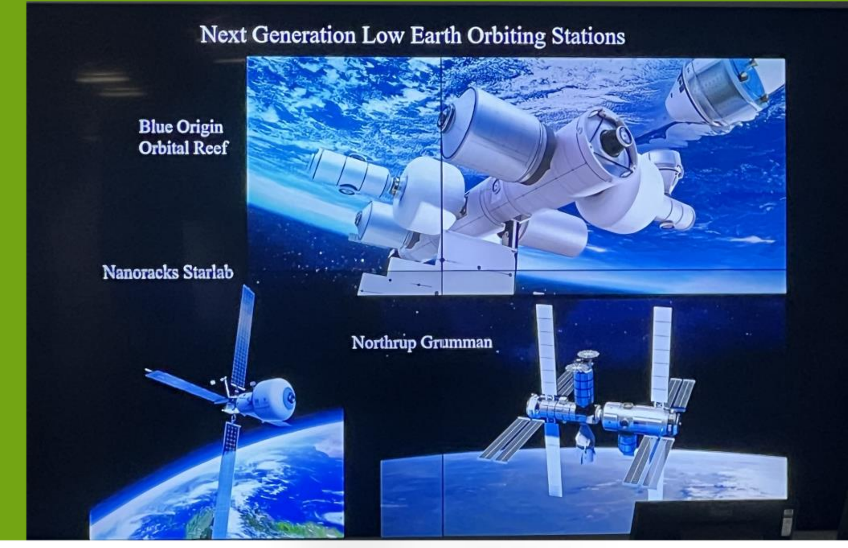
Counteracting Micro-Gravity Induced Bone Loss in Astronauts:

A systematic Review

Harvey White - Hull York Medical School



Abstract

My project explores the current literature on the potential use of anti-resorptive drugs, namely bisphosphonates; to counteract microgravity induced bone loss.

Goals:

1. Identify current limitations bone loss has on the future goals of human space flight
2. Briefly outline countermeasures used onboard the ISS
3. Evaluate the use of Bisphosphonate therapy as a countermeasure for micro-gravity induced bone loss

Introduction

- Current evidence suggests that every month spent in space causes a 0.4-1.6% loss in bone mineral density (BMD) [1].
- This loss is seen with AERD (Advanced Exercise Resistance Devices), involving 2.5 hours 6x a week training sessions. Of which involves specialised and complicated equipment [1].
- Current mean International Space Station (ISS) flight times around 5-6 months and plans for trans planetary fly-bys to Mars by the 2030s; these missions could take up to 3 years.
- This would expose astronauts to unsustainable bone loss and muscle atrophy. Would not be possible for AERD's on Martian missions [2].
- Extrapolation of current data could predict up to ~14.4% reduction in whole BMD, with the pelvis and lumber spine effected greater, with 50.5% and 39.6% loss.

Methodology

My database search focused on in vivo and in vitro use of bisphosphonates such as alendronate sodium as a countermeasure against microgravity induced bone loss.

- Searches of EMBASE (n=39) and OVID Medline (n=28)
- Papers were then filtered for relevance (n=19), access (n=4) and duplicates (n=3), 13 studies remained.

1	astronaut?
2	(low adj3 gravity)
3	space?flight
4	cosmonaut?
5	1 or 2 or 3 or 4
6	Bisphosphonate?
7	alendronate
8	fosumax
9	amino?bisphosphonate?
10	6 or 7 or 8 or 9
11	(Bone adj3 density)
12	Bone mineral density
13	(bone adj3 loss)
14	T?score
15	osteoporo*
16	osteopeni*
17	11 or 12 or 13 or 14 or 15 or 16
18	5 and 10 and 17

Figure 3 – EMBASE search criteria

Side Effects:

Oral alendronate sodium:
- Nonulcerative dyspepsia [3]
- Oesophagitis
  - Indigestion-like problems – removed if IV Injection used instead (Risedronate)

Potential Generic Bisphosphonate Side Effects:
- Atypical Femoral fractures [7]
  - 7.9 incidences per 10000 person years
- Altered bone architecture
  - Increased trabecular bone formation (Alteration in structural integrity?)
- Osteonecrosis of jaw [8]
  - 0.01-0.04% total risk
- Reduced risk of renal calculi [9]
  - Increased renal Calcium loss, reduces renal stone formation

Results

- Sibonga et al. [3]
This study looked at the use of 70mg weekly alendronate on 10 astronauts alongside AERD, with an average mission length of 5.5 month. Results vs AERD seen on the right –figure 4.

DXA and QCT scans were performed an average of 114 days pre-flight and 7-14 days post-flight. Pre- and post-flight biochemical samples were taken.

RESULTS:
All results were significant p<0.005 for bisphosphonate vs pre-AERD groups while bisphosphonate vs ARED was significant at the total hip and lumber spine but not at the pelvis or trochanter (p=0.15, 0.16).

