PAMIDRONATE MAY PREVENT MUSCLE PROTEIN BREAKDOWN IN BURNS BY INDIRECTLY AFFECTING CYTOKINES

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INTRODUCTION

- Pamidronate given to children <10d post-burn
- Prevents resorptive bone loss (Osteoporos Int 2005; 16:631-5) for up to 2 yr (Bone 2007; 41: 297-302)
- Prevents muscle protein breakdown (J Bone Miner Res 2014; 29: 1369-72)
- In vitro Ca modulates inflammatory response by affecting monocyte chemokine production (Semin Cell Dev Biol 2016; 49: 52-56)

HYPOTHESIS AND AIM

- Hypothesis: pamidronate affects muscle protein breakdown by altering chemokine/cytokine concentration directly or indirectly via lowering blood ionized (i) Ca.
- Aim: to correlate biomarkers of muscle structure and function with iCa concentration in a retrospective study

METHODS

- We retrospectively reviewed the data obtained from bioplex measurements of cytokines on 22 subjects(2-21 yr) who participated in the pamidronate randomized controlled trial:
- Controls n=10, pamidronate n=12 with a mean of 8 data points per control subject and 10 data points per pamidronate subject spread over the first 60d post-burn

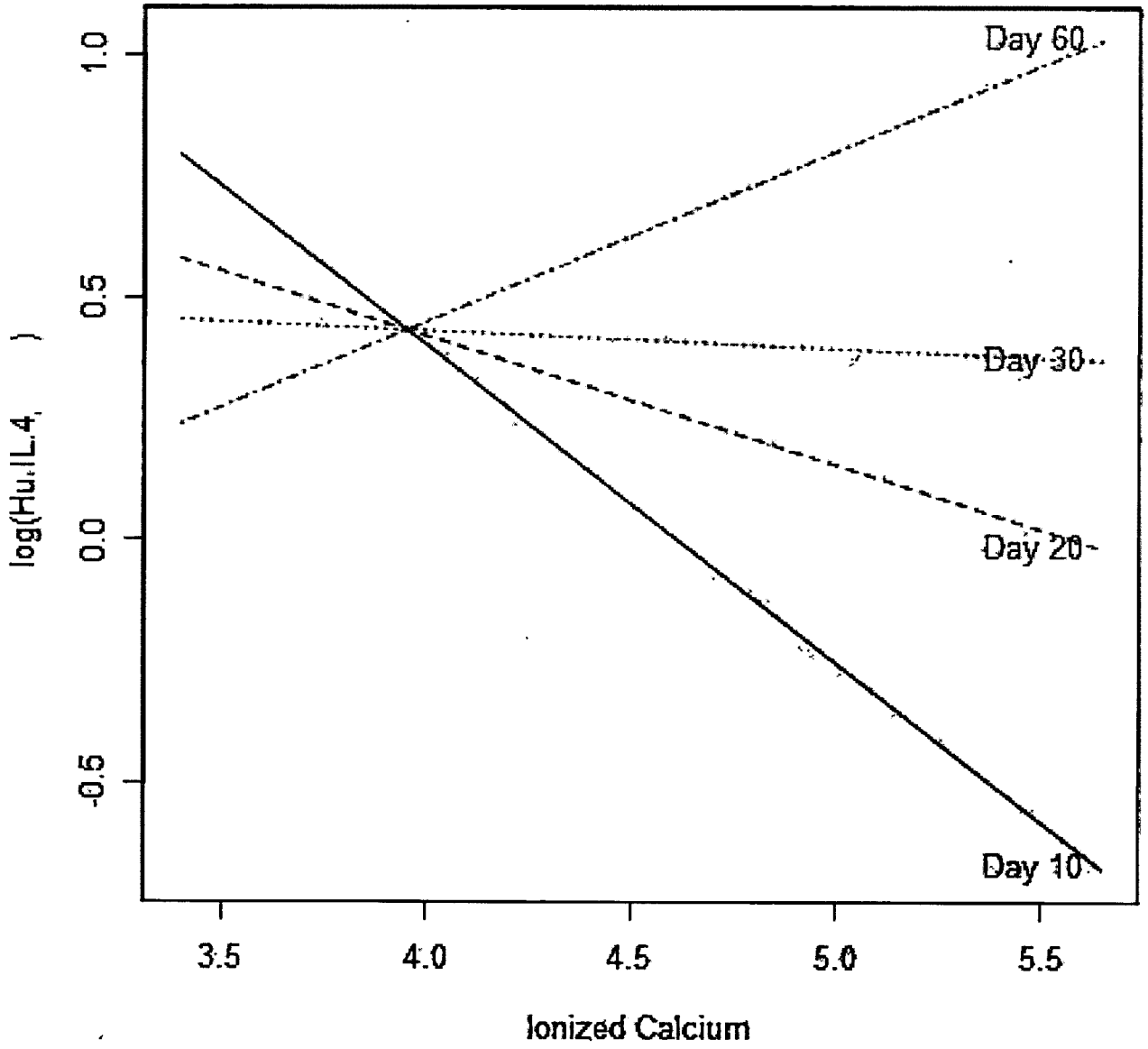
DATA ANALYSIS

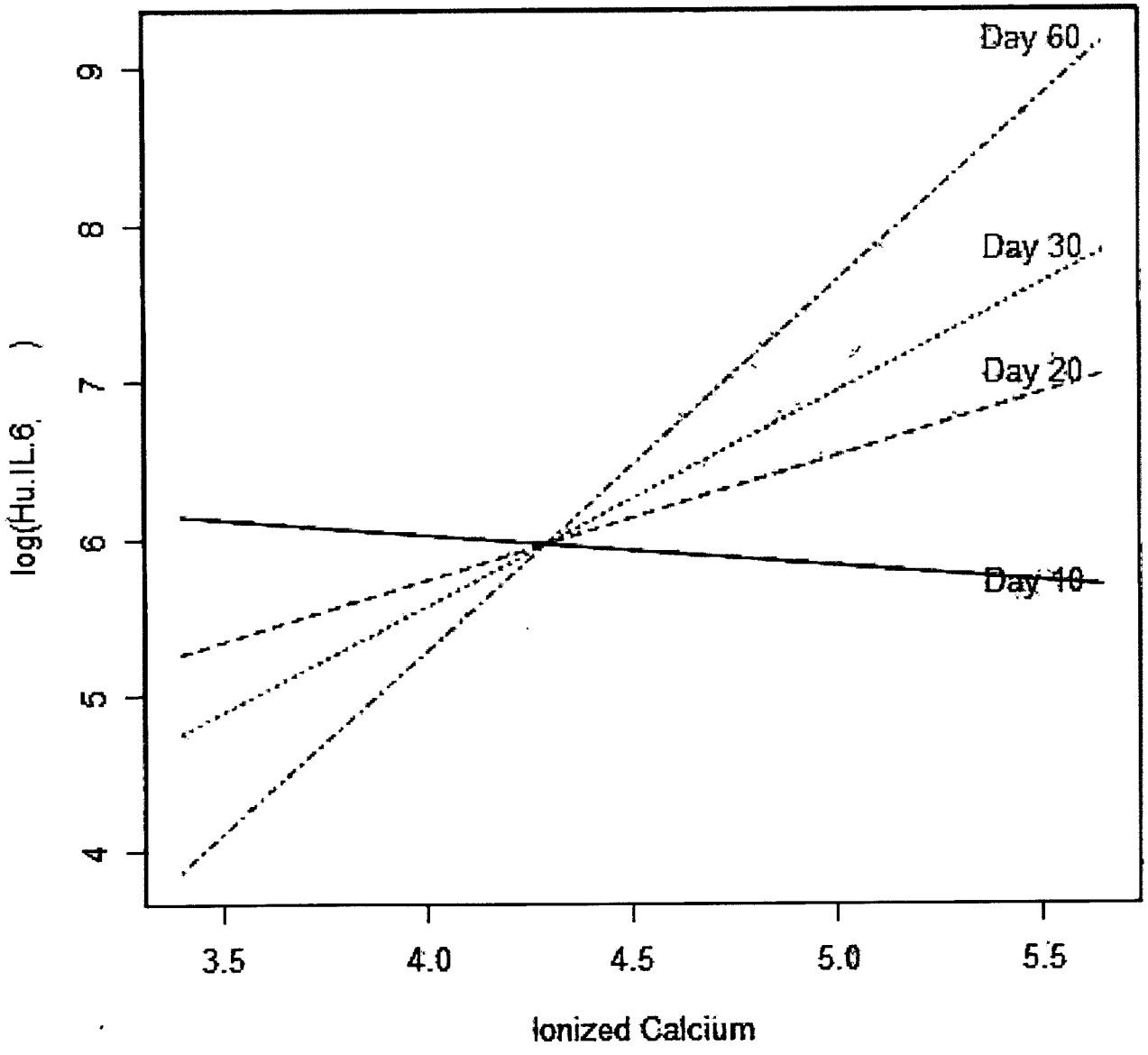
- Relationship between cytokine and treatment group: mixed ANOVA
- Relationship between ionized Ca and treatment group: mixed multiple regression
- Each analysis adjusted for age, burned surface area, and time from admission
- Allows for an interaction between time and group but blocks on subject to control for repeated measures

