Section: Anaesthesia

Original Research Article

COMPARATIVE EFFICACY OF ULTRASOUND GUIDED ALCOHOLIC NEUROLYSIS OF GENICULAR NERVES ALONG WITH PRP OR PROLOTHERAPY IN PATIENTS SUFFERING FROM CHRONIC KNEE PAIN DUE TO OSTEOARTHRITIS

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Abstract

Background: Osteoarthritis (OA) of the knee joint is most common disease of joints in the elderly, causing adverse impact on physical activity, quality of life and socio-economical life. Currently, regenerative therapy has been introduced. The main aim of our study was to compare the clinical effectiveness of USG guided neurolysis of genicular nerve with intraarticular knee injection of either 25% dextrose versus autologous platelet rich plasma in treating chronic osteoarthritis knee using standard scoring systems [WOMAC SCORING-MODIFIED CRD PUNE]. **Materials and Methods:** A total of 60 patients after written and informed consent who fulfilled the inclusion criteria were enrolled. Following admission, patients were evaluated using WOMAC score, VAS score ISK score, ROM (flexion at affected knee joint. Group A received USG Guided 5 ml of PRP with alcoholic neurolysis of genicular nerves whereas Group B recieved USG guided 5 ml of 25% dextrose prolotherapy with alcoholic neurolysis of genicular nerves. The scores were compared post intervention at 1 month, 3 months and 6 months. **Result:** On inter group analysis, statistically significant reduction in both WOMAC and ISK scores was noted in group A and B at 3 months ($p=0.0016$ and $p<0.001$) and at 6 months ($p=0.00068$ and $p<0.001$) respectively. Statistically significant reduction in VAS scores were seen between PRP and prolotherapy groups at both – 3 months($p=0.063$) and 6 months ($p=0.012$) from baseline. Increase in ROM was found to be statistically significant on inter group analysis at both 3 months($p<0.001$) and at 6 months ($p<0.001$). **Conclusion:** We concluded that alcoholic neurolysis of genicular nerves with PRP was better than alcoholic neurolysis of genicular nerves with 25%-dextrose. However, prolotherapy with alcoholic neurolysis can be used for pain relief and functional improvement in patients of KL Grade 2 and 3 primary osteoarthritis of knee.

INTRODUCTION

Osteoarthritis (OA), being the most common disease of the joints in the elderly, frequently affects the knee joint causing a major source of disability owing to pain and significant loss of function.[1] OA is characterized by progressive loss of articular cartilage followed by attempted repair of articular cartilage, remodelling and sclerosis of subchondral bone and in many instances formation of subchondral bone cyst and osteophytes. The severity of the disease can be graded according to the radiographical findings by the Kellgren–Lawrence (KL) system. Source of pain is mainly attributed to changes to the non-cartilaginous components of the joint like the joint capsule, synovium, subchondral bone, ligaments, and peri-articular muscles.

In OA, multiple inflammatory mediators including plasma proteins (C-reactive protein, proposed as a marker for development and progression of OA), prostaglandins (PGE2), leukotrienes (LKB4), cytokines (TNF, IL1β, IL6, IL15, IL17, IL18, IL21), growth factors (TGFβ, FGFs, VEGF, NGF), nitric oxide, and complement components have been found in the synovial fluid. All of these components locally result in cartilage breakdown secondary to

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proteoglycan and collagen destruction induced by matrix metalloproteinases and other hydrolytic enzymes (including cyclooxygenase two and prostaglandin E).

The Goals of treatment of OA are to alleviate pain, minimize loss of physical function, and to minimize disease progression or even try to revert it. Comprehensive therapy consists of a multimodality approach including nonpharmacologic, pharmacologic, and surgical elements. there are many patients who refuse to undergo surgery so there is always a search of new treatment alternatives that might arise new horizons of treatment for patients. Recently there has been a stronger emphasis placed on developing new modalities that aim to slow the disease progression or even reverse the process in OA knee.

