective of the study was to evaluate the treatment of giardiasis with commercial metronidazole and the compounding medicine in a rural hospital in the south of Ethiopia.

Material and Methods

Location

A cross sectional observational study was carried out at the Gambo Rural General Hospital (HGRG), Ethiopia. The hospital is located within the region of Oromia, at city of Arsi Negele, a city 245 km south-east of capital city of Addis Ababa. The hospital has a laboratory clinic where the analysis of faecal samples of patients with diarrhoea were analysed.

Patients

The diagnosis of Giardiasis was identified by studying presence of parasites on fresh faeces with lugol's technique. Giardiasis sp. presence in faeces was medically identified by the presence of cysts or trophozoites within samples, following the WHO's recommendations [10]. Basic variable information data was collected for all patients, such as epidemiological variables together with information of the source of drinkable water in each case.

Research details

On one hand, patients who attended at first phase from the 1st-18th July 2014 were treated with commercially produced metronidazole (Metazol®, [Cadila, Mumbay, India] 250 mg capsules of metronidazole or Camezol [SB laboratory Monbai, India]: metronidazole in oral suspension: 125 mg/5ml. These medicines were dispensed by PFSA (Pharmaceutical Fund and Supply Agency). On the other hand, patients diagnosed with intestinal giardiasis

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condition from 16th July to 9th August were treated with the metronidazole compounding medicine. The main active substance was "metronidazole Fagrom" (enriched 100%). Pharmaceutical forms used were metronidazole 500 mg capsules, metronidazole 250 mg capsules and metronidazole 125mg/5ml oral suspension. Metronidazole compounding pharmaceutical forms: oral capsules "0" with non-medicinal ingredients microcrystalline cellulose and riboflavin. The compounding formulae prepared by the hospital pharmacist followed Good Manufacturing Practices Guidelines (GMP) for capsules [11], liquid preparations, creams and ointments [12] according to the regulations of the European Commission [13] of the HGRG pharmacy service.

Dose, dosage and administration

Metronidazole is administered orally following the recommendations of the Therapeutic Drug Guide of the Ethiopian Health Ministry [14].

Adults, metronidazole 500 mg every 8 hours, orally for 7 days.

Children with body weigh between 20 kg to 40 kg, metronidazole 250 mg every 8 hours, orally for 7 days.

Children weighed less than 20 kg, metronidazole 125 mg / 5 ml in oral suspension every 8 hours, orally for 7 days.

As part of the study, all patients were requested for a follow-up appointment 3 to 7 days after the finalisation of the treatment. The aim of appointment was to carry out a new faecal study to confirm parasitic elimination. Basic epidemiologic variables and drinking water were collected from all patients. Condition was considered cured if no *Giardia intestinalis* was found in the second in patient's post-study sample after treatment.

Data analysis

The variables were populated in a 2011 Excel datasheet and analysed by SPSS (version 21) database. The comparison between both treatments was analysed using (two nominal variable) Fisher's exact Test statistical method. This was deemed significantly $P<0.05$. This study was approved prior start by the Research Ethical's Committee of HGRG and also by the Ethiopian Catholic Secretariat.

Results

A starting population of 55 patients were included within the period of study, although only 37 returned (final sample) to the hospital for the second appointment to fulfill all study information. Details of the patients who were included in the study can be seen in Figure 1 as well of those excluded. Finally, 12 patients were treated with commercial medicine whilst 25 were treated with compounding medicine. The age of patients was similar in both groups. There were no gender associations or differences regarding the source of drinkable water (Table 1) within both groups. Three out of the 12 patients treated with commercial medicine failure treat (25%), nevertheless no failures within the 25 patients treated with

