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Introduction and Objective: Bone mass density (BMD) has been shown to be altered in people with hemophilia, most probably due the lack of physical activity. Alterations in sub-condral bone are also well described after repetitive bleed episodes in hemophilic patients. Exercise has been recommended as being beneficial for people with hemophilia to counteract the consequences of hemarthrosis and to improve the quality of life, but a lack of exercise-related evidence is available to support it. So our objective was to provide and evaluate the effect of an aquatic training program on BMD and bone turnover markers in an animal model of blood-induced joint damage.

**Material and Methods:** The arthropathy was induced in male Wistar rats by eight weekly intraarticular injections of 0.1mL autologous blood into their right knees. Animals were divided into Control Group (CG; n=8), Hemarthrosis Group (HG; n=8), Swimming + Hemarthrosis Group (SHG; n=10). SHG group performed an 8-week swimming protocol of 60 minutes (5 x per week) with 5% body weight attached to their tails. BMD was assessed using dual-energy Xray absorptiometry (whole-body, tibia, femur and knee joint) before and after the end of exercise protocol. Blood samples were collected at sacrifice and procollagen type 1 amino-terminal propeptide (P1NP, bone formation marker) and C-terminal telopeptide (CTX-1, bone re-absorption marker) were measured (ELISA).

**Results:** Hemarthrosis group has significant lower BMD compared to SHG at femur (0.33 $\pm$ 0.01 vs. 0.41 $\pm$ 0.02 g/cm<sup>2</sup>; p<0.0001), tibia (0.24 $\pm$ 0.02 vs. 0.28 $\pm$ 0.01 g/cm<sup>2</sup>; p<0.0001) and knee region (0.23 $\pm$ 0.01 vs. 0.26 $\pm$ 0.01 g/cm<sup>2</sup>; p<0.0001) **Figure 1**. No difference were found between experimental groups on whole body BMD (0.15 vs. 0.17; p=0.858). P1NP serum levels was higher (p=0.0028) in SHG (50.52 $\pm$ 10.77 ng/mL) then HG (36.46 $\pm$ 3.82 ng/mL) while CTX was lower (p=0.0006) in SHG (111.33 $\pm$ 11.93 ng/mL) compared to HG (161.77 $\pm$ 27.25 ng/mL) **Figure 2**.

## Swimming exercise prevents bone mass density alteration and modulates bone turnover in an animal model of blood-induced joint damage



**Fig 1.** Bone mineral density (BMD) values before (initial) and after (final) the exercise protocol at the (a) femur, (b) tibia and (c) knee joint of the experimental legs. Control Group (CG, n=8), Hemarthrosis Group (HG, n=8) and Swimming-Hemarthrosis Group (SHG, n=10). \*p<0.0001 *vs*. CG, #p<0.0001 *vs*. SHG.



**Fig. 2.** Plasma concentration of P1NP (a) and CTX (b) in the Control Group (CG, n=8), Hemarthrosis Group (HG, n=8) and Swimming-Hemarthrosis group (SHG, n=10). The results are presented as the mean±SD. \*p<0.01 vs. CG, #p<0.01 vs. SHG.

**Conclusions:** This is the first time that the beneficial effects of swimming exercise on bone density and bone metabolism has been shown on an animal model of blood-induced joint damage.

•Mansouritorghabeh, H., Rezaieyazdi, Z. & Badiei, Z. (2008) Are individuals with severe haemophilia A prone to reduced bone density? Rheumatology International, **28**, 1079–1083.

•Wallny, T.A., Scholz, D.T., Oldenburg, J., Nicolay, C., Ezziddin, S., Pennekamp, P.H., Stoffel-Wagner, B. & Kraft, C.N. (2007) Osteoporosis in haemophilia – an underestimated comorbidity? Haemophilia, **13**, 79–84.

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