

Comparison between antibiotic therapy of *Brucellosis* with and without vitamin A

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Abstract

Background: Brucellosis is one of the endemic diseases in our country and it can be in the types of acute, sub-acute or chronic. It estimates that about 20% of Brucellosis may change from acute to chronic. Because cell mediated immunity (CMI) is the main defense of body against *Brucella* species, it seems that some degree of Immunologic disorders existed in the patients with chronic form of diseases and some supplements such as Vitamin A (Vit A) as an immunomodulator can stimulate CMI and may decrease the rate of chronicity.

Materials and Methods: In a single-blind randomized clinical trial 120 patients with the clinical and serological diagnosed Brucellosis were randomized. A total of 60 patients received streptomycin and Doxycycline as standard therapy for 6 weeks and others in addition to this Regimen received Vit A for about 4 weeks.

Results: In the case group, only 1 case (1.6%) relapsed and in the control group 8 (13.5%) with significant difference ($P < 0.005$) between two groups. Morbidity of disease was different between two groups.

Conclusion: Vit A therapy in the patients with Brucellosis with may reduce the disease morbidity and rate of chronicity.

Key Words: Brucellosis, immunity, vitamin A

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INTRODUCTION

Brucellosis is one of the endemic diseases in Iran, especially in our city Isfahan. Unpasteurized dairy products are the main causes of transmission to human also it is a zoonotic disease.

It is a disease of animal (Zoonosis) that under certain circumstances can be transmitted to humans.^[1]

Although it occurs world-wide, brucellosis is more common in countries that do not have effective animal health program.^[2,3]

As one of the first bacteria to be weaponized, *Brucella* remains a potential bioterrorism agent^[4,5] and all confirmed cases should have epidemiologic evaluation.^[6]

Musculoskeletal involvement is the main problem, morbidity, and debility frequently was seen in this disease.

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Spink reports 20% chronicity in about 2,000 cases of brucellosis which it elongates greater than 1 year.^[7]

Because cell mediated immunity (CMI) is the main defensive mechanism of body in this disease,^[8] it's seems that immunodeficient and malnourished patient more susceptible to this form of disease.

In Kurmanova *et al.* study, a clinical trials, demonstrated that the use of Vitamin A (Vit A) in a dose of 33,000 IU thrice a day for 10-12 days during the complex treatment of patients with acute (36 persons) and sub-acute (57 persons) brucellosis lowered the average period of manifestation of the disease (clinical signs)^[9] because it formation of antibodies, the lymphocyte blast cell transformation, the total number and subpopulation of the active T-cells. In Dizer *et al.* study levamisole administration as a supplement concomitantly with conventional antibiotic therapy has no immunostimulating effect on the basis of the lymphocyte subgroups ratios and the ability of phagocytosis measured.^[10]

In Chandra study, showed that deficiency of, Fe, Zn, Vit B6, Vit A, Cu, Na and Vit D had long-term effect on CMI.^[11]

In a pilot study by Salehi, it was revealed that Vit A as a supplement therapy can reduce the late complications of bruceelosis such as relapse.^[12]

The main object of this study was comparison between the standard therapy of brucellosis with and without Vit A.

MATERIALS AND METHODS

In a research project with the number of 75,005, which was approved by the Ethics Committee of Isfahan University of medical sciences, a semiexperimental and prospective clinical trial study was done on 120 cases of brucellosis. Inclusion criteria were: Documentation of positive serologic enzyme-linked immuno sorbent assay (ELISA) test and then confirmation by standard tube agglutination test (STA).

Exclusion criteria were patients < 8 years old, disorders of eye, ear and kidney and pregnant women.

By random selection, 60 patients received standard treatment of brucellosis streptomycin 15 mg/kg/d and Doxycylin 100 mg twice daly for about 6 weeks and 25,000 unit Vit A daily for about 4 weeks (case group), and 60 patient received only standard therapy of Brucellosis (control group) all the patients were unaware about the received drugs. Patients in

both groups were clinically followed and examined continuously and by filling the questionnaires based on subjective symptoms such as fever, chills, sweating, anorexia, arthralgia, myalgia, anorexia, and objective signs such as fever and arthritis.

Duration of subjective symptoms and sings, chronicity and relapses in both group compared for about 1 year [Figure 1].

Results were analyzed by using the SPSS software version 20.

RESULTS

In both groups, 40 persons (66%) were men and 20 persons (34%) were women [Table 1].

