The effect of synovial tissue volume shrinking on pain relief for knee osteoarthritis was overestimated or not?

We read with deep interest the article by O’Neill et al. aimed to examine whether synovitis changes following intra-articular steroid therapy. This open-label trial indicated that synovial tissue volume (STV) in knee osteoarthritis (OA) shrinks following steroid therapy and rebounds in those whose pain relapses. Thus, the authors thought that STV can be considered as a treatment target in symptomatic knee OA. We really appreciate the work that was done by the authors. The results supported the potential role of targeted therapies for synovitis in the treatment of knee OA, especially for pain relief. However, there are some worthwhile issues that need to be explored.

The authors reported that pain decreased following steroid injection, as did mean STV, and most of the patients whose pain relapsed suffered from increased STV. The persistent responders did not suffer from increased STV. Thus, the authors concluded that the fluctuation of STV correlates with the severity of knee pain. However, it should be noted that intra-articular steroid can shrink STV, and can be very effective in pain relief directly. The effect of pain relief can be resulted from the decreased STV or the intra-articular steroid. We, therefore, considered the effect of STV shrinking on pain relief for knee OA was overestimated. In order to examine the net effect of STV shrinking on pain relief, several randomised controlled trials regarding arthroscopic debridement for the treatment of knee OA can be considered as a reference. These randomised controlled trials came to a conflict result, even arthroscopic debridement for knee OA had been overused. Felson et al. indicated that arthroscopic debridement may simply remove some of the evidence while the destructive forces of OA, such as malalignment, muscle weakness, instability and obesity, continue to work. For intra-articular steroid, there were some positive effects, such as relieving pain, anti-inflammatory action and relieving swelling, other than shrinking STV. These additional effects can’t be neglected.

In addition to all the above, there are some other issues need to be mentioned. First, the coefficient of correlation between change in STV and pain score was small, which further indicated that there may exist some other confounding factors. We wonder whether there is a parallel association between STV and pain level, rather than causation. Second, 6.4% of included patients belonged to Kellgren–Lawrence (K/L) grade 4. On the one hand, it is hard to inject patients with knee OA of K/L grade 4 in our clinical practice. On the other hand, we suggest to conduct a sensitivity analysis by excluding these patients. Third, fixed-effect multiple linear panel regression (generalised multiple linear regression) was used to evaluate the association between change in pain and STV. But the authors did not mention the reason why chose this advanced statistical method, which is very strange for most of the readers. More explanation is worthy of expectation. Fourth, there were over two-thirds (64.9%) had significant patellofemoral involvement. We are not sure whether the results were adjusted by this confounding factor. Fifth, there was no difference in K/L grade between responders and non-responders. However, we have no idea whether there was no difference in tibiofemoral K/L grade as well. Sixth, the authors did not mention the use of painkillers between the follow-up and the final visits, especially for the patients whose pain relapsed. This may influence the results. Lastly, those whose pain recurred to within 20% were defined as having relapsed. Maybe the word “within” should be replaced by “over”, or did we misunderstand some important information?

We respect the great contributions of the authors, and we would also be very interested in the authors’ response to these issues.

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