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TITLE: Efficacy of Calcium and Vitamin D Supplementation for the Prevention of Stress Fractures in Female Naval Recruits

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14. ABSTRACT The goal of this project is to determine if calcium and vitamin D intervention can reduce the incidence of stress fracture by at least 50% in female Naval recruits during basic training. The secondary goal is to examine the potential mechanisms for increasing bone adaptation to intense mechanical loading. We will recruit 5200 recruits who will be randomly assigned to an intervention group given calcium 2000 mg and vitamin D 800 I.U. per day or a control placebo group. The intervention and stress fracture monitoring will continue through 8 weeks of basic training. In a subset of 560 subjects, we will obtain peripheral quantitative computed tomography(pQCT)measurements of the tibia at baseline and end of training to determine changes in moment of inertia. To date we have enrolled 4606 subjects and completed 3518. We have enrolled 113 into the pQCT substudy. We continue to enroll and collect data. To date, 249 subjects have sustained stress fractures. There have been no adverse events since the last annual report. We have requested a no-cost extension to complete the study. We have no findings to report.					
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INTRODUCTION

Stress fractures during military basic training remain a major concern despite training modifications that have decreased stress fracture incidence. Stress fractures are especially prominent in women. These injuries result in loss of manpower and high medical expense, occasionally incurring service-related disability. Supplementing female recruits with calcium and vitamin D may supply nutrients needed to meet training demands and thereby significantly reduce risk of fracture. Inadequate calcium and vitamin D intake may limit bone adaptation since recruits under 30 years of age have not achieved peak bone mass, training stimulates bone formation and micro-fracture repair, calcium intakes are normally low, and substantial dermal calcium losses occur during training. The goal of this project is to determine if calcium and vitamin D intervention can reduce the incidence of stress fracture by at least 50% in female Naval recruits during basic training. The secondary goal is to examine the potential mechanisms for increasing bone adaptation to intense mechanical loading. We will recruit 5200 recruits who will be randomly assigned to an intervention group given calcium 2000 mg and vitamin D 800 I.U. per day or a control placebo group. The recruit intervention and stress fracture monitoring will continue through 8 weeks of basic training. In a subset of 560 subjects, we will obtain peripheral quantitative computed tomography (pQCT) measurements of the tibia at baseline and end of training to determine changes in moment of inertia. Positive findings from this study would provide support for the Navy to adopt an easy, low cost method of further decreasing incidence of stress fractures.

BODY

Key Research Accomplishments

- Implementation of a project that does not interfere with the flow of Naval basic training
- Prompt restart of the project twice, including hiring and training of new study personnel
- Enrollment of 4606 subjects
- Completion of 3518 subjects
- Retention of 76% of enrolled subjects
- Implementation of pQCT substudy

Research accomplishments associated with each task outlined in the approved Statement of Work are outlined in Table 1.

	Original	Actual/Projected	Explanation of discrepancies
Planning and set up	7/01-12/01	9/01-5/02	Although the project was funded 9/01, the DOD did not approve us to start until 4/02. We started one month after approval.
Enrollment, intervention and data collection	1/01 - 12/03	5/02 - 4/06	About 4.5 months after startup, enrollment was put on hold by the Great Lakes IRB for nearly 12 months (9/02-8/03). Great Lakes Command directed us to stop recruitment for another 8 months (1/05-8/05).
Data clean up and analysis	1/04-6/04	5/06 - 9/06	Delayed as described above

After receiving notification of funding, we worked with the DOD regulatory persons and the Creighton and Great Lakes Institutional Review Boards (IRB's) as quickly as possible to obtain approval for starting the study. We did not receive final approval from the DOD until April 2002. We started recruitment one month later. We were actively recruiting until September 26, 2002 when we were notified by the Great Lakes IRB that we were to stop recruitment and put the study on hold. We understand that all active clinical projects were stopped at the Great Lakes at that time. We were allowed to complete follow up of enrolled subjects.

The project was re-approved by the Great Lakes IRB and allowed to resume on August 7, 2003. We needed to hire new staff members since we had no funds to maintain our original staff during the shutdown period. Within five weeks after re-approval we hired and trained new staff, and we resumed recruitment on September 18, 2003. Thus, we were delayed nearly a year with recruitment and data collection.

In September 2003, we were provided money from the DOD to purchase a Stratec peripheral quantitative computed tomography (pQCT) device. We submitted the protocol amendment for the pQCT measurements to the Great Lakes IRB in September 2003 and received approval in January 2004. We immediately requested that the DOD approve the protocol amendment, but we did not receive that approval until June 2004. We then hired and trained a person to do the pQCT measurements and started the pQCT sub-study in July, 2004. We completed the pQCT precision study, and then in October 2004 the pQCT started to malfunction. The first year warranty that was included in the purchase price expired while we were waiting for approval to start the pQCT study. The repair estimate was \$10,000. We asked for extra funds from the DOD to repair the pQCT in November 2004. In the meantime, we selected a contractor, obtained a repair quote and put in a purchase order with the university so that we could have the pQCT repaired. In January 2005, the Great Lakes Command directed that we stop all recruitment until we were able to use the pQCT.

We had the device repaired and hired and trained a new technician since our first one had taken another job. We also did a small precision study to assure that the repaired device had reliability. We were ready to restart in June 2005, but the Recruit Training Command at the Great Lakes asked us to wait until August 2005 to restart the study, which we did. We are currently enrolling subjects and collecting data. Since the beginning of the pQCT study, 74% of those consenting for the overall studied have agreed to participate in the pQCT substudy.

To date we have enrolled 4606 study participants in the overall study. We have enrolled 113 participants into the pQCT sub-study, but none of those have finished training to date. We have a retention rate of 76%.

The mean age of the study participants is 20.2 (± 2.7) years. The ethnic/racial breakdown is as follows: American Indian/Alaskan 3.41%; Asian 4.16%; Black/non-Hispanic 17.94%; Hispanic or Latino 12.66%; White/non-Hispanic 58.87% and other 2.95%. To date, 249 of the study subjects have sustained a stress fracture. Stress fractures are confirmed by either radiograph or technetium bone scan and adjudicated by Dr. Recker..

Table 2 shows descriptive characteristics of a portion of the sample. We have Creighton University Academic Services scan bubble sheets containing participant answers to the questionnaire. Since we do this in batches, the data describe less than the entire sample at this time.

Variable	N	Median (range)
Dairy servings/wk	2420	6 (1-26)
Alcohol drinks/wk	716	3 (1-12)
Cigarette packyears	765	3 (1-24)
Birth control pills (yrs use)	1102	2 (1-17)
Depomedroxyprogesterone	403	1 (1-11)
Progesterone implant	17	1 (1-7)

Reportable Outcomes

We have made three presentations on this study:

Ahlf, R., Lappe, J., Cullen, D., Thompson, K. (2005) Efficacy of calcium and vitamin D supplementation for the prevention of stress fractures in female Naval recruits. Oral presentation at the Accessions Research & Best Practices Symposium, August 23-25, Lincolnshire IL.

Lappe, J., Cullen, D., Thompson, K.(2004) An update on the study of calcium and vitamin D to prevent stress fractures. Oral presentation to the GlaxoSmithKline Calcium Board. Seattle, September 28.

Lappe, J. (2004) Efficacy of calcium and vitamin D supplementation for the prevention of stress fractures in female naval recruits. Oral presentation. U.S. Army Accessions Command, Accessions Research Consortium, Fort Jackson S.C.

Conclusions

We are drawing no conclusions at this time since we have not completed the study.

References

None

Appendices

None