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Umbilical Cord– Derived Stem Cells for the Treatment of Knee **OSTEOARTHRITIS**

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Knee Osteoarthritis: Knee osteoarthritis is a condition that's caused by degeneration of the cartilage between the bones of the knee joint. Cartilage is the cushioning that protects the bones from friction and impact. When cartilage wears away, the bones rub against each other, causing pain, stiffness, inflammation, and limited movement. The condition also affects the bone underneath the cartilage and the nearby soft tissues. Osteoarthritis gets worse over time and may require surgery.

Prevalence: The pooled global prevalence of knee OA was **16.0%** in individuals aged 15 and over and was 22·9% in individuals aged 40 and over. Correspondingly, there are around 654·million individuals (40 years and older) with knee OA in 2020 worldwide.

Purpose: To review the literature to evaluate the efficacy of umbilical cord–derived MSCs in the treatment of OA of the knee joint.

Case study: A total of 7 studies met inclusion criteria, including **385 patients** undergoing injection of **HUC-MSCs (mean age, 59.7 years)**. The mean follow-up was **23.4 months**. The overall percentage of male patients was **43.2%** . Weighted averages of the WOMAC, macroscopic ICRS, subjective IKDC, and VAS scores.

TABLE 1
Studies Included[a]

Lead Author (Year)	LOE	Knees, n[b]	Patient age, y	Follow-up, months	BMI	Sex, % Male
Castellanos (2019)[5]	2	20	71.0 ± 6.4	6.0	29.7 ± 4.3	25.0
Chung (2021)[6]	2	93	56.6 (43.0-65.0)	20.4 (12.0-42.0)	25.8 (20.9-33.2)	NR
Dilogo (2020)[9]	2	57	58.3 ± 9.6	12.0	27.1 ± 4.4	58.6
Matas (2019)[24]	1	18	56.4 (40.0-65.0)	12.0	27.8 ± 2.6	61.1
Mead (2020)[26]	3	42	74.1 ± 9.0 (52.0-94.0)	12.0	27.7 ± 4.1 (20.3-35.3)	57.1
Park (2017)[29]	2	7	58.7 ± 15.4 (29.0-77.0)	72.9 (12.0-84.0)	26.4	28.6
Song (2020)[33]	4	128	56.5 ± 7.9 (40.0-78.0)	36.1 ± 6.4 (25.0-47.0)	24.6 ± 3.6 (17.0-45.8)	32.8
Total	—	385	59.7 (29.0-94.0)	23.4 (12.0-84.0)	26.1 (17.0-45.8)	43.2

[a]Patient age, follow-up, and BMI are reported as mean ± SD (range) (if reported), with the "Total" row reported as a weighted average. BMI, body mass index; LOE, level of evidence; NR, not reported. Dashes indicate not applicable.
[b]Number of knees injected with human umbilical cord mesenchymal stem cells in each study.

Isolation of Stem Cells: Umbilical cords were obtained from full-term placentas by cesarean delivery and stored in sterile phosphate-buffered saline, mixed with 100-U/mL penicillin and 100-mg/mL streptomycin. Wharton jelly was cut into small pieces, seeded into culture plates, and mixed with MEM Eagle Alpha Modifications (Gibco) high glucose, 10% heat-inactive FBS, 1% penicillin/streptomycin, and 2 mM L-glutamine (Gibco). At 80% confluence, cells were detached by treatment with TrypLE TM Express (Gibco) and then harvested and preserved in Profreeze (Lonza).

Injection Method: Injections were administered superolaterally into the intra-articular space under direct visualization, using an arthroscopic portal approach, whereas another study described using an anterolateral approach with the knee in 90° flexion.

Administration Strategy: Four studies administered 1 injection to each patient. In 1 study,9 patients were injected once with HUC-MSCs and then an additional 2 times with hyaluronic acid (HA) at 1-week intervals. Another study described administering 1 injection for all patients and, for those who did not demonstrate a>30% reduction in pain based on the WOMAC pain sub score, a second injection was given 6 weeks later.

Number of HUC-MSCs: Three studies used HUC-MSC dosages of 500 mL/cm^6 of chondral defect with a cell concentration of 5×10^6 cells/ml. Two studies used cell concentrations of 20×10^6 and 10×10^6 cells/mL, respectively.

TABLE 2
Results of MCMS Evaluation[a]

Study	MCMS
Castellanos (2019)[5]	68
Chung (2021)[6]	73
Dilogo (2020)[9]	70
Matas (2019)[24]	78
Mead (2020)[26]	64
Park (2017)[29]	66
Song (2020)[33]	72
Total, mean ± SD	70.1 ± 4.7

[a]MCMS, Modified Coleman Methodology Score.

TABLE 3
Outcome Scores[a]

Study	Preinjection	Postinjection	*P*
WOMAC score[b]			
Chung (2021)[6]	44.5 ± 15.1	11.0 ± 3.7	**<.001**
Dilogo (2020)[9]	24.66	14.7	.06
Song (2020)[33]	57.3 ± 11.4	10.2 ± 7.9	**.000**
Matas (2019)[24]	35.6 ± 10.1	4.2 ± 3.9	**.04**
Total	39.3	11.0	—
IKDC score			
Chung (2021)[6]	39.0 ± 10.4	71.3 ± 5.9	**<.001**
Dilogo (2020)[9]	51.4	60.7	.14
Song (2020)[33]	24.3 ± 11.1	68.5 ± 12.7	**.000**
Park (2017)[29]	39.1	63.2	.18
Total	40.9	67.3	—
VAS pain score			
Dilogo (2020)[9]	45.3	27.5	.16
Song (2020)[33]	76.4 ± 16.6	12.8 ± 11.7	**.000**
Matas (2019)[24]	39.4 ± 21.4	2.4 ± 2.1	**.02**
Park (2017)[29]	49.1	19.3	.18
Total	50.7	17.7	—
Macroscopic ICRS score			
Chung (2021)[6]	4.0	2.14 ± 0.54	NR
Song (2020)[33]	NR	1.57 ± 0.51	NR
Park (2017)[29]	4.0	2 ± 0	NR
Total	4.0	1.8	—

[a]Scores are reported as a mean ± SD (when reported, or just the mean) at latest follow-up, with the Total row reported as a weighted mean. Boldface *P* values indicate statistically significant difference between pre- and postinjection ($P < .05$). Dashes indicate not applicable. ICRS, International Cartilage Regeneration & Joint Preservation Society; IKDC, International Knee Documentation Committee; NR, not reported; VAS, visual analog scale for pain; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

[b]One study did not report exact numerical data for this score and was excluded from this table.[5]

Conclusion: Patients undergoing treatment of knee OA with HUC-MSCs might be expected to experience improvements in clinical outcomes. The results illustrated positive clinical outcomes in the assessment of both pain and function at short-term follow-up.

Furthermore, 3 studies included in this review evaluated the macroscopic ICRS score with all 3 reporting improvement in scores, indicating that HUC MSCs may actually repair cartilage damage from knee OA.

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