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Resistance Exercise Potentiates Antibiotics in the Treatment of Typhoid Fever

Ibrahim Oladayo Mustafa

Department of Human Physiology, College of Medical Sciences, Ahmadu Bello University, Zaria, Nigeria.

*Corresponding author:** Ibrahim Oladayo Mustafa, Department of Human Physiology, College of Medical Sciences, Ahmadu Bello University, Zaria, Nigeria.

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Abstract
Exercise generally has been known to improve immunity thereby offering a better protection against infection. Typhoid fever on the other hand is caused by an infection from bacteria known as Salmonella typhi.

This study investigated the effect of resistance exercise, which includes regular lifting of weights in the gym in amateur bodybuilders that are treating typhoid fever with known antibiotics.

Fifty (50) regular gymnasium goers (also known as gym rats) that train with weights regularly were recruited for the study. Another 50 volunteers who do not weight-train were also recruited to serve as control group. Both groups were on similar class of antibiotics used in the treatment of typhoid fever, with continued exercise – albeit of less intensity – among the gym goer group. About 3mL of blood sample was taken from each of the participants on Day 1, Day 3, Day 5 and Day 7 of antibiotic use. Haematological studies (Packed Cell Volume {PCV}, White Blood Cell Count {WBC}, Lymphocytes and Haemoglobin) were conducted on the blood samples and data in both groups compared with each other. In addition, data on the symptoms felt by each participant was obtained via well-designed questionnaire.

On Day 1 all participants were symptomatic. The group of amateur bodybuilders steadily improved both in symptoms and in haematological indices (PCV, WBC, Lymphocytes and Haemoglobin), with total disappearance of symptoms in 70% of subjects by Day 5. The control group however, reported a slower improvement in symptoms and even a dip in haematological indices on Day 3, with less than 80% reporting total disappearance of symptoms by Day 7.

The results from this study show that regular resistance exercise prior to, or while taking antibiotics potentiates the antibiotics, ensuring and speeding up recovery from typhoid fever.

Introduction

Typhoid fever is caused by the Gram-negative bacteria known as Salmonella typhi [1]. It has become a significant public health issue in less developed countries [2]. In a World Health Organization report, about 11 to 20 million people across the world fall ill due to this disease, with mortality rate of 145,000 individuals each year [3]. In Nigeria, lack of proper sewage management system, inadequate supply of drinkable water and insufficient health facilities are some of the major factors that contribute to the spread of the disease [4].

Patients do not always seek health care treatment at hospitals, nor through the use of laboratory services due to costs. Rather, they rely on self-medication with known or pharmacist-prescribed antibiotics [5]. To begin with, available and affordable tests for typhoid fever such as the Widal test have been reported severally to have limited diagnostic utility and are unreliable [6]. Instead, clinical presentations such as fever, headache, diarrhoea, abdominal cramp and chronic lethargy are mostly used by health professionals (in the absence of malaria) to begin treatment [7].

Leukopenia on the other hand has been described as one of the characteristic findings in Salmonella typhi infection [8] with leucocytosis occurring only in the early asymptomatic stage of infection [9]. Lymphocytopenia was found in about 76% of typhoid fever patients in a study by Abdool Gaffar et al. [10]. Even though not severe, anaemia has been reported in typhoid fever [11] due to the effect of the toxin produced by the bacteria, and reduction in haemoglobin concentration is known to occur [12]. Typhoid fever, in most cases can be treated with oral antibiotics and regular follow-ups especially when treated by the symptomatic stage before complications set in [7]. Appropriate antibiotic treatment (the right drug, dose, and duration) is critical to curing typhoid, and the newer quinolones or third generation cephalosporins are associated with higher cure rates [13,14].

Exercise has been shown to mobilise immune cells with high functional capacity after each session, and the cumulative effect of this process is known to protect the body from pathogens [15]. Skeletal muscles (the major targets of resistance exercise) release signalling proteins known as myokines in response to exercise that reduce inflammation (Interleukin-6), and assist with lymphocyte proliferation (Interleukin-7) [16-19]. Also, it is being suggested that muscle-derived release of Interleukin-15 may assist with trafficking of natural killer cells towards vulnerable areas of the body that encounter pathogens [15].