Almost all cases had consumed unpasteurized dairy products. 84 persons (70%) of all cases were from around of Isfahan (Rehnan, Khomeini shahr, Fereidan, Zarinshahr and shahreza) and 36 cases (30%) from Isfahan.

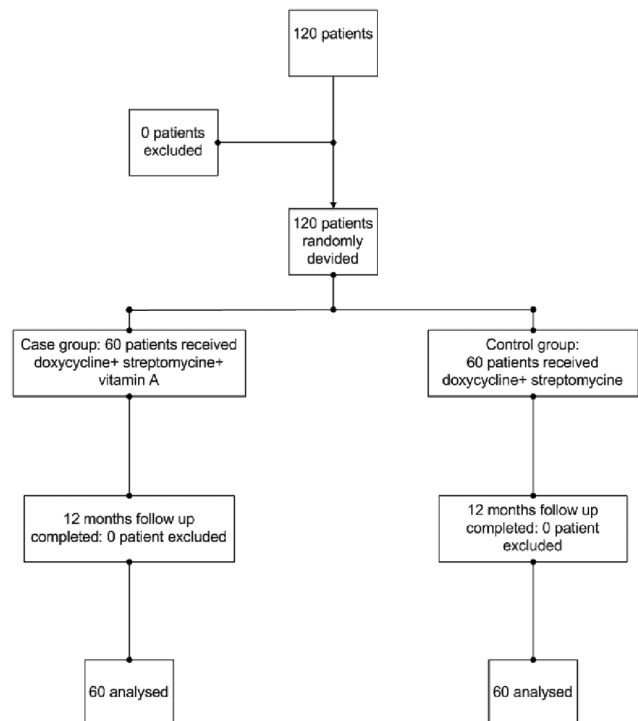


Figure 1: Patients who entered the study, where divided in two study groups, followed up and analysed

Table 1: Brucellosis patient's by sex and location

Group sex	Case G (No %)	Control G (No %)	Location	
			Isfahan	Urban
Men	40 (66)	40 (66)	36 (30%)	84 (70%)
Women	20 (34)	20 (34)		
Total	60 (100)	60 (100)	120	

Almost all cases (about 85%) had musculoskeletal involvement such as sacroileitis (with low back pain), knee and hip arthritis. Furthermore, they had evening and night fever and sweating. Serology by Enzyme limulus assay test and confirmatory STA test were positive in all cases and its ranges were between $\frac{1}{160}$ and $\frac{1}{1560}$.

Comparison of signs and symptoms showed defervescence (4, 6 days), pain and restriction of range of motion in joints (10, 14 days), sweating (5, 6 days), Arthralgia and myalgia (12, 14 days) and Anorexia (2, 2 weeks) were in case and control groups respectively [Table 2].

In the case group, 1 case (1.6%) was changed to the chronic and 1 case (1.6%) relapsed, and in control group, 5 cases (8%) became chronic and 8 cases (13.5%) relapsed. The statistical analysis was carried out by one-way ANOVA, which showed significant differences between two groups ($P < 0.005$) [Table 3].

DISCUSSION

Brucellosis is a Zoonotic disease and in this study, its incidence and prevalence in men is more than women, which is compatible with Corbel and Nicholas study.^[13]

Mosculoskeletal involvement was the most frequent complication up to 80% in Colmenero *et al.* study^[14] and in our study it was seen in 85% of cases and it is compatible with study that study. For treatment of Brucellosis the combination of doxycycline plus gentamycin provides excellent results.^[15,16] In Lulu *et al.* study, two drug combinations of streptomycin and tetra cycline, streptomycin and rifampicin or streptomycin and doxycycline were effective, but one of five patients with the chronic brucellosis

relapsed. A combination of streptomycin, tetracycline, and rifampicin with or without steroids was used successfully in complications of brucellosis.^[17]

In Kurmanova *et al.* clinical trial study demonstrated that the use of Vit A during the complex of patients with acute and sub-acute Brucellosis lowered the average period of manifestation of the disease clinical signs^[9] and also in our study mean duration of clinical signs and symptoms decreased [Table 3].

In my pilot study in 2000 Vit A as a supplementation therapy could influence on outcome of brucellosis and reducing the late complication of brucellosis such as relapse.^[11] This study is also compatible with the pilot study of Salehi.^[12]

Comparison of chronicity between case and the control group was 1.6% and 8% respectively with significant difference meaning ($P = 0.005$) and also relapses was 1.6% and 13.5% in case and control group respectively with significant difference meaning ($P < 0.005$). The limitation of this study was small sample size and further studies with more cases are needed.

