

## Steroids and Osteoarthritis

Celine Perkins<sup>1</sup>, Bethan Whiting<sup>1</sup> and Paul YF Lee<sup>1,2\*</sup>

<sup>1</sup>Welshbone, South Wales Orthopaedics Research Network, Wales, UK

<sup>2</sup>LEO institute, Grantham and District Hospital, United Lincolnshire Hospitals NHS Trust, England

\*Corresponding author: Paul YF Lee, Welshbone, South Wales Orthopaedics Research Network, Wales, UK, Tel: +447764614688; E-mail: paul@welshbone.com

Received date: May 22, 2017; Accepted date: May 24, 2017; Published date: June 07, 2017

Copyright: © 2017 Lee PYF, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

### Editorial

Corticosteroids are used in the treatment of arthritis. Despite the differences in the aetiology of rheumatoid and osteoarthritis; joint pain, stiffness, swelling and deformity remain features of both conditions. These factors contribute to the disability of both conditions and impact patients' quality of life [1]. Current management is focused on reducing joint pain and inflammation, whilst improving or maintaining joint function [2] Although not recommended as the first line treatment in rheumatoid or osteoarthritis, steroids have been used selectively in the management of these symptoms. Corticosteroids are used in combination with other treatments and in various preparations. Other injectable substances are available and is explained by Golding et al in this issue. For the purpose of this editorial we will focus on the use of injected corticosteroids.

There is no standardised preparation of corticosteroid injection; make up varies locally based on a combination of clinical experience and personal preference. The different mechanisms of action can guide selection in particular clinical situations and properties are modified to optimise anti-inflammatory action [3]. Different drug delivery systems are used to increase drug residence including thermo-gelling, pH-sensitive gels and bio-adhesive materials [4]. Methylprednisolone is commonly used universally with triamcinolone hexacetonide being effective when injected into large joints and hydrocortisone into small joints [3,5].

In theory, during acute inflammation, glucocorticoids work by decreasing vascular permeability and inhibiting the migration and accumulation of polymorphonuclear lymphocytes into tissues. Apoptosis in lymphoid cells is induced, inhibiting expansion of T and B lymphocytes and reducing circulating eosinophils, basophils and monocytes. Glucocorticoids also inhibit the migration of neutrophils and inhibit the activity of fibroblasts, reducing fibrosis and scar formation. The systemic action of steroids is proven and they are consequently beneficial in managing rheumatoid arthritis. This systemic action is applied locally to intra-articular injections in osteoarthritis despite the differences in pathology to rheumatoid arthritis. The most notable contrast between the two is that rheumatoid arthritis is characterised by synovial inflammation and erosion of cartilage and bone, whereas osteoarthritis is believed to be caused by mechanical forces. Osteoarthritis exhibits the growth of osteophytes and little evidence of the typical form of inflammation only what is limited to the cartilage and bone [6].

Despite avoiding the well-known side effects of oral steroids, injected corticosteroids are not without their own potential side effects. These include pain and swelling at the site of the injection lasting a couple days and an increased risk of infection, blushing, thinning or lightening of the skin. Rare cases of sudden loss of visual acuity have been reported following injections [7]. Attention is required when

prescribing injected steroids to patients with diabetes as a temporary increase in blood sugar occurs following intramuscular injections, though this is minimal after intra-articular injections [8]. Common problems are the presence of comorbidities in which patients are taking anticoagulants. Due to the risk of bleeding into a joint these patients may need their INR monitored before an intraarticular injection [8].

Intra-articular injection of corticosteroids has been a part of the treatment of osteoarthritis for over 50 years despite limited evidence of its efficacy [9]. The recommendation (NICE guideline 117 section 1.5.12) for their use, in addition to core treatment, is based on evidence that they may be effective in providing short term relief of pain and improvement in function [10]. It is not, by any means, the first choice in managing the condition, but if physical therapies such as strength and fitness exercises and pharmacological methods are ineffective or not tolerated well, it can be an effective short-term option when used as a one off. However, the most current reviews on the use of corticosteroids in osteoarthritis still stress the need for further experimental research in order to confirm or refute the true effects of the injections, both in the short and the long term [9,10].

The traditional approach of focusing on the treatment of late stage osteoarthritis has not yielded effective disease modifying treatments, consequently clinical care focuses on palliation until joint replacement is indicated [11]. Both total hip and knee arthroplasty are cost effective procedures, with total hip replacement being slightly superior in terms of value per QALY [12]. Joint replacement is major surgery not without its complications and a growing concern is that younger patients will have an increased requirement for revision surgery [13].