Platelet Rich Plasma (PRP) is an autologous concentration of a high number of platelets derived from patient's own blood in a small volume of plasma. Platelets contain large number of growth factors and cytokines which can stimulate cellular growth, vascularization, proliferation, tissue regeneration and collagen synthesis and have a beneficial effect on tendon and cartilage tissue regeneration.[2,3]

In dextrose prolotherapy, increase extracellular glucose has been revealed to increase the amount of numerous polypeptide growth factors in a diversity of human cells.[4-8] Additionally contact of various human cells to a hypertonic

dextrose solution may lead to an increase in levels of growth factors.[9,10]

Another recent technique to provide analgesia is the Ultrasound guided (USG) genicular nerve block. Genicular nerves, which are the branches of the tibial, common peroneal, and obturator nerves provides innervation to the capsule of the knee joint, as well as to the intra-articular and extra-articular ligaments. Radio frequency ablation of these nerves have recently been of considerable interest as an effective technique to alleviated knee pain, particularly in patients with knee OA.[11-14] Disadvantages of genicular nerve ablation include high procedure and equipment costs, longer procedural time, procedure-related pain, and a nonresponse rate over 25%.[15]

The main aim of our study was to compare the clinical effectiveness of USG guided neurolysis of genicular nerve with intraarticular knee injection of either 25% dextrose versus autologous platelet rich plasma in treating chronic osteoarthritis knee using standard scoring systems [WOMAC SCORING-MODIFIED CRD PUNE]. Secondary Objectives were to evaluate the degree of pain relief, to assess the improvement in range of movement of the knee joint and to study the adverse effects, if any.

MATERIALS AND METHODS

After taking ethical committee approval, from institutional ethics committee, S N Medical College Agra, wide their letter no. IEC/2021/30 a prospective comparative study was conducted between October 2019 to December 2021 on patients visiting the department of Orthopedic Medicine and Anaesthesia-pain clinic, S. N. Medical college Agra . Sixty Patients of age group between 18 and 75 years with H/O chronic knee pain ≥3 months with VAS score >4 and X-ray knee showing degenerative changes of the joint (KL grade 2–3) meeting ACR Criteria (revised 2016) were included in the study. All patients were randomized by using serially numbered opaque sealed envelope (SNOSE) technique and allocated into two groups:

Group [A] (PRP GROUP)- PRP(5ml) with alcoholic neurolysis of genicular nerves.

Group [B] (PROLOTHERAPY GROUP)- 25%dextrose(5ml) prolotherapy with alcoholic neurolysis of genicular nerves.

Written and informed consent was taken from patients and the procedure was explained. Before the procedure, all patient underwent basic laboratory and hematologic screening and were evaluated with non-weight-bearing x-ray of affected knee. All interventions were performed in an operating theatre under strict aseptic conditions. Pre injection and post injection evaluation was performed in both groups using WOMAC, ISK score, VAS score and range of motion.

The patient was laid supine with a small pillow or bolster under the knee to place the joint in mild flexion, and monitors (ECG, pulse oximeter, non-invasive blood pressure device) as per ASA standard were attached, and an intravenous access secured. High frequency(15-6MHz) linear USG probe (SONOSITE M-Turbo) was used to visualize 3 genicular nerves [superior medial genicular nerve, superior lateral genicular nerve, inferior medial genicular nerve] and diagnostic genicular nerve block was given using a volume of 2.0 ml of lignocaine 2% was injected around nerves. If the block resulted in more than 50% reduction in pain intensity for more than 2 hours at rest, on movement, and on walking for 5 minutes, it was considered successful. Therapeutic neurolysis was done afterwards using 1mL of absolute alcohol mixed with 0.25% bupivacaine injected under ultrasonographic guidance, for each of 3 nerves. The spread of drug was further confirmed with visualization of spread of drug at desired point.

