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Journal Name:	International Journal of TROPICAL DISEASE & Health
Manuscript Number:	Ms_IJTDH_27075
Title of the Manuscript:	How do metronidazole drawbacks impact patient compliance and therapeutic outcomes in treating amoebiasis in Rwanda
Type of the Article	Original Research Article

General guideline for Peer Review process:

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty**', provided the manuscript is scientifically robust and technically sound.

To know the complete guideline for Peer Review process, reviewers are requested to visit this link:

(<http://www.sciencedomain.org/page.php?id=sdi-general-editorial-policy#Peer-Review-Guideline>)



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PART 1: Review Comments

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)																																													
Compulsory REVISION comments	AMEBIASIS (<i>Entamoeba histolytica</i>) <table> <tr> <th>Drug</th><th>Adult dosage</th><th>Pediatric</th></tr> <tr> <td>asymptomatic</td><td></td><td></td></tr> <tr> <td>Drug of choice: Iodoquinol¹</td><td>650 mg PO tid x 20d</td><td>30-40 3 do</td></tr> <tr> <td>OR Paromomycin²</td><td>25-35 mg/kg/d PO in 3 doses x 7d</td><td>25-35 7d</td></tr> <tr> <td>OR Diloxanide furoate^{3*}</td><td>500 mg PO tid x 10d</td><td>20 mg</td></tr> <tr> <td>mild to moderate intestinal disease</td><td></td><td></td></tr> <tr> <td>Drug of choice:⁴ Metronidazole</td><td>500-750 mg PO tid x 7-10d</td><td>35-50 7-10d</td></tr> <tr> <td>OR Tinidazole⁵</td><td>2 g once PO daily x 3d</td><td>≥3yrs in 1</td></tr> <tr> <td>either followed by Iodoquinol¹</td><td>650 mg PO tid x 20d</td><td>30-40 3 do</td></tr> <tr> <td>OR Paromomycin²</td><td>25-35 mg/kg/d PO in 3 doses x 7d</td><td>25-35 7d</td></tr> <tr> <td>severe intestinal and extraintestinal disease</td><td></td><td></td></tr> <tr> <td>Drug of choice: Metronidazole</td><td>750 mg PO tid x 7-10d</td><td>35-50 7-10d</td></tr> <tr> <td>OR Tinidazole⁵</td><td>2 g once PO daily x 5d</td><td>≥3yrs in 1</td></tr> <tr> <td>either followed by Iodoquinol¹</td><td>650 mg PO tid x 20d</td><td>30-40 3 do</td></tr> <tr> <td>OR Paromomycin²</td><td>25-35 mg/kg/d PO in 3 doses x 7d</td><td>25-35 7d</td></tr> </table> * Availability problems. See table below. 1. Iodoquinol should be taken after meals.	Drug	Adult dosage	Pediatric	asymptomatic			Drug of choice: Iodoquinol ¹	650 mg PO tid x 20d	30-40 3 do	OR Paromomycin ²	25-35 mg/kg/d PO in 3 doses x 7d	25-35 7d	OR Diloxanide furoate ^{3*}	500 mg PO tid x 10d	20 mg	mild to moderate intestinal disease			Drug of choice: ⁴ Metronidazole	500-750 mg PO tid x 7-10d	35-50 7-10d	OR Tinidazole ⁵	2 g once PO daily x 3d	≥3yrs in 1	either followed by Iodoquinol ¹	650 mg PO tid x 20d	30-40 3 do	OR Paromomycin ²	25-35 mg/kg/d PO in 3 doses x 7d	25-35 7d	severe intestinal and extraintestinal disease			Drug of choice: Metronidazole	750 mg PO tid x 7-10d	35-50 7-10d	OR Tinidazole ⁵	2 g once PO daily x 5d	≥3yrs in 1	either followed by Iodoquinol ¹	650 mg PO tid x 20d	30-40 3 do	OR Paromomycin ²	25-35 mg/kg/d PO in 3 doses x 7d	25-35 7d	The common treatment is 500-750mg PO tidx7-10d We were not interested by asymptomatic patients. That is why symptomatic patients were given metronidazole; but the findings detected lumen agents were not prescribed. The inadequate treatment influences cure rate and not compliance in this case
