What is the role of erythropoietin prolotherapy on pain relief of knee osteoarthritis?

Sir,

Knee osteoarthritis is one of the prevailing chronic joint diseases in the world. Doctors have always searched for the new, effective treatment methods with the least side effects. Intra-articular prolotherapy is one of the recent treatment methods to address chronic and severe pain. Using growth-stimulating substances, this method activates an inflammatory cascade and releases inflammatory factors resulting in cellular growth and accelerated cartilage building.[1,2] Erythropoietin is a blood cell proliferation and growth-stimulant substance recently used in damaged ligaments and muscles prolotherapy.[3,4]

Research has found that growth factors such as necrosis factor beta, erythrocytes growth factor, and the factor released from platelets (which is released from fibroblasts) result in cell proliferation increase.[3,5] The effect of inflammatory factors on cartilage restoration has been demonstrated in different studies.[6,7] Inflammation causes secondary growth factor production and injecting inflammatory factors without inflicting damage starts the proliferation phase. However, after discovering erythropoietin receptors outside hematopoietic system, many studies were carried out on its effects on nonhematopoietic parts.[1,3] In many studies, the effect of erythropoietin on musculoskeletal system has been surveyed.[1,6] It has been suggested that this hormone affects bone tissue directly (activating bone marrow cells) and indirectly (through channels transferring messages to basic cells). In the novel study conducted by Rahimzadeh *et al*. published in this journal, the authors planned to compare the ability of three methods of intra articular knee joint therapies with erythropoietin, dextrose, and pulsed radiofrequency. Intra-articular prolotherapy with erythropoietin was more effective in terms of pain level reduction and range of motion improvement compared with dextrose and pulsed radiofrequency [Tables 1-4].[4]

These studies suggest that increasing the administration dose of erythropoietin in future studies may lead to even better results. Considering the various beneficial effects of erythropoietin on nonhematopoietic tissues, more studies with more cases and higher administration doses are required to prove its probable beneficial effects on joint cartilage tissue.

Table 1: Demographic data of the patients

	Total	EPO group	Dextrose group
Patients	40	20	20
Age (mean±SD)	59.05±8.08	61.15±7.47	56.95±8.31
Male	17	9	8
Female	23	11	12

SD=Standard deviation; EPO= Erythropoietin

Table 2: Pain scores in the two groups (a maximum visual analog scale score of 10)

VAS (mean±SD)	EPO group	Dextrose group	*P* (for *t*-test)
Before intervention	6.65±0.98	7.05±0.99	0.626
2 weeks	3.15±1.08*	3.85±0.58	0.039
4 weeks	3.15±0.87	3.95±0.60	0.047
12 weeks	3.50±1.23	4.00±0.72	0.013

*Data are presented as mean±SD. SD=Standard deviation; VAS=Visual analog scale; EPO= Erythropoietin

Table 3: Knee joint range of motion over time

Range of motion (mean±SD)	EPO group	Dextrose group	*P*
Before intervention	95±19.73	104±15.18	0.562
2 weeks	105±20.60*	110±14.64	0.141
4 weeks	110±21.16	114±14.55	0.149
12 weeks	113±21.60	117±15.60	0.250

*Data are presented as mean±SD. SD=Standard deviation; EPO= erythropoietin

Table 4: Satisfaction score in the two groups

Group	Satisfaction score				Total
	Excellent	Good	Relative	Dissatisfied	
EPO group (%)	3 (15)	11 (55)	6 (30)	-	20
Dextrose group (%)	-	8 (40)	11 (55)	1 (5)	20

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Conflicts of interest

There are no conflicts of interest.

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