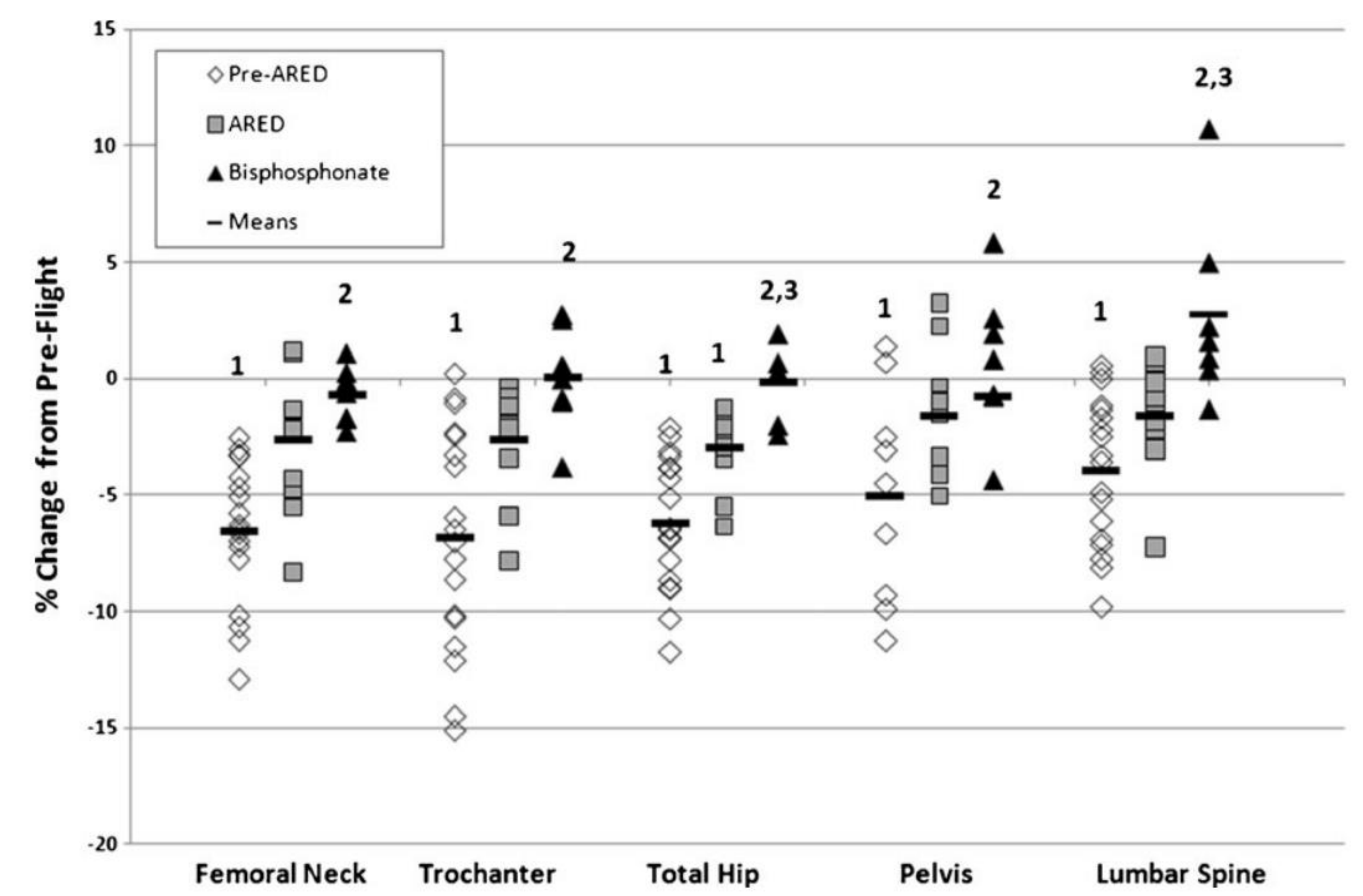
- Spector et al. [4]
Another study looking at 7 ISS crewmembers treated with 70mg/day alendronate. Mean flight time 164 +-15 days. Control group of 9 performing AERD. Mean flight time 158 +-21 days.

RESULTS:

Control (DXA results %BMD)	Treated
- lumber spine -2.6 +-1.9	- LS +2.8 +-4.0
- total hip -3.5 +-2.2	- TH -0.2 +-1.5
- trochanter -4.1 +-2.7	- T +0.02 +-2.3
- femoral neck -1.9 +-4.1	- FN -0.7 +-1.2

- Scott et al. [5]
This adult rat study performed artificial weightlessness to assess effectiveness of pretreatment with zoledronate injections 3 days prior to 3 weeks of unloading.

RESULTS:
- qCT showed 32% increase in trabecular bone volume in treated rats vs saline, 45% reduction in osteoclast surface.
- Zoledronate group: -40% in mineralizing surface, -54% bone formation rate.
- Unloaded control: -31% cancellous bone, -38% mineralizing surface, -50% reduced bone formation rate.



ˆFigure 4 – graph of BP vs AERD with % BMD change on Y, region on X [3]

- Elizondo et al. [6]
An adult rat study, testing effectiveness of 4 weeks pretreatment with 3x/week alendronate vs risedronate. Via simulated 4 weeks of hind limb unloading.

RESULTS:
- Unloaded control -28% tibia, -17% femur compared to ambulated rats
- Risedronate and alendronate similar to ambulated rats, risedronate even had higher at femur

Conclusion

In conclusion, bisphosphonates have the potential to counteract and even reverse bone density changes caused by low gravity environments. They are relatievly cheap, weigh little and have a manageable side effect profile; if route of use chosen correctly.

Further consideration for use in future trans-planetary flight and future mid-long term lunar missions, where the cumulative time effect of gravity will put astronauts at risk of fractures as a service-related complication in the long term.

Limitations include, small study sizes, with variation in effect between individuals (potentially due to lower study power). Therefore, larger astronaut studies are needed to gain further information on rates of side effects in flight and whether this chemically preserved bone maintains its structural quality in the long term.

References

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