hematoxylin and eosin (H and E) staining, Van Gieson staining, Masson's trichrome and fluorochrome labelling indicated PTEN inhibition provided protective effects against ethanol on bone tissue. Interestingly, our data revealed that the mRNA of PETN, paralleled with PTENP1, was increased in a time-dependent manner upon ethanol stimulation, which resulted in increasing PTEN protein level. In addition, ethanol increased PTEN expression while decreased p-PTEN expression in a time-dependent manner, which indicated the generation of more functional PTEN.

Conclusions: Taken together, dual regulations of PTEN by ethanol via transcriptional and post-transcriptional process impaired the downstream signalling of Akt/GSK3 β / β -catenin and osteogenic differentiation of hBMSC. Therefore, we propose that PTEN inhibition treatment for Akt/GSK3 β / β -catenin activation could be tested in the clinic as a potential therapeutic approach to preventing the development of alcohol-induced osteopenia.

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Cartilage, synovium and bone

SAT0048 ANALYSIS OF DIFFERENT THERAPEUTIC REGIMES IN PATIENTS WITH HEMOPHILIC ARTHROPATHY

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Background: The greater morbidity of the patient with haemophilia is due to hemarthrosis. The treatment is based on the administration of deficient coagulation factor (FC). The treatment is divided into prophylactic (TP) and on demand (AD). Prophylaxis consists in the administration of FC in order to maintain adequate levels of factor to prevent or reduce spontaneous bleeding and AD is the application of the factor when there is clinical evidence of bleeding. The TP is the recommended treatment in severe haemophilia, plasma and recombinant concentrates are used, safe and effective, but with a short half-life, which requires frequent intravenous infusions, being a barrier to compliance. Another drawback of the current treatment in haemophilia A (HA) is that up to 30% develop inhibitor (antibodies that neutralise the activity of a CF).

New subcutaneous drugs (NSD) have begun to be used in clinical trials, such as:

- Emicizumab: Bispecific anti-IXa/X monoclonal antibody.
- Concizumab: Anti-TFPI antibody.

This new therapeutic strategy can have implications both from a clinical and economic point of view.

Objectives: To analyse the different treatment regimens and their economic implications in a cohort of patients with hemophilic arthropathy (HA).

Evolution of hemarthroses in patients with AH after starting treatment with NSD in the clinical trial phase.

Methods: Retrospective descriptive study, in the Haemophilia Unit of our hospital (regional reference), in patients with AH (Haemophilia A and moderate-severe B), followed in consultation with episodes of joint bleeding, from January 2007 to October 2017. Gravity of the haemophilia determined by the percentage of FC activity (VIII and IX), moderate from 1% to 5%, severe <1%. The number of joint bleeds was analysed 6 months before and after the start of treatment with the NFS in patients who have participated in a multicenter phase III study and continue with the treatment

Results: We included 89 patients (88 men and 1 carrier woman), mean age 31 $\pm$ 17 years, HA (severe 56%, moderate 26%), HB (severe 15%, moderate 1%). 17% develop inhibitor (10 severe HA, 3 moderate HA, 3 severe HB). Treatment on demand 44% and prophylaxis 38%. Replacement therapy: FC VIII (44% severe HA, 22% moderate HA), FC IX (11% severe HB, 1% moderate HB), recombinant active factor VII (rFVIIa) (2 patients with severe HB with inhibitor).

In treatment with monoclonal antibody (patients currently in Clinical Trial): 15% Emicizumab, of these 4 are with inhibitor (2 severe HA, 1 moderate HA, 1 severe HB and 1% Concizumab (severe 1HB with inhibitor).

The number of hemarthroses was analysed 1 year before the administration of NFS until now, achieving a statistically significant reduction in the rate of joint bleeding of 86% ($p < 0.005$) compared to conventional pre-treatment.

Conclusions: The majority of patients with severe and moderate haemophilia are on demand treatment, despite existing recommendations.

It can also be said that there are drugs in the research phase that may involve a paradigm shift in the therapeutic approach of patients with haemophilia, which will allow more personalised treatment, to achieve better joint protection and a better quality of life.

Disclosure of Interest: None declared

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SAT0049 11BETA-HYDROXYSTEROID DEHYDROGENASE TYPE 1 REGULATES CHRONIC SYNOVITIS WITH LOCAL AND SYSTEMIC COMPLICATIONS

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Background: Inflammation, local joint destruction and systemic bone loss are common complications in patients with rheumatoid arthritis (RA). We have identified that localised pre-receptor activation of glucocorticoids (GC) by the enzyme 11 β -hydroxysteroid dehydrogenase type 1 (11 β -HSD1) is increased within sites of inflammation and surrounding tissues, such as synovium and bone. Whilst this greatly increases local bioavailability of cortisol, which supports resolution of inflammation, in chronic disease, GCs drive may drive catabolic pathways that contribute to joint destruction and systemic bone loss.

Objectives: To determine the contribution of 11 β -HSD1 activated glucocorticoids to joint destruction and inflammatory bone loss, we crossed an 11 β -HSD1 null mouse onto a transgenic murine model of chronic polyarthritis (TNF-Tg) to generate TNF-Tg^{11 β KO} mice.

Methods: Clinical measures of joint inflammation, mobility and behaviour were collected between 4 and 9 weeks of age. Paw swelling was determined using calliper measurements. Histology was assessed in formalin fixed sections following staining with haematoxylin and eosin, safranin O or TRAP staining. Juxta articular and systemic bone losses were measured by micro-Ct. synovitis was determined by Image J analysis of histology sections.

Results: 11 β -HSD1 was completely knocked out within sites of inflammation in the TNF-Tg^{11 β KO} mouse. At 9 weeks, both clinical and inflammation scores were markedly exacerbated in TNF-Tg^{11 β KO} animals relative to TNF-Tg counterparts (inflammation score; TNF-Tg, 4.3 $\pm$ 2.26 versus TNF-Tg^{11 β KO}, 11.08 $\pm$ 0.86; $p < 0.001$). This was supported by marked increases in joint swelling and juxta articular bone loss from these animals (erosion scores, TNF-Tg, 5.2 $\pm$ 0.61 versus TNF-Tg^{11 β KO}, 9.0 $\pm$ 0.66; $p < 0.005$). Closer examination of joint destruction revealed that the pannus was larger and more extensive within subchondral bone, whilst evidence of cartilage degradation was significantly worse in the TNF-Tg^{11 β KO} mouse (synovitis size, TNF-Tg, 26 763 (AU) $\pm$ 3200 versus TNF-Tg^{11 β KO}, 530276 $\pm$ 3225; $p < 0.005$). Systemic bone loss determined by bone volume to tissue volume (BV/TV), trabecular thickness (TT) and trabecular number (TN) was also greatly exacerbated within the TNF-Tg^{11 β KO} mouse (TNF-Tg, BV/TV 5.7 $\pm$ 0.75, TT 73.5 $\pm$ 6.4, TN 0.00077 $\pm$ 0.00004 versus TNF-Tg^{11 β KO} BV/TV 1.8 $\pm$ 0.36, TT 7359.77 $\pm$ 3.7, TN 0.0003 $\pm$ 0.00005; $p < 0.001$, $p < 0.005$, $p < 0.001$ respectively).

Conclusions: This study demonstrates that rather than contributing to catabolic pathways of tissue destruction, local GC activation by 11 β -HSD1 is critical in mediating the suppression inflammation, joint destruction, synovitis and inflammatory bone loss in this murine model of chronic polyarthritis.

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