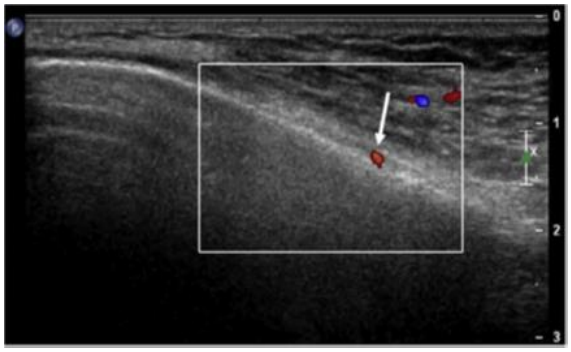

Image 1: Musculoskeletal USG image of genicular artery at the superolateral supracondylar area of

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femur, genicular nerves are located just adjacent to genicular artery)

The PRP was prepared as described by Abate et al,[1] 25 patients were given three PRP injections while the patients in other group received 5 ml of 25% dextrose in the affected knee at ~2-wk interval. The injection was made into the suprapatellar bursa of the affected knee using musculoskeletal ultrasound (SONOSITE M-Turbo) with a 15-6 MHz linear transducer to ensure proper 23G-spinal needle placement. This large bursa was chosen because it communicates freely with the articular cavity of knee joint and is easily visualized on ultrasound. Immediately after the injection, passive flexion and extension of the affected knee was performed Five to Ten times, followed by 30 mins of resting supine. Patients were given inj. Tramadol and Paracetamol for pain and instructed to limit the use of their affected knee for 24-hrs post injection, after which normal activities could resume. No standardized physical therapy protocol was used during the treatment and post injection phases.

They were discouraged and instructed not to use NSAIDs (non-steroidal anti- inflammatory), other analgesics and from starting any kind of other therapies for their osteoarthritis during the study period (6 month).

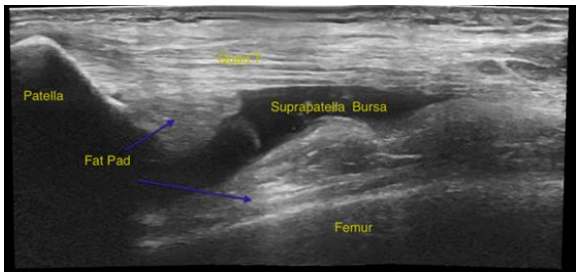

Image 2: Musculoskeltal USG image of suprapatellar bursa

Statistical analysis: The data on relevant study variables were collected and stored in pre-designed Microsoft Excel datasheets. Data was examined and verified with original proforma or any missing observations. Data were described by mean and standard deviation or in percentage as applicable. Two sample independent t-test was used to compare mean levels between groups at different time points which is 03 months and 06 months from baseline in the study. All tests were carried out with 5% level of significance as two-sided unless stated otherwise. The statistical analysis was performed by using the software IBM SPSS Statistics v 22.0 for Windows (Armonk, NY, USA).

RESULTS

Out of 60 Patients enrolled in study, 8 patients from both group were lost to follow-up so final analysis includes 52 patients. There was no significant difference between two groups in terms of baseline characteristics like age, sex, BMI, K-L grade and pain severity (table 1). Patients were clinically evaluated for pain, stiffness and difficulty in motion by WOMAC (modified CRD-pune version) & ISK score.

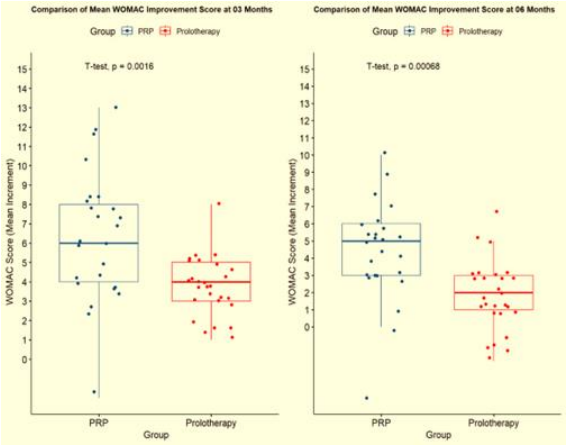

Figure 1: Inter group analysis of mean WOMAC improvement scores at 3 months and 6 months