Improvements in vascular function are a well-established adaptation to regular exercise especially weight training and these improvements in blood flow could assist with immune cell recirculation between the blood, lymphatic system and peripheral tissues in the event of infection [20]. In addition, exercise increases the flow of immune cells through the lymphatic system in five folds (resistance exercise even more), with even a mild exercise-activity stimulating this movement [21,22]. Accruing evidences of exercise improving immunity and helping to fight diseases prompted the necessity for this study to investigate the extent of amelioration that resistance exercise offers in the treatment of typhoid fever with oral antibiotics.

Methods

Geographical Location

The study was carried out in Zaria, a city located in North-western Nigeria, with a population of 700,000 (National Population Commission, 2016). The city coordinates are latitudes 11o 06' and 60o 00' North of the Equator and longitudes 7o 43' and 59o 00' East of the Greenwich Meridian.

Study Design

One hundred (100) volunteers that had typhoid fever and self-medicating on anti-typhoid antibiotics were recruited for the study. Fifty of the volunteers are amateur bodybuilders that visit the gym regularly while the remaining fifty do not involve in bodybuilding exercises at all. The antibiotics used by all participants were either Levofloxacin, a third-generation fluoroquinolone or Cefixime, a third-generation cephalosporin. Usage of the antibiotics lasted for seven (7) days [14]. All participants reported experiencing the classical symptoms of typhoid fever namely; severe fever, headache, diarrhoea, abdominal cramp and chronic lethargy at the beginning of the study. The bodybuilder group continued their resistance exercise – though of lesser intensity – during the course of the study.

Questionnaire

Information on the symptoms participants experienced before commencing the self-treatment (usage of the antibiotics) was obtained via a well-designed questionnaire. Information on the symptoms that persisted or disappeared during the course of treatment was also recorded in the questionnaire.

Ethics approval and consent to participate

The study was approved by the ABU Ethics Committee on Human Research with the Approval No: ABUCUHSR/2018/002. The consent of each participant in this study was sought and gotten, with the Consent Form duly signed by the participants.

Collection of blood sample

A little volume of blood of about 3mL was collected from the each participant at an interval of two days starting from the first day, for duration of seven days (Days 1, 3, 5 and 7). The blood samples were analysed for Packed Cell Volume (PCV), Haemoglobin, White Blood Cell (WBC) and Lymphocyte count using automated TC20™ cell counter by Bio-Rad Laboratories.

Results

The haematological components that are affected during Salmonella typhi infection (typhoid fever), and used as indices in determining extent of infection were measured in both bodybuilders and non-bodybuilders with an interval of two days, as the self-treatment progressed. The values were compared in both groups and across different days as shown in Table 1.

Table 1: Haematological indices taken with the progression of typhoid treatment in bodybuilders and non-bodybuilders. Values are in mean ± standard deviation (SD).

		PCV (%)	WBC ($\times 10^3/\mu L$)	Lymphocytes ($\times 10^3/\mu L$)	Haemoglobin (g/dL)
Day 1	Bodybuilders	39±2.0	3.7±0.2	1.7±0.4	12.3±1.0
	Non-Bodybuilders	38±1.4	3.6±0.3	1.2±0.3	11.2±0.7
Day 3	Bodybuilders	42±2.6	4.0±1.5	2.2±0.2	13.2±1.1
	Non-Bodybuilders	37±1.1	3.7±1.1	1.6±0.5	11.0±0.7
Day 5	Bodybuilders	^{z}*45±3.5	^{z}*6.9±2.0	^{z}*2.5±0.3	^{z}*15.1±1.6
	Non-Bodybuilders	40±2.5	4.1±1.8	1.7±0.1	12.8±1.5
Day 7	Bodybuilders	^{z}*45±4.0	^{z}*8.7±2.2	^{z}*2.6±0.8	^{z}*15.5±0.9
	Non-Bodybuilders	^{z}41±2.0	^{z}6.0±2.9	^{z}2.3±0.4	^{z}13.4±1.2

The asterisk (*) indicates significant difference between Bodybuilders and Non-bodybuilders for a particular Day, at the level of $P < 0.05$ while the zee sign (^{z}) indicates significant difference between a particular Day and Day 1 of the study at the level of $P < 0.05$. PCV = Packed Cell Volume and WBC = White Blood Cell count.