Corticosteroid injections are used as a standard treatment to 'buy time' before joint surgery and is widely accepted due to no other alternative treatments. When considering the efficacy of corticosteroids in the short term, for example 3 months after injection, they are reported effective at reducing both patient reported outcomes of pain and objective measures. However, when looking long term, the benefit of an intraarticular corticosteroid injection is poor and is considered a quick fix [6,14-17]. Worryingly, recent studies have found that the dose of corticosteroid injected in osteoarthritis can actually cause chondrocyte death which could actually be exacerbating the loss of chondrocyte extra-cellular matrix, destructive loss of the dynamic cartilage system and the basis of osteoarthritis [18-20]. Moreover, corticosteroids have been undoubtedly injected with local anaesthetics without consideration to their influence on this dynamic environment within the joint capsule. Put simply, local anaesthetic has been injected to reduce the pain patients are experiencing without addressing the cause or processes of osteoarthritis which led to the pain initially. The local anaesthetic has a short term benefit to the patient without any disease modifying effects. There is an increasing bank of evidence

demonstrating local anaesthetics to be detrimental to chondrocyte viability and proliferation, consequently accelerating the processes believed central to the aetiology of osteoarthritis itself [21-25].

Additionally, in the view of pharmaceutical companies, combining corticosteroids and local anaesthetic is considered mixing your own drug. Therefore, interactions between the two agents were not considered or tested before intraarticular injections became common practice. Evidence now indicates a synergistic effect of corticosteroid and local anaesthetic on chondrocyte viability and proliferation, on top of the negative effects already imposed from these individual treatments [26]. For such a huge public health issue, osteoarthritis being the world's third biggest cause of disability, it would seem arrogant to dismiss other forms of treatment on the basis of tradition and these avenues must be explored. Would it not make more sense to inject something native into joints to facilitate joint homeostasis? With the aim to cure or at least stabilise the severity of osteoarthritis rather than compromise the cartilage, clinically promising results have been observed after injecting hyaluronic acid and platelet-rich plasma alone [14,27-29]. What is the science behind a maximum three intra-articular injections? Is it because after three injections there are no chondrocytes left to gain any benefit.

An element of the conservative management of osteoarthritis is physiotherapy [30]. The aim of which is to reduce joint stiffness, maintain range of movement and increase the strength of muscles surrounding affected joints. The possibility that the aspect of strength is impaired by a one-off steroid treatment needs consideration. It is not known whether the effects on muscle mass from a single intra-articular corticosteroid injection are similar to those previously demonstrated of intramuscular injections. However, given the known association between BMI and osteoarthritis, it may be relevant to investigate whether this treatment could be contributing to an altered body composition in these patients, consequently impairing strength gains.

In summary, there is not enough evidence for the use of steroids in osteoarthritis, we assume they are anti-inflammatory and apply systemic knowledge to local joints. Rheumatoid and osteoarthritis are very different, steroids may provide temporary pain relief but have very toxic local effects to injured cartilage and joints in osteoarthritis. Whilst in rheumatoid arthritis steroids reduce synovial inflammation, in osteoarthritis the synovium is the only source of food supply to the chondrocytes, so killing it doesn't make any logical sense. The benefits and indications for treatment with oral, intramuscular, intravenous and intra-articular steroids should not be confused or used interchangeably without a stronger evidence base. Neither should random combinations of steroid and local anaesthetic be mixed by doctors, changing the pharmacodynamics of the drug till it is no longer known what is really being injected. We need a call for the 'steroid' label of a quick fix to stop and maybe we would be better off using a more consistent treatment which doesn't require random mixing such as injecting native joint elements like hyaluronic acid.

