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Q/ Is intra-articular platelet-rich plasma injection an effective treatment for knee OA?

EVIDENCE-BASED ANSWER

A/ PROBABLY NOT, based on the balance of evidence. While low-quality evidence may suggest potential benefit, the balance of evidence suggests it is no better than placebo.

Compared with saline placebo, platelet-rich plasma (PRP) injections may improve standardized scores for knee osteoarthritis (OA) pain, function, and stiffness by 24% to 70% for periods of 6 to 52 weeks in patients with early to moderate OA (strength of recommendation [SOR]: **B**,

small randomized controlled trials [RCTs] with methodologic flaws).

Compared with hyaluronic acid (HA), PRP probably improves scores by a similar amount for periods of 8 to 52 weeks (SOR: **B**, multiple RCTs with conflicting results favoring no difference). However, since HA alone likely doesn't improve scores more than placebo (SOR: **B**, RCTs of moderate quality), if both HA and PRP are about the same, then both are not better than placebo.

Evidence summary

PRP vs placebo. Three RCTs compared PRP with saline placebo injections and 2 found that PRP improved the Western Ontario and McMaster Universities Arthritis Index (WOMAC, a standardized scale assessing knee pain, function, and stiffness) by 40% to 70%; the third found 24% to 32% improvements in the EuroQol visual analog scale (EQ-VAS) scores at 6 months¹⁻³ (TABLE¹⁻¹²).

The first 2 studies enrolled patients (mean age early 60s, approximately 50% women) with clinically and radiographically evaluated knee OA of mostly moderate severity (baseline WOMAC scores about 50).^{1,2} Investigators in the first RCT injected PRP once in one subgroup and twice in another subgroup, compared with a single injection of saline in a third subgroup.¹ They gave 3 weekly injections of PRP or saline in the second RCT.²

The third study enrolled mainly patients with early osteoarthritis (mean age early 50s,

slightly more women). Investigators injected PRP 3 times in one subgroup and once (plus 2 saline injections) in another, compared with 3 saline injections, and evaluated patients at baseline and 6 months.³

PRP vs HA. Nine RCTs compared PRP with HA injections. Six studies (673 patients) found no significant difference; 3 studies (376 patients) found that PRP improved standardized knee assessment scores by 35% to 40% at 24-48 weeks.^{7,8,10} All studies enrolled patients (mean age early 60s, approximately 50% women) with clinically and radiographically evaluated knee OA of mostly moderate severity. In 7 RCTs,^{4-6,9-12} investigators injected PRP or HA weekly for 3 weeks, in one RCT⁸ they gave 4 weekly injections, and in one⁷ they gave 2 PRP injections separated by 4 weeks.

Three RCTs used the International Knee Documentation Committee (IKDC) score, considered the most reliable standardized scoring system, which quantifies

TABLE

How platelet-rich plasma injections compare with saline or hyaluronic acid for knee osteoarthritis

Comparison	Number of patients	Outcome evaluated	Intervention sequence	Net Improvement (%) after injections				Comments
				4-8 wk	12 wk	24-26 wk	48-52 wk	
PRP vs saline	78 (156 knees) ¹	WOMAC	PRP x 1 vs saline x 1	50	54	46	—	<i>P</i> <.01 for all comparisons vs saline
			PRP x 2 vs saline x 1	50	48	40	—	
	30 ²	WOMAC	PRP x 3 vs saline x 3	36	56	68	68	<i>P</i> <.01 for all comparisons vs saline
	79 ³	EQ-VAS	PRP x 3 vs saline x 3	—	—	32	—	<i>P</i> <.05 for all comparisons vs saline
74 ³	EQ-VAS	PRP x 1 and saline x 2 vs saline x 3	—	—	24	—	<i>P</i> <.05 for all comparisons vs saline	
PRP vs HA	111 ⁴	WOMAC	PRP x 3 vs HA x 3	NS	NS	NS	NS	
	192 ⁵	IKDC score	PRP x 3 vs HA x 3	NS	—	NS	NS	
	176 ⁶	WOMAC	PGRF x 3 vs HA x 3	—	—	NS	—	
	160 ⁷	WOMAC	PRP x 2 vs HA x 3	—	—	—	40	<i>P</i> <.001 for improvement over HA
	120 ⁸	WOMAC	PRP x 4 vs HA x 4	8	25	35	—	<i>P</i> <.001 for all comparisons over HA
	109 ⁹	IKDC score	PRP x 3 vs HA x 3	NS	—	NS	NS	
	96 ¹⁰	WOMAC	PGRF x 3 vs HA x 3	—	—	—	39	<i>P</i> <.001 for improvement over HA
	55 ¹¹	KOOS and EuroQol scores	PRP x 3 vs HA x 3	—	NS	NS	—	Didn't supply raw scores
30 ¹²	IKDC score	PRP x 3 vs HA x 3	—	NS	NS	—		

EQ-VAS, EuroQol International Knee Documentation Committee (scores symptoms, activity, function) visual analog scale; EuroQol, International Knee Documentation Committee (scores symptoms, activity, function); HA, hyaluronic acid; IKDC, International Knee Documentation Committee Score (range 0-100, where high values are better); KOOS, Knee and Osteoarthritis Outcome System (scores symptoms, stiffness, pain, and function); NS, not significant; PGRF=plasma rich in growth factors (a preparation of PRP); PRP, platelet-rich plasma; WOMAC, Western Ontario and McMaster Universities Arthritis Index Score (range 0-100, where low values are better).

subjective symptoms (pain, stiffness, swelling, giving way), activity (climbing stairs, rising from a chair, squatting, jumping), and function pre- and postintervention.^{5,9,12} All 3 studies using the IKDC found no difference between PRP and HA injections. Most RCTs used the WOMAC standardized scale, scoring 5 items for pain, 2 for stiffness, and 17 for function.^{1,2,4,6-8,10}

Risk for bias

A systematic review¹³ that evaluated methodologic quality of the 3 studies comparing PRP with placebo rated 2^{1,3} at high risk of bias and one² at moderate risk. Another meta-analysis¹⁴ performed a quality assessment including 4 of the 9 RCTs^{8-10,12} comparing PRP with HA and concluded that 3 had a high risk

of bias; the fourth RCT had a moderate risk. No independent quality assessments of the other RCTs were available.^{4-7,11}

Recommendations

The American Academy of Orthopaedic Surgeons doesn't recommend for or against PRP injections because of insufficient evidence and strongly recommends against HA injections based on multiple RCTs of moderate quality that found no difference between HA and placebo.¹⁵

JFP

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