The graph of the values of each of the haematological indices was then plotted against the days (Days 1, 3, 5 and 7) they were measured (Figures 1-4).

The study participants were also asked how they felt as the treatment progressed and their responses recorded in the questionnaire. Responses that were obtained every two-day interval were classified as either asymptomatic or symptomatic and compared across both groups (bodybuilders and non-bodybuilders) and across days (Table 2).

Table 2: Showing number of asymptomatic and symptomatic study-participants among bodybuilders and non-bodybuilders as typhoid treatment progressed.

		Asymptomatic (n)	Symptomatic (n)
Day 1	Bodybuilders	0	50
	Non-Bodybuilders	0	50
Day 3	Bodybuilders	22	28
	Non-Bodybuilders	15	35
Day 5	Bodybuilders	^{z}*35	15
	Non-Bodybuilders	24	26
Day 7	Bodybuilders	^{z}42	8
	Non-Bodybuilders	^{z}37	13

The asterisk (*) indicates significant difference between Bodybuilders and Non-bodybuilders for a particular Day, at the level of $P < 0.05$ while the zee sign (^{z}) indicates significant difference between a particular Day and Day 1 of the study at the level of $P < 0.05$.

Discussion

Despite it being ill-advised, the use of self-prescribed over-the-counter drugs by an average Nigerian, due to unaffordability of standard health facilities, has been recognized to save lives.

Even though severe anaemia is reported to be a rare occurrence in typhoid fever except in a case of intestinal haemorrhage, mild to moderate acute anaemia due to haemolysis, and haemoglobinuria was observed among some subjects in an earlier study [8,23]. It is seen from the results of this study that though the PCV and haemoglobin concentrations of all subjects increased continuously across both groups as treatment progressed, it is especially so among the bodybuilders; with even a slight decrease in PCV by Day 3 among the non-bodybuilders, perhaps due to the arrest in maturation of the cell lines in the bone marrow, a situation that ensues due to the toxins released by the salmonella bacteria [11]. This is evident in the dip observed in the graph of non-bodybuilders from Day 1 to Day 3 as seen in Fig 1 and Fig 4. For the bodybuilders, exercise of various types, durations, and intensities is said to induce recruitment of all blood cells including cells of the immune system, and this is suggested as the reason for a more rapid normalization of PCV and haemoglobin observed in that group, as better immunity results to less bacteria and less haemolysis-causing toxins [24].

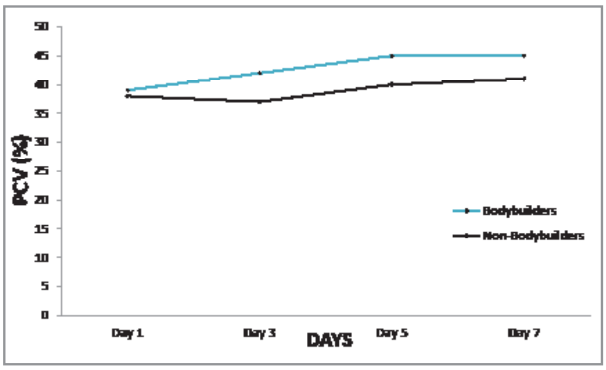

Figure 1: The PCV (Packed Cell Volume) in study participants as the treatment progressed

