ORA Annual Scientific Meeting May 2021: The Evolution of Understanding and Treatment of Rheumatic Diseases

Submitted by Osk Jenkins

I was fortunate to attend to a lecture by Michelle Petri, a rheumatologist from John Hopkins who specializes in SLE.

I have summarized her entire lecture and highlighted her clinical pearls. I found PEARLS 5,6,7 and 8 particularly interesting as an allied health professional.

- **PEARL 1-** Dr. Petri suggests that we all need to track SLE patients more closely
- **PEARL 2**- She advocates that if prednisone is used it should be below 6 mg a day. Using a combination of two treatments may allow lower dose of prednisone.
- **PEARL 3**-She advocated that Lupus patients need to be screened and educated about the risks of: High BP and cholesterol as well as smoking.
- **PEARL 4**- She says all Lupus patients should be on Plaquenil.
- **PEARL 5**- Turmeric is not appropriate in SLE patients
- **PEARL 6**- Cannabidiol – accelerates proteinuria in SLE.
- **PEARL 7-** PPIs can attenuate risk of osteoporotic fractures. Not a good choice for Lupus patients.
- **PEARL 8**- There are type 1 and type 2 symptoms. Medications address Type 1 symptoms ie) rash, swollen joints, but have no effect on TYPE 2 SYMPTOMS ie) fatigue, anxiety, sleep disturbance.
- **PEARL 9-** Nephrons lost are lost forever!
- **PEARL 10**- Patients with LLDAS (Lupus Low Disease Activity Scale) showed a 50% reduction in organ failure if they are in LLDAS 50 percent of the time. 50/50 rule.

Below are the expanded pearls except 3, 6, and 7 which did not have further information.

P1- MONITORING; She says pick a criterion and stick to it. She suggests using one of the following criteria.

- SLICC criteria or
- EULAR/ACR criteria.

P2- PREDNISONE; 6 mg of prednisone or below is suggested but even at that amount there is a significant risk of organ damage. For example, she notes atherosclerotic events increase with prednisone use. CVA: at 10 mgs of prednisone the risk increases by 2.5 times and at 20 mgs it is increased to 5 times.

She was advocating to keep Lupus patients off prednisone or at the lowest dose possible. The cumulative organ damage with prednisone, is significant. She says 80% is attributable to prednisone (ocular, bone) but does acknowledge all damage is not just prednisone related but is also directly

attributable to disease activity in Lupus. Lowering steroids can be achieved by using two treatments i.e.) voclosporin patients at 20 mg did well with only 1 mg of prednisone.

P4-PLAQUENIL- No patients should be over 400 mg a day even if obese.
She acknowledges that there is more retinopathy than previously suspected but advocates for routine optical coherence tomograms (OCT). She says it is easily evident on OCT with the "flying saucer sign." She says the retina is at increased risk after 16 years of use. 11% at that time will have retinopathy. 90 percent of patients will have no issues with retinopathy for years and years on Plaquenil.
She advocates for regular monitoring of blood levels to ensure that the patient is at a therapeutic level. Regular dosing is 4.5 mg -6 mg/ kg, but she says that doesn't always correlate with blood levels. Plaquenil does decrease the risk of thrombus events in SLE patients. The blood level needs to be optimal at 1000.

She says treatment options should be based on symptoms and tolerance.
Methotrexate is good for skin and joints.
Mycophenolate Mofeteil is good for Renal, Skin and for serological activity.
Leflunomide is good for joints and Renal.
Azathioprine is good for skin, renal, joints and is safe in pregnancy.

There are some new choices for medications (US based information);

- Anafrolumab
- Baracitinib – JAK 1-2, MOA IL6
- IL2s- T cell regulated with good benefit at 24 weeks.
- Belinumab (Benlysta)

P5- TURMERIC -Complications include gallbladder obstruction, kidney stones, stomach hyperacidity/ulcers. It also increases tacrolimus levels, aggravates CNS pathology, attenuates murine lupus by inhibiting NLRP3 inflammasome.

P8- TYPE 2 SYMPTOMS- Ensuring patient understand that TYPE 2 symptoms require other management or approaches such as mindfulness meditation, sleep hygiene, energy conservation etc. She referenced an article from Dr. David Pisetsky (see below) that she finds helpful in counselling her patient re; symptoms she can help them with and those she may need to refer them to someone else to address ie) OT or PT, counsellor etc.

P9- NEPHRONS- She referenced some worrisome statistics such as 20 percent of Lupus patients will be on dialysis within 20 years, noting that may Lupus patients are diagnosed young. 20 years may be a patient who was diagnosed at 20 and is only 40 years old now.

With the first episode of Lupus nephritis 1/3 of nephrons are gone for good. We all lose nephrons over time but this is s a significant decline in early Lupus. Renal flares need to be treated aggressively to protect as many nephrons as possible. Target is urine protein/creatinine 0.5 g/day

- Treatments are aimed at managing renal flares. Some recent trials show promise;

- Kidney Function at 24-104 weeks showed eGFR slope on belimumab decreased and was statistically significant. It also decreased time to first renal flare (even Class 5 CKD).
- Cyclophosphamide – no efficacy. At 6 months if MMF non-responder then add cylclophosphamide or Belinumab. BLISS trial successful .5 - .7 durability of medication demonstrated > 2 years.
- LUNAR trial- Obinutuzumab had renal benefit.
- FDA approved voclasporin as it showed more favourable results even against MMF. It is a calcinueron inhibitor. FOREST trial showed voclasporin better than MMF.
- IL 16 can be measured in urine. Chemotactic pathways in kidneys are impacted. Rheumatologists can't do kidney biopsies routinely so urine tests will be coming soon and will become standard of care.

P10- LLDAS- Low Lupus Disease Activity Score is defined as;

- SLEDAI < OR = 4, PGA < or = 1,
- no major organ involvement,
- no new activity and
- prednisone <7.5 mg a day.

Lupus is complex. It is more severe in males. It is multifactorial (skin, joints, CV, renal, CNS)

If you are interested in the Pisetsky article here is the reference:
Pisetsky DS, Clowse MEB, Criscione-Schreiber LG, Rogers JL. A Novel System to Categorize the Symptoms of Systemic Lupus Erythematosus. Arthritis Care Res (Hoboken). 2019 Jun;71(6):735-741. doi: 10.1002/acr.23794. Epub 2019 Apr 23. PMID: 30354033.