situations and look beyond prejudice and misconceptions, to discover whether there are pharmacological and clinical data to support the use of medical cannabis and cannabinoids in musculoskeletal conditions and arthritis. Aside from media and social discussions, we will try to answer to the current hot question for a clinician is "Is it possible to recommend medical cannabis as a new analgesic option in musculoskeletal conditions?"

Disclosure of Interests: None declared

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SP0147

ETHICAL ISSUES IN MEDICAL CANNABIS USE

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Background: The human history of *Cannabis* is chequered.

We have evidence from the Ebers papyrus of ancient Egypt (1450 BCE) that 'shm-shm-t' was used as a medication for what appears to have been topical inflammatory issues. In the Atharva Veda (~1500 BCE), 'bhang' was considered one of the five sacred plants of India. The Old Testament refers to 'kaneh-bosm' as a component of a ceremonial anointing oil. In the UK's Elizabethan era, *Cannabis*, as hemp, was grown widely for fibre to make rope and sail for the Royal Navy. In Victorian times, WB O'Shaughnessy brought back from India to the UK the medicinal use of *Cannabis* preparations for its reputed analgesic, anti-emetic, anti-inflammatory and anti-convulsant properties. In the modern era, *Cannabis* is a Schedule 1 drug in many countries - a legal status defined as having high abuse potential with no currently accepted medical value.

Objectives: To consider the ethical issues associated with the use of Cannabis-derived preparations for medicinal purposes.

Conclusion: *Cannabis* is unique among the Schedule 1 list, because extracts from the plant are licensed medicines in different parts of the world. The two most widely-researched metabolites from the plant are Δ^9 -tetrahydrocannabinol and cannabidiol (THC and CBD). The clinical uses of nabiximols (THC:CBD 1:1, combined with other minor cannabinoids) and nabilone (a synthetic THC analogue) for multiple sclerosis and antiemesis, respectively, as well as cannabidiol and dronabinol ((-)-*trans*-THC) for childhood intractable epilepsy and cachexia, respectively, identify that *Cannabis*-derived medicinal products have therapeutic value.

Cannabis or THC in acute administration has a remarkably low association with mortality, however, there are a number of potential issues in the use of *Cannabis* itself rather than the above-mentioned extracts/compounds. Long-term heavy use of *Cannabis* is associated with the risk of addiction in about 10% of individuals. Severe anxiety attacks and psychotic episodes have been linked to higher doses of THC, although this has not been systematically identified. Both THC and CBD have identified metabolic profiles which might influence the turnover of other drugs.

A major feature of the use of *Cannabis* itself is the variability observed. In part, this derives from the natural product nature of the plant and the associated variation in the metabolites between different parts of the plant, different plants, different methods of harvesting, storage as well as method, dose and frequency of administration, the subject's prior exposure to *Cannabis* and the immediate environmental context. Even with the well-controlled clinical trials, there has been identified a variability in plasma levels of the administered agents. In those countries where medicinal *Cannabis* is more freely available, there are also concerns about patient use of black market sources.

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FRIDAY, 14 JUNE 2019

15:30:00 – 17:00:00

Reproductive issues in rheumatology

SP0148

DOES PREGNANCY REALLY AMELIORATE DISEASE ACTIVITY OF WOMEN WITH CHRONIC ARTHRITIS? OLD BELIEFS VS NEW PARADIGMS

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Rheumatoid arthritis (RA) and Spondyloarthritis (SpA) are chronic inflammatory diseases whose onset can occur during childbearing age. Juvenile Idiopathic Arthritis (JIA) can be active still during adulthood. Therefore, the disease course during pregnancy has been a topic of interest over the decades [1]. The approach towards the management of pregnancy in the rheumatic diseases has greatly changed in the last 30 years, as it became evident that active maternal disease is associated with adverse pregnancy outcomes, such as miscarriage, pre-term

birth, small-for-gestational age babies. A well-controlled maternal disease during pregnancy is associated with a better pregnancy outcome: the key-point is the treatment of maternal disease with drugs which are not harmful for the fetus. To achieve this "ideal setting" is of fundamental importance to perform a preconception counselling a tailor the management of the patient according to the individual risk stratification [2].