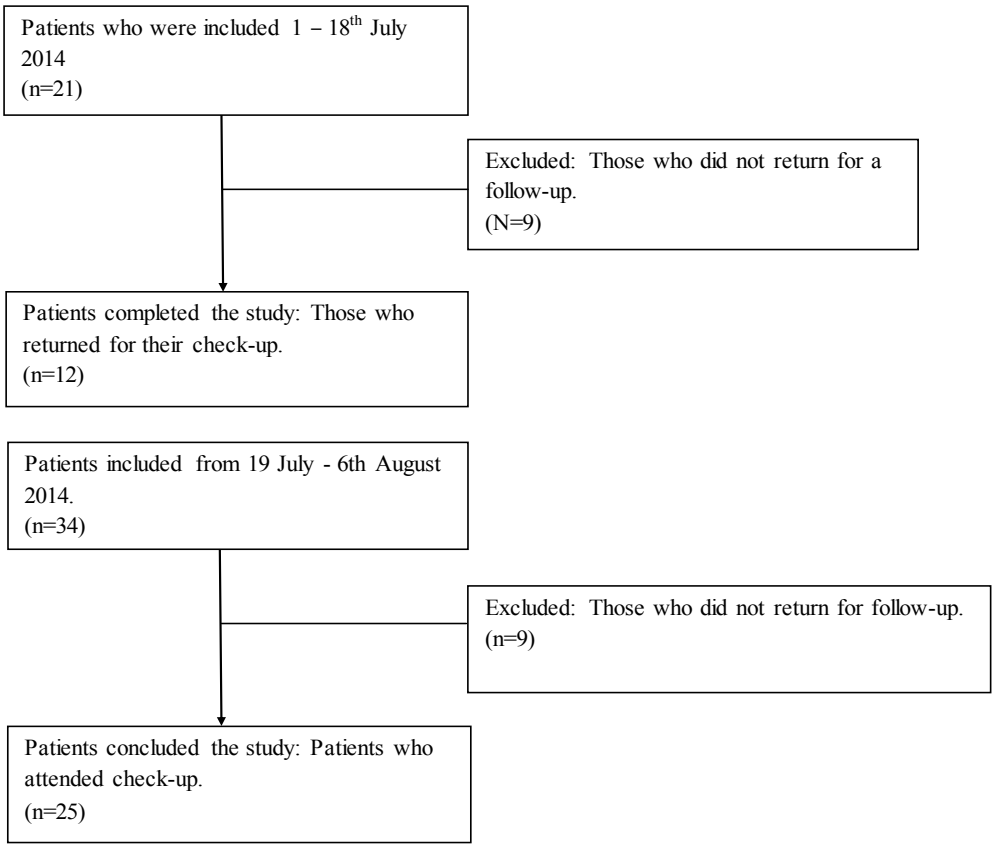

Figure 1: Details of the patients who were included in the study.

Table 1: Demographic details of patients included in the study.

		Patients treated with commercial metronidazole			Patients treated with the compounding medicine		
	Total patients (n= 55)	**Total Patients (n=21)**	**Patients included (n= 12)**	**Patients excluded (n= 9)**	**Total Patients (n=34)**	**Patients included (n=25)**	**Patients excluded (n= 9)**
Age, average, (range)	20 (26)	26 (33.5)	23 (29)	30 (45)	19 (22)	16 (21)	30 (36)
Gender							
Masculine (%)	30 (55.5)	13 (23.6)	7 (12.7)	6 (10.9)	17 (30.1)	13 (23.6)	4 (7.3)
Feminine (%)	25 (44.5)	8 (14.5)	5 (9.1)	3 (5.4)	17 (30.1)	12 (21.8)	5 (9.1)
Water source:							
Well (%)	26 (47.3)	12 (21.8)	9 (16.4)	3 (5.4)	14 (25.5)	11 (20)	3 (5.5)
River (%)	23 (41.8)	9 (16.4)	3 (5.5)	6 (10.9)	14 (25.5)	9 (16.4)	5 (9.1)
Tap (%)	1 (1.8)	0 (0)	0 (0)	0 (0)	1 (1.8)	0 (0)	1 (1.8%
River and Well (%)	5 (9.1)	0 (0)	0 (0)	0 (0)	5 (9.1)	5 (9.1)	0 (0)

DE (Standard deviation)

In brackets is the %

compounding medicine (0%) (p=0.03) occurred (25% difference in results: confidence intervals: 95%: 0.3%-57.1%).

Discussion

This study showed a better response on patients treated with metronidazole compounding medicines rather than metronidazole commercial medicine. However, it should be noted, that this result may be considered with careful limitation due to missing data for the loss of patients in the group treated with metronidazole commercial medication within this study. Another limitation of this study may be connected to the quality and chemical stability of the commercial medicines used [15]. This difference shown in this study may also be related to other factors, such as the possibility of non-appropriate storage conditions at the pharmacy service at the HGRG as neither proper temperature control of room was measured nor humidity was follow-up [16]. Another factor could be a lack of good distribution practices as well as a low quality of the medication connected to poor transportation of the drugs [16]. On the other hand, it seems that the in-house manufacturing compound medicines using commercial intermediate formulation medicines may be a better strategy for the treatment of Giardiasis at hospitals with low resources, where a pharmacist is available and pharmacological protocol complies with European standards. It is though that, the compounding medicine maintains its quality and properties within its manufacturing limits, better than the commercial produced medicine due an early administration after production and elimination of transport factors [6,7]. Medicine manufactured in-house at the hospital, may be more efficient when storage and moisture conditions are not the best. However, there is no sufficient data to confirm this conclusion within this study. For the future it will be worthy to study whether effectiveness is due the lack of best therapeutic efficacy or a loss of efficacy before administration of the medication due to falsified medicines, lack of manufacturing quality and/or storage/ transport conditions. This study has the limitation of the missing data due to loss of patients at the second appointment. This loss was higher in the group treated with commercial medication than compounding medication. The medication used with commercial intermediate formulation substance may be a good strategy for the treatment of Giardiasis condition in hospitals with low resources. A confirmation of these results will need carrying out more similar studies but with greater number of samples for both groups.

Conclusions

This study showed a better response on patients treated with metronidazole compounding medicines rather than metronidazole commercial medicine. Metronidazole compounding medicine was a better alternative against commercial marketed metronidazole for the treatment of giardiasis condition in a country with limited/ low resources.

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