Leucocyte count increases continuously with increasing bouts of exercise intermitted by some moments of rest as is typical of resistance exercise routine. For this study, the leucocyte count (WBC) increased steadily in both groups as treatment progressed from Day 1 to Day 7, but significantly more so among the bodybuilders, already reaching normal level of leucocyte count by Day 5 in that group (Fig 2) [25]. It has also been reported that one of the more pronounced features of physical activity on immune parameters is the prolonged neutrocytosis after acute long-term exercise, and a boost in neutrophil functions; chemotaxis, phagocytosis, and oxidative burst activity [26-28]. Extreme exercise though is said to reduce these functions, with the exception of chemotaxis which is not affected [29]. Extreme exercise however is associated mostly with endurance exercise such as running, cycling, swimming, etc. and seldom with weight lifting or resistance exercise. In addition, ordinary exercises such as endurance exercises alone may not increase leukocyte functionality whereas resistance exercise has been shown to elevate all the cells of innate immunity in circulation and increase effective redistribution of leukocyte [30]. This would explain why in this study, the recovery from typhoid fever was significantly more rapid among the bodybuilders than the non-bodybuilders. Just as we observe from Table 2 that significantly more subjects from the bodybuilders' group became asymptomatic by Day 5 compared with the non-bodybuilders' group which only reached a similar number of asymptomatic subjects by Day 7. In corroboration to the findings of this study, lymphocyte proliferation has been found to increase after exercise [31]. Explaining why there were significantly more lymphocytes among the bodybuilders by Days 5 and 7 when compared with Day 1 of the study and when compared with same Days among the non-bodybuilders (Fig 3).

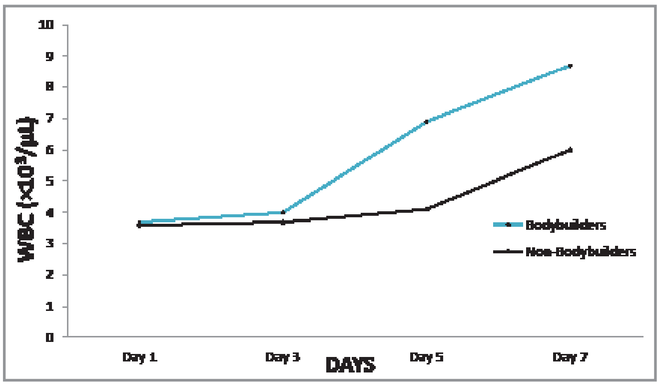

Figure 2: The WBC (White Blood Cell) count in study participants as the treatment progressed

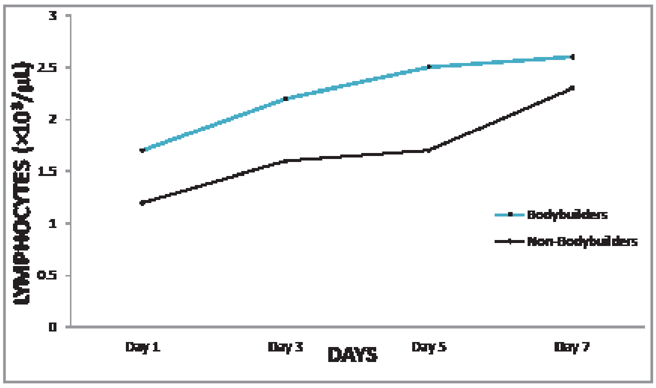

Figure 3: The Lymphocyte count in study participants as the treatment progressed

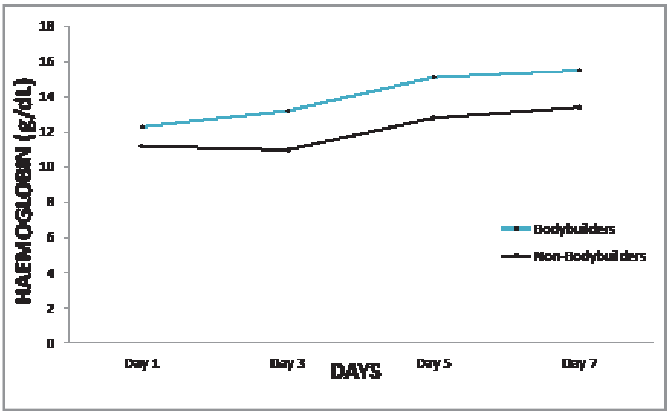

Figure 4: The haemoglobin level in study participants as the treatment progressed

In alignment with the necessity and results of this study, Rall et al. earlier noted that determining the potential therapeutic impact of resistance exercise on chronic illnesses (such as typhoid fever) is an important area of research that has received little attention [32].