Historically, pregnancy has been considered to have a beneficial effect upon RA, with around 90% of women improving and up to 75% going into remission, followed by flares in puerperium in about 80% [3]. Modern prospective studies using validated measures of disease activity reveal less impressive ameliorative effects of pregnancy on RA [4]. A recent systematic review of prospective studies, using serial and objective evaluations of inflammatory disease, reported that RA improves in 60% of patients through pregnancy and flares in 46.7% of cases after delivery [5].

What are the possible explanations for this shift in the course of RA during pregnancy over decades? 1) methodological issues are obviously present (different study design; different patient population in terms of disease subset, duration, and severity); 2) disease activity as a "self-reported outcome" vs use of validated indices [6]; 3) change in treatment strategies over time: in the '80s women with RA were likely to be treated with steroids only and probably those women with active disease despite treatment were not able to carry out a pregnancy, therefore it is possible that only patients with mild-moderate form of RA were observed during pregnancy. Conversely, the current wide therapeutic armamentarium allows to reach disease remission also in patients with aggressive forms of RA, therefore it is likely to observe disease flares (rather than amelioration) during pregnancy if the drug is stopped at conception. Interestingly, among 75 prospectively-followed RA pregnancies, in patients treated with tumor necrosis factors inhibitors (TNFi) before conception, the discontinuation of the TNFi early in pregnancy resulted in increased risk for disease flares during pregnancy [7]. On the other hand, if disease is well controlled with drugs which are maintained during pregnancy, then there is little room to detect any improvement during pregnancy.

Spondyloarthritis (SpA) is a heterogeneous group of diseases and limited data are available about the disease course of different subsets (axial SpA –axSpA– and Psoriatic Arthritis –PsA–) during pregnancy. Recently, prospective data from the RevNatus registry showed that the majority of women with r-axSpA had stable or low disease activity from preconception period to 1 year after delivery with a small increase in the second trimester [8]. Previous studies reported that axSpA tend to be stable or to get worse [9]. Only one small retrospective work showed that the majority of women with AS displayed a decrease in disease activity during pregnancy [10]. In a recent report of 61 pregnant women with axSpA prospectively followed the discontinuation of TNFi early in pregnancy was a risk factor for flare [7]. Regarding PsA, data are scarce. The only two prospective studies demonstrated improvement during pregnancy and deterioration in the postpartum period [11, 12]. Similarly to axSpA, discontinuation of TNFi at conception is associated with an increased number of flares during pregnancy [13].

In general, it seems that the changes in management of chronic arthritis has determined a shift in paradigm in the disease course during pregnancy. The major determinant of this change has been the growing confidence in using anti-rheumatic drugs during pregnancy and breastfeeding. The increasing evidence about the safety of the majority of anti-rheumatic drugs has been recognized by many national and international working groups under the umbrella of scientific societies which endorsed guidelines and points to consider about this topic [14, 15].

Regarding biologic agents (bDMARDs), they can differ in molecular structure; however, they are all big size proteins which cannot passively diffuse and reach the fetus during the first trimester of gestation. Based on this assumption, unintended pregnancies exposed to these drugs are not a problem. As the active transport of IgG immunoglobulins across the placenta becomes significant after week 16 of gestation, it is understood that those bDMARDs which are IgG monoclonal antibodies will be transferred to the fetus. It was demonstrated that the drug concentration of monoclonal antibodies was higher in the newborn as compared to the mother, as expected for any IgG. Therefore, it is recommended to stop bDMARDs (with different timing according to their structure) in the second trimester – early third trimester in order to minimize the exposure to the drug and avoid that the new born will be immunosuppressed because of the drug received from the mother [14, 15]. Among TNFi, certolizumab pegol (CTZ) does not have the Fc portion needed for transplacental passage and no to minimal drug was detectable in the blood of neonates whose mothers received the drug until delivery [16]. Regarding breastfeeding, it is possible to consider bDMARDs as a homogenous class. They are all large proteins, which are unlikely excreted into breastmilk due to their high molecular weight. But even if they were present in breastmilk, bDMARDs will be degraded in the newborn's digestive tract with no chance for absorption (consider that bDMARDs are administered intravenously or subcutaneously, not orally). CTZ was shown to be absent in the breastmilk and breastfed children did not show any particular adverse event [17].

The exposure to immunosuppressive drugs, especially to bDMARDs, during late pregnancy poses the question about the immune competence of the neonate and the approach towards vaccinations. Data from large administrative US databases showed that children exposed during the third trimester to TNFi did not have an