Author’s response to reviews

Title: Ofloxacin Plus Rifampicin Versus Doxycycline Plus Rifampicin In The Treatment Of Brucellosis. A Randomized Clinical Trial

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Dear editor

we wrote the changes which were done in our manuscript by us.
1. We removed “cepholosporins and macrolides” from the list of the most commonly used antibiotics in the treatment of brucellosis
2. We changed all incorrectly written terms of doxycycline
3. We corrected the term of quinolones
4. Page 6 line 19 Brucellosis is replaced with brucellosis (page 8 line 7).
5. Public health terms is excluded from the manuscript (first paragraph of discussion part)
6. Reference 13 was corrected
7. Reference 14 is deleted
8. Following sentences have been removed from the discussion section.
   (Page 7 line 18) The first quinolone was produced from nalidixic acid. It is active against brucella infections. There is considerable interest at the possible effectiveness of the new group of fluorinated quinolones in human brucellosis"
9. Parameter word in the table has been replaced with Clinical findings
10. Sentence (Finding in the group) was removed from table (page 11 )
11. P values column has been removed and, only significant values were reported in table 1 (page 11)
12. Arthralgia is corrected
13. Below sentence is added to patients and methods section:
   Patients who met the criteria for entry were randomly assigned to receive in a 1:1 ratio in doxycycline plus rifampicin or ofloxacin plus rifampicin groups.
14. This part is added to patients and methods section.

The primary end point was existence of clinical relapse. Relapse was defined as the reappearance of symptoms and sign of the disease accompanied by increasing titers of the serological tests and / or a positive culture during the follow-up period after treatment was stopped. The secondary end point was accepted as the duration of fever after starting treatment. Fever of patients who were started to treatment was measured by axillary route and recorded every hour until it decreased to 37 degreesC
15. This sentence is added to patients and methods section:
   Sample size was determined according to the patients who were admitted to the study with brucella infection in the study period.
16. We added below paragraph which is located before conclusion in the text

It is important to consider the limitations of this study. In the present study, 14 cases were evaluated in doxycycline plus rifampicin group and 15 in ofloxacin and rifampicin group. In order to detect a minimum difference of 14% between two groups of patients, the beta error would be 0.52. On the
other hand, a true difference between regimens (i.e., alpha = 0.05 and beta = 0.20) would require 26 patients to be allocated to each of the treatment groups. Our study group was small and thus might lack power to distinguish a true difference between the treated group and the control group. We think that further studies, especially larger well-designed ones, are needed to therapy for brucella infection.

17. we removed "recent antibiotic use" words in exclusion criteria. (page 4: line 24)  
18. Treatment method (page 5 line 1 ) part in the patients and methods section has been located to the sample size and randomization part which has been just added. Exclusion section and assessment of efficacy parts were added to the new version.  
19. Reference 1 and 2 were changed with  
20. The order of references in the text has been corrected.  
21. We have removed all p-values relating to such endpoints (compare baseline characteristics or to compare adverse event rates) from Table 1 and from page 6 of the text.  
22. The statistical significance tests are excluded from the manuscript. We reported simply the means and standard deviations of the durations of follow-up.  
23. Below paragraph has been added to the patients and method (Exclusion) section. Four patients were excluded from doxycycline plus rifampicin group. Because they felt well, and didn't complete the therapy. One patient was excluded in the ofloxacin plus rifampicin group because he didn't want to use drugs two weeks after starting to the treatment. As a result five patients were excluded from the study.  
24. That part has been added to patients and methods section as assessment of efficacy part. The primary end point was existence of clinical relapse. Relapse was defined as the reappearance of symptoms and sign of the disease accompanied by increasing titers of the serological tests and / or a positive culture during the follow-up period after treatment was stopped. The secondary end point was accepted as the duration of fever after starting treatment. Fever of patients who were started to treatment was measured and recorded every hour until it decreased to 37 degreesC.