Lastly, the study of resistance training and immunology is said to be an important area of research that provides a useful model for understanding how the immune system reacts to diseases and how.

Conclusion

It is seen that rather than due to hardiness, quicker recovery observed among those who exercise, especially those involved in resistance exercise, is due to better and faster immune response to infection. Specific effect of resistance exercise on individual leucocyte type such as leukocyte redistribution is controlled [30]. neutrophils, monocytes, eosinophils and basophils during typhoid treatment remains to be investigated in the nearest future.

Conflict of Interest

No conflict of interest declared.

Funding

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References

1. Mweu, E., & English, M. (2008). Typhoid fever in children in Africa. Tropical Medicine & International Health, 13(4), 532–540.
2. Ahmad, S., Tsagkaris, C., Aborode, A. T., Ul Haque, M. T., Khan, S. I., Khawaja, U. A., Carla Dos Santos Costa, A., Essar, M. Y., & Lucero-Prisno, D. E., 3rd (2021). A skeleton in the closet: The implications of COVID-19 on XDR strain of typhoid in Pakistan. Public health in practice (Oxford, England), 2, 100084. https://doi.org/10.1016/j.puhip.2021.100084
3. World Health Organization. (2018). Typhoid. Retrieved April 30, 2021, from https://www.who.int/news-room/fact-sheets/detail/typhoid
4. Akinyemi, K. O., Oyefolu, A. O. B., Mutiu, W. B., Iwalokun, B. A., Ayeni, E. S., Ajose, S. O., & Obaro, S. K. (2018). Typhoid Fever: Tracking the Trend in Nigeria. The American journal of tropical medicine and hygiene, 99(3_Suppl), 41–47. https://doi.org/10.4269/ajtmh.18-0045
5. Bassey, E. E., Hasan, M. M., Costa, A. C. D. S., Tsagkaris, C., Aborode, A. T., Karra-Aly, A., Essar, M. Y., & Ahmad, S. (2021). Typhoid fever and COVID-19 pandemic in Nigeria: a call for coordinated action. Einstein (Sao Paulo, Brazil), 19, eCE6796. https://doi.org/10.31744/einstein_journal/2021CE6796
6. Bhutta, Z. A., & Mansurali, N. (1999). Rapid serologic diagnosis of pediatric typhoid fever in an endemic area: A prospective comparative evaluation of two dot-enzyme immunoassays and the Widal test. American Journal of Tropical Medicine and Hygiene, 61(4), 654–657.
7. Bhutta, Z. A. (2006). Current concepts in the diagnosis and treatment of typhoid fever. BMJ, 333(7558), 78–82.
8. Ndako, J. A., Dojumo, V. T., Akinwumi, J. A., Fajobi, V. O., Owolabi, A. O., & Olatinsu, O. (2020). Changes in some haematological parameters in typhoid fever patients attending Landmark University Medical Center, Omuaran-Nigeria. Heliyon, 6(5), e04002. https://doi.org/10.1016/j.heliyon.2020.e04002
9. Hatta, M., & Smits, H. L. (2007). Detection of Salmonella typhi by nested polymerase chain reaction in blood, urine, and stool samples. American Journal of Tropical Medicine and Hygiene, 76(1), 139–143.
10. Abdool Gaffar, M. S., Seedat, Y. K., Coovadia, Y. M., & Khan, Q. (1992). The white cell count in typhoid fever. Tropical and Geographical Medicine, 44(1), 23–27.
11. Crump, J. A., & Mintz, E. D. (2010). Global trends in typhoid and paratyphoid fever. Clinical Infectious Diseases, 50(2), 241–246.
12. Brooks, W. A., Hossain, A., Goswami, D., Nahar, K., Alam, K., Ahmed, N., Naheed, A., Nair, G. B., Luby, S., & Breiman, R. F. (2005). Bacteremic typhoid fever in children in an urban slum, Bangladesh. Emerging infectious diseases, 11(2), 326–329. https://doi.org/10.3201/eid1102.040422
13. Van den Bergh, E. T., Gasem, M. H., Keuter, M., & Dolmans, M. V. (1999). Outcome in three groups of patients with typhoid fever in Indonesia between 1948 and 1990. Tropical Medicine & International Health, 4(3), 211–215.
14. World Health Organization. (2003). Background document: The diagnosis, prevention and treatment of typhoid fever (pp. 19–23). Geneva: WHO. Retrieved from https://www.who.int/entity/vaccineresearch/documents/en/typhoid_diagnosis.pdf
15. Duggal, N. A. (2019). Can physical activity ameliorate immunosenescence and thereby reduce age-related multi-morbidity? Nature Reviews Immunology, 19(9), 563–572.
16. Pedersen, B. K. (2012). Muscles, exercise and obesity: Skeletal muscle as a secretory organ. Nature Reviews Endocrinology, 8(8), 457–465.