## References

- Kramer HR, Fontaine KR, Bathon JM, Giles JT (2012) Muscle density in rheumatoid arthritis: associations with disease features and functional outcomes. *Arthritis Rheum* 64: 2438-2450.
- Cole BJ, Schumacher HR Jr (2005) Injectable corticosteroids in modern practice. *J Am Acad Orthop Surg* 13: 37-46.
- Foster ZJ, Voss TT, Hatch J, Frimodig A (2015) Corticosteroid Injections for Common Musculoskeletal Conditions. *Am Fam Physician* 92: 694-649.
- Butoescu N, Jordan O, Doelker E (2009) Intra-articular drug delivery systems for the treatment of rheumatic diseases: a review of the factors influencing their performance. *Eur J Pharm Biopharm* 73: 205-218.
- Garg N, Perry L, Deodhar A (2014) Intra-articular and soft tissue injections, a systematic review of relative efficacy of various corticosteroids. *Clin Rheumatol* 33: 1695-1706.
- Bannuru RR, Natov NS, Obadan IE, Price LL, Schmid CH, et al. (2009) Therapeutic trajectory of hyaluronic acid versus corticosteroids in the treatment of knee osteoarthritis: a systematic review and meta-analysis. *Arthritis Rheum* 61: 1704-1711.
- Balakrishnan S, Apsingi S, Manjure SB (2008) Sudden loss of visual acuity following intra-articular steroid injection in to the knee joint: a case report. *Cases J* 1: 428.
- Stephens MB, Beutler AI, O'Connor FG (2008) Musculoskeletal injections: a review of the evidence. *Am Fam Physician* 78: 971-976.
- Juni P, Hari R, Rutjes AW, Fischer R, Silletta MG, et al. (2015) Intra-articular corticosteroid for knee osteoarthritis. *Cochrane Database Syst Rev* 22: CD005328.
- McCabe PS, Maricar N, Parkes MJ, Felson DT, O'Neill TW (2016) The efficacy of intra-articular steroids in hip osteoarthritis: a systematic review. *Osteoarthritis Cartilage* 24: 1509-1517.
- Chu CR, Millis MB, Olson SA (2014) Osteoarthritis: From Palliation to Prevention: AOA Critical Issues. *J Bone Joint Surg Am* 96: e130.
- Jenkins PJ, Clement ND, Hamilton DF, Gaston P, Patton JT, et al. (2013) Predicting the cost-effectiveness of total hip and knee replacement: a health economic analysis. *Bone Joint J* 95: 115-121.
- Labeck G, Thaler M, Janda W, Agreiter M, Stockl B (2011) Revision rates after total joint replacement: cumulative results from worldwide joint register datasets. *J Bone Joint Surg Br* 93: 293-297.
- Iannitti T, Lodi D, Palmieri B (2011) Intra-articular injections for the treatment of osteoarthritis: focus on the clinical use of hyaluronic acid. *Drugs RD* 11: 13-27.
- Farkas B, Kvell K, Czömpöly T, Illés T, Bárdos T (2010) Increased Chondrocyte Death after Steroid and Local Anesthetic Combination. *Clin Orthop Relat Res* 468: 3112-3120.
- Raynauld JP, Buckland-Wright C, Ward R, Choquette D, Haraoui B, et al. (2003) Safety and efficacy of long-term intraarticular steroid injections in osteoarthritis of the knee: a randomized, double-blind, placebo-controlled trial. *Arthritis Rheum* 48: 370-377.
- Lambert RG, Hutchings EJ, Grace MG, Jhangri GS, Conner-Spady B, et al. (2007) Steroid injection for osteoarthritis of the hip: a randomized, double-blind, placebo-controlled trial. *Arthritis Rheum* 56: 2278-2287.
- Fubini SL, Todhunter RJ, Burton-Wurster N, Vernier-Singer M, MacLeod JN (2001) Corticosteroids alter the differentiated phenotype of articular chondrocytes. *J Orthop Res* 19: 688-695.
- Nakazawa F, Matsuno H, Yudoh K, Watanabe Y, Katayama R, et al. (2002) Corticosteroid treatment induces chondrocyte apoptosis in an experimental arthritis model and in chondrocyte cultures. *Clin Exp Rheumatol* 20: 773-781.
- Blanco FJ, Guitian R, Vazquez-Martul E, de Toro FJ, Galdo F (1998) Osteoarthritis chondrocytes die by apoptosis. A possible pathway for osteoarthritis pathology. *Arthritis Rheum* 41: 284-289.
- Piper SL, Kramer JD, Kim HT, Feeley BT (2011) Effects of local anesthetics on articular cartilage. *Am J Sports Med* 39: 2245-2253.
- Chu CR, Coyle CH, Chu CT, Szczodry M, Seshadri V, et al. (2010) In vivo effects of single intra-articular injection of 0.5% bupivacaine on articular cartilage. *J Bone Joint Surg Am* 92: 599-608.
- Dragoo JL, Korotkova T, Kanwar R, Wood B (2008) The effect of local anesthetics administered via pain pump on chondrocyte viability. *Am J Sports Med* 36: 1484-1488.
- Dragoo JL, Korotkova T, Kim HJ, Jagadish A (2010) Chondrotoxicity of low pH, epinephrine, and preservatives found in local anesthetics containing epinephrine. *Am J Sports Med* 38: 1154-1159.

- 
25. Piper SL, Kim HT (2008) Comparison of ropivacaine and bupivacaine toxicity in human articular chondrocytes. *J Bone Joint Surg Am* 90: 986-991.
  26. Bogatch MT, Ferachi DG, Kyle B, Popinchalk S, Howell MH, et al. (2010) Is chemical incompatibility responsible for chondrocyte death induced by local anesthetics? *Am J Sports Med* 38: 520-526.
  27. Filardo G, Kon E, Di Martino A, Di Matteo B, Merli ML, et al. (2012) Platelet-rich plasma vs hyaluronic acid to treat knee degenerative pathology: study design and preliminary results of a randomized controlled trial. *BMC Musculoskeletal Disorders* 13: 229.
  28. Rodriguez-Merchan EC (2013) Intraarticular Injections of Platelet-rich Plasma (PRP) in the Management of Knee Osteoarthritis. *Arch Bone Jt Surg* 1: 5-8.
  29. Sánchez M, Fiz N, Azofra J, Usabiaga J, Aduriz Recalde E, et al. (2012) A randomized clinical trial evaluating plasma rich in growth factors (PRGF-Endoret) versus hyaluronic acid in the short-term treatment of symptomatic knee osteoarthritis. *Arthroscopy* 28: 1070-1078.
  30. Page CJ, Hinman RS, Bennell KL (2011) Physiotherapy management of knee osteoarthritis. *Int J Rheum Dis* 14: 145-151.