CONCLUSION

Treatment of Brucellosis with antibiotics and Vit A as a supplement and immunomedulator can reduce the morbidity and chronicity of disease.

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REFERENCES

1. Pappas G, Akritidis N, Bosilkovski M, Tsianos E. Brucellosis. *N Engl J Med* 2005;352:2325-36.
2. Kozukeev TB, Ajeilat S, Maes E, Favorov M, Centers for Disease Control and Prevention (CDC). Risk factors for brucellosis – Leylek and Kadamjay districts, Batken Oblast, Kyrgyzstan, January-November, 2003. *MMWR Morb Mortal Wkly Rep* 2006;55:31-4.
3. Pappas G, Papadimitriou P, Akritidis N, Christou L, Tsianos EV. The new global map of human brucellosis. *Lancet Infect Dis* 2006;6:91-9.
4. Chang MH, Glynn MK, Groseclose SL. Endemic, notifiable bioterrorism-related diseases, United States, 1992-1999. *Emerg Infect Dis* 2003;9:556-64.
5. Yagupsky P, Baron EJ. Laboratory exposures to *brucellae* and implications for bioterrorism. *Emerg Infect Dis* 2005;11:1180-5.
6. Centers for Disease Control and Prevention (CDC). Suspected brucellosis case prompts investigation of possible bioterrorism-related activity – New Hampshire and Massachusetts, 1999. *MMWR Morb Mortal Wkly Rep* 2000;49:509-12.
7. Spink WW, Farreras P, Pedro-Pons A. What is chronic brucellosis? *Ann Intern Med* 1951;35:258-74.
8. Yingst S, Hoover DL. T cell immunity to brucellosis. *Crit Rev Microbiol* 2003;29:313-31.

Table 2: Brucellosis patient's by recovery of signs and symptoms

Group Signs/symp	Case group mean days	Control group mean days
Fever	4	6
Chills	5	6.5
Sweating	6	7.5
Arthritis	10	15
Arthralgia	12	20
Myalgia	12	20
Anorexia	14	14

Table 3: Brucellosis patient's by chronicity and relapse

Group	Case group (No %)	Control group (No %)
Chronicity	1 (1.6)	5 (8)
Relapse	1 (1.6)	8 (13.5)

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9. Kurmanova KB, Ishchanova RZh, Sakhisheva SSh, Studentsova VK, Tsirel'son LE, Alshinbaeva GU. Increasing the effectiveness of antibiotic therapy by correcting immunologic disorders with vitamin A in patients with brucellosis. *Antibiot Khimioter* 1990;35:35-8.
10. Dizer U, Hayat L, Beker CM, Görenek L, Ozgüven V, Pahsa A. The effect of the doxycycline-rifampicin and levamisole combination on lymphocyte subgroups and functions of phagocytic cells in patients with chronic brucellosis. *Chemotherapy* 2005;51:27-31.
11. Chandra PK. Nutrient and Immunoregulation. *J Nutr.* 1992;122 Suppl 3:754-7.
12. Salehi H. Comparing standard treatment of brucellosis with and without Vitaamin A. *J Isfahan Med Sch (I.U.M.S)* 2003;20:56-8.
13. Michael J.Cobel, Nicholas J.Beeching. Brucellosis. *Harrison's Principle's Internal Medicine.* 18th ed., Vol. 1. Chapter 157. 2012. p. 1299-300.
14. Colmenero JD, Reguera JM, Martos F, Sánchez-De-Mora D, Delgado M, Causse M, *et al.* Complications associated with *Brucella melitensis* infection: A study of 530 cases. *Medicine (Baltimore)* 1996;75:195-211.
15. Solera J, Geijo P, Largo J, Rodríguez-Zapata M, Gijón J, Martínez-Alfaro E, *et al.* A randomized, double-blind study to assess the optimal duration of doxycycline treatment for human brucellosis. *Clin Infect Dis* 2004;39:1776-82.
16. Hasanjani Roushan MR, Mohraz M, Hajiahmadi M, Ramzani A, Valayati AA. Efficacy of gentamicin plus doxycycline versus streptomycin plus doxycycline in the treatment of brucellosis in humans. *Clin Infect Dis* 2006;42:1075-80.
17. Lulu AR, Araj GF, Khateeb MI, Mustafa MY, Yusuf AR, Fenech FF. Human brucellosis in Kuwait: A prospective study of 400 cases. *Q J Med* 1988;66:39-54.

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