17. Ellingsgaard, H. (2019). Exercise and health — emerging roles of IL-6. Current Opinion in Physiology, 10, 49–54.
18. Wallace, D. L. (2006). Prolonged exposure of naïve CD8+ T cells to interleukin-7 or interleukin-15 stimulates proliferation without differentiation or loss of telomere length. Immunology, 119(2), 243–253.
19. Haugen, F. (2010). IL-7 is expressed and secreted by human skeletal muscle cells. American Journal of Physiology-Cell Physiology, 298(4), C807–C816.
20. Green, D. J. (2017). Vascular adaptation to exercise in humans: Role of hemodynamic stimuli. Physiological Reviews, 97(2), 495–528.
21. Coates, G. (1993). Hindlimb and lung lymph flows during prolonged exercise. Journal of Applied Physiology, 75(2), 633–638.
22. Havas, E. (2000). Albumin clearance from human skeletal muscle during prolonged steady-state running. Experimental Physiology, 85(6), 863–868.
23. Bakshi, S., & Jasmer, S. (1972). Acute haemolytic anaemia in typhoid fever. The Indian Journal of Pediatrics, 39(7), 270–273.
24. Pedersen, B. K., & Ullum, H. (1994). NK cell response to physical activity: Possible mechanisms of action. Medicine & Science in Sports & Exercise, 26(2), 140–146.
25. Rohde, T., Maclean, D., & Pedersen, B. K. (1998). Effect of glutamine on changes in the immune system induced by repeated exercise. Medicine & Science in Sports & Exercise, 30(6), 856–862.
26. McCarthy, D. A., & Dale, M. M. (1988). The leucocytosis of exercise: A review and model. Sports Medicine, 6(6), 333–363.
27. Brines, R., Hoffman-Goetz, L., & Pedersen, B. K. (1996). Can you exercise to make your immune system fitter? Immunology Today, 17(6), 252–254.
28. Smith, J. A., McKenzie, S. J., Telford, R. D., & Weidemann, M. J. (1992). Why does moderate exercise enhance, but intense training depress immunity? In Behavior and Immunity (pp. 155–168).
29. Ortega, E., Collazos, M. E., Maynar, M., Barriga, C., & De La Fuente, M. (1993). Stimulation of the phagocytic function of neutrophils in sedentary men after acute moderate exercise. European Journal of Applied Physiology, 66(1), 60–64.
30. Freidenreich, D. J., & Volek, J. S. (2012). Immune responses to resistance exercise. Exercise Immunology Review, 18, 8–41.
31. Field, C. J., Gougeon, R., & Marliss, E. B. (1991). Circulating mononuclear cell numbers and function during intense exercise and recovery. Journal of Applied Physiology, 71(3), 1089–1097.
32. Rall, L. C., Roubenoff, R., Cannon, J. G., Abad, L. W., Dinarello, C. A., & Meydani, S. N. (1996). Effects of progressive resistance training on immune response in aging and chronic inflammation. Medicine and science in sports and exercise, 28(11), 1356–1365. https://doi.org/10.1097/00005768-199611000-00003

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