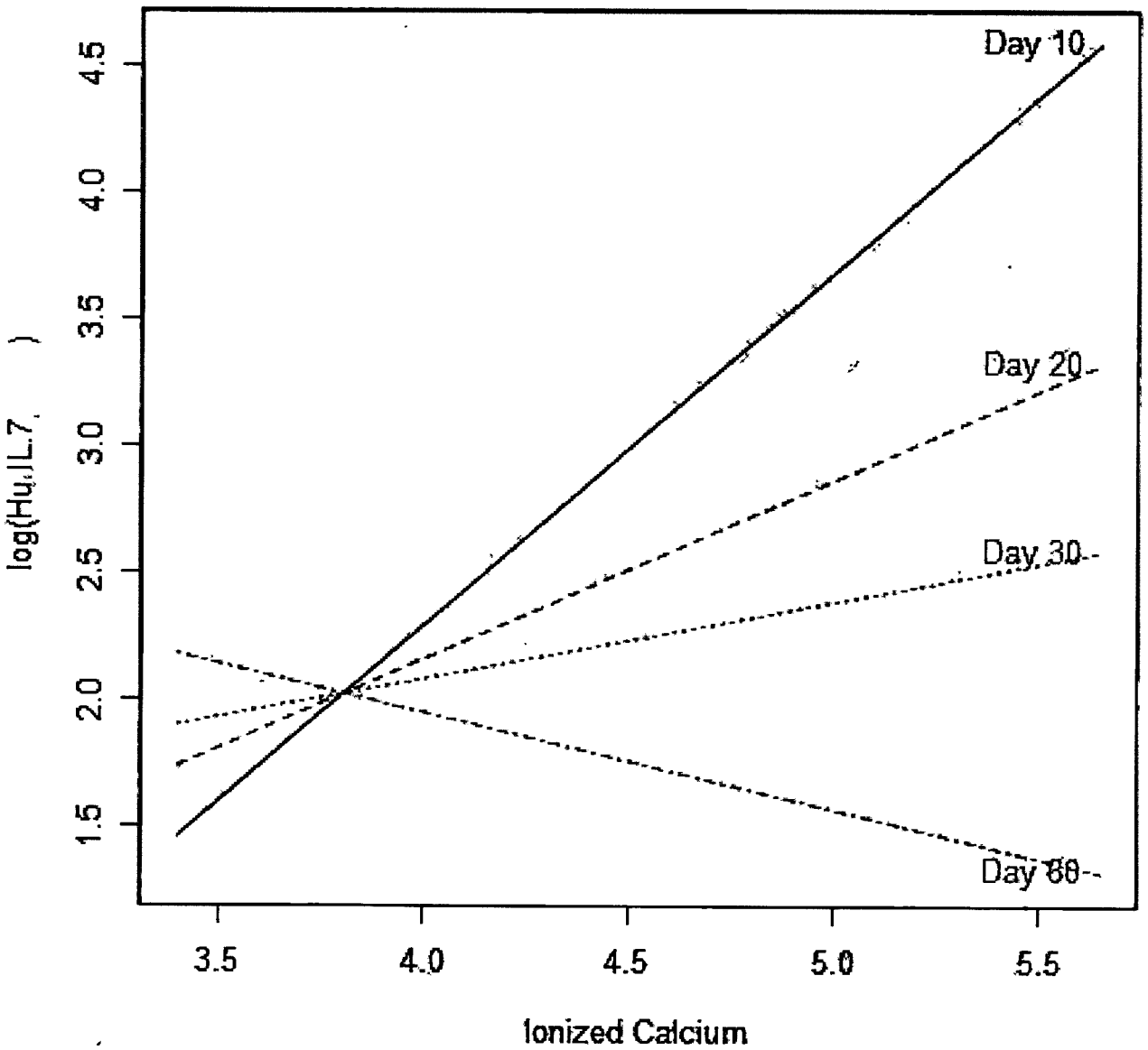
RESULTS

- IL7 marginally different between treatment groups(p=0.048)
- IL4 inversely correlated with ionized Ca (p=0.048)
- IL6 directly correlated with ionized Ca, p=0.036
- IL7 directly correlated with ionized Ca, p=0.032
- TGFβ not different between groups

Figures depict plots of log serum cytokine concentration against blood ionized Ca four time points post-burn. ANOVA results given separately.


Day 60
Day 30
Day 20
Day 10
1.0
0.5
0.0
-0.5
log(Hu.IL.4,)
3.5
4.0
4.5
5.0
5.5
Ionized Calcium


Day 60
Day 30
Day 20
Day 10
log(Hu.IL.6.)
4
5
6
7
8
9
3.5
4.0
4.5
5.0
5.5
Ionized Calcium


Day 10
Day 20
Day 30
Day 60
log(Hu.IL.7)
1.5
2.0
2.5
3.0
3.5
4.0
4.5
3.5
4.0
4.5
5.0
5.5
Ionized Calcium

RESULTS CONTINUED

- IL4 inversely correlated with ionized Ca, stimulates myotube differentiation from satellite cells.
- IL6 is associated with muscle wasting
- IL7 may impair myotube differentiation

CONCLUSIONS

- No differences in ionized Ca between pamidronate and treatment group at specific time points measured
- Inverse correlation between blood ionized Ca and cytokines facilitating muscle breakdown
- Direct correlation between blood ionized Ca and cytokines stimulating muscle breakdown