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	This table indicates the normal treatment in amoebiasis. Certainly, doctors should update about complete treatment in your country. For asymptomatic infections, iodoquinol, paromomycin, or diloxanide furoate are the drugs of choice. For symptomatic intestinal disease, or extraintestinal, infections (e.g., hepatic abscess), the drugs of choice are metronidazole or tinidazole, immediately followed by treatment with iodoquinol, paromomycin, or diloxanide furoate. That is why the high percentage of non-compliance that you obtained due to an inadequate treatment. Another point to clarify is that whenever you report in any Parasitology Laboratory tetra nucleated cyst of <i>Entamoeba</i> you ought report <i>Entamoeba histolytica/Entamoeba dispar</i> because you cannot morphologically discriminate between these two amoebas. Then, as <i>E. dispar</i> infection is consider as asymptomatic in humans how many cases of asymptomatic carriers did you have under metronidazol treatment and how many were symptomatic ones? Have all patients in your study had Bacteriology stool cultures to discard bacterial infections? You would probably have in your study asymptomatic carriers under metronidazol treatment, bt in fact they were infected, for instance by <i>Salmonella</i>, enteropathogenic <i>E. coli</i> strains, <i>Campylobacter</i>, <i>Clostridium difficile</i>, etc. This could be partially explain your results. You should detail the Parasitological records and techniques by all your subjects were diagnosed. They were only infected by <i>Entamoeba histolytica/E. dispar</i> or you recorded co-infections with other helminths or protozoan of medical importance	Only symptomatic cases were considered because that is when patients are sick and consult. Bacterial infections were excluded. We are far from doing identification of strains in this study. The clinical markers limited to symptoms of amoebiasis, particularly, diarrhea, dysentery, colic. Again we should make difference between a SURVEY study assessing patients' point of view and a CONTROLLED CLINICAL TRIAL. This is a survey, so we cannot go far to diagnose all infectious agents; this is theory you are developing, Fix mind in the context of the work. At least only participants who recognized having been diagnosed with entamoeba
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		histolytica were selected. All these pathogens you mention have each its own clinical profile. <i>C. difficile</i> is also sensitive to metronidazole. We repeat that we are far from doing identification of strains in this study. The clinical markers limit to symptoms of amoebiasis, particularly, diarrhea, dysentery, colic. Again you should make difference between a SURVEY study assessing patients' point of view and a CONTROLLED CLINICAL TRIAL. So this is out of scope
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Minor REVISION comments	Keywords: Metronidazole, not metronidazole Introduction • Amebiasis, also called amoebic dysentery (No, amoebic dysentery is one of the clinical forms of amebiasis, which according to WHO is the infection of <i>Entamoeba histolytica</i> regardless the symptoms) • This parasite lives in the intestines and produces eggs (cysts) (From the Parasitological point of view is not correct to say that produce eggs, just cyst and trophozoites) • metronidazole resistance is well documented for various bacteria and protozoan species. Metronidazole resistance in the protozoan parasite <i>Entamoeba histolytica</i> is associated with increased expression of ironcontaining superoxide dismutase and peroxiredoxin and decreased expression..... (This entire paragraph is not part of your results, so I would consider to delete it) • Numbers from Figure 1 should fix with what you cited in the text	Corrected We adapted sentence Revised
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<u>Optional/General</u> comments	There is a good purpose in this article that is to show how a bad practice could drawbacks impact patient compliance and therapeutic outcomes in treating amoebiasis in Rwanda. There is a nice work but still there is a need for more parasitological data on it.	Thanks This is a survey, so we cannot go far to diagnose all infectious agents; this is theory. We fix mind in the context of the work.