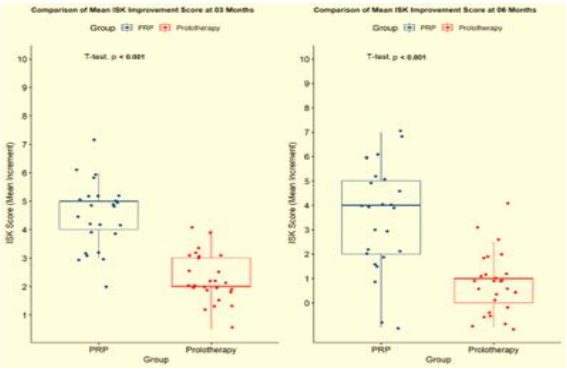

Figure 2: Inter group analysis of mean ISK improvement scores at 3 months and 6 months

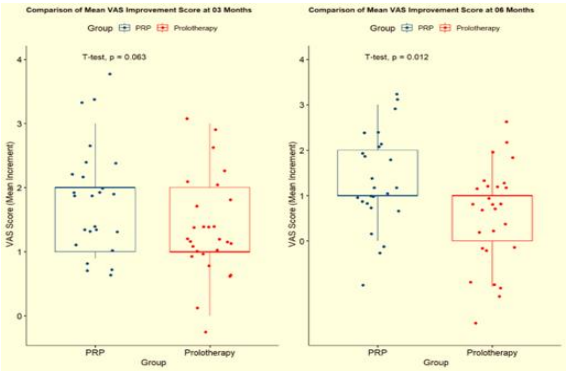

Figure 3: Inter group analysis of mean VAS improvement scores at 3 months and 6 months

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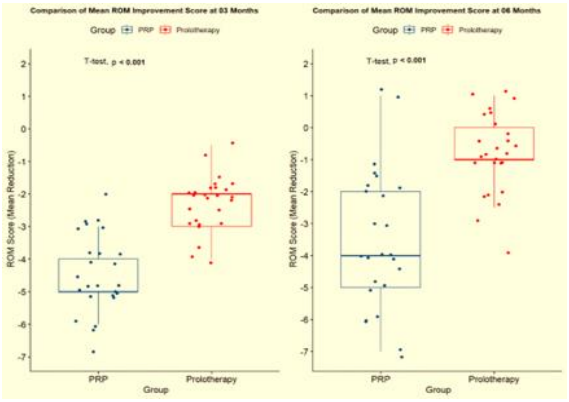

Figure 4: Inter group analysis of mean ROM improvement scores at 3 months and 6 months

Mean values of WOMAC and ISK score at baseline in group A were 37.84+7.531 and 11.580+1.0962 respectively which dropped to 31.56+8.237 and 7.120+0.9712 at the end of 3rd month and to 33.48+8.771 and 8.080+2.0447 at the end of 6 months. Meanwhile, the baseline WOMAC and ISK scores in group B were 35.30+7.824 and 11.580+1.1688 respectively which dropped to 31.56+8.064 and 9.204+1.3248 at the end of 3rd month and to 33.48+8.355 and 10.630+1.5102 at the end of 6 months [Table 2].

On inter group analysis, statistically significant reduction in both WOMAC and ISK scores was noted – 3 months($p=0.0016$ and $p<0.001$) and at 6 months ($p=0.00068$ and $p<0.001$) [Figure 1&2].

Mean values of VAS score at baseline were 6.72+1.173 and 6.33+1.109 in group A and group B respectively which dropped to 4.96+1.485 and 5.00+1.330 at the end of 3rd month and to 5.40+1.472 and 5.78+1.368 at the end of 6th month [Table 2]. Statistically significant reduction in VAS scores were seen between PRP and prolotherapy groups at both – 3 months($p=0.063$) and 6 months($p=0.012$) from baseline [Figure 3].

Mean values of ROM in group A and group B at baseline were 94.12+5.897 and 92.52+5.323 respectively which increased to 104.04+6.147 and 99.74+7.294 at the end of 3rd month and to 98.60+7.687 and 96.04+6.757 at the end of 6th month [Table 2]. ROM was found to be statistically significant on inter group analysis at both 3 months ($p<0.001$) and at 6 months($p<0.001$) at baseline [Figure 4]. No adverse effects were seen in any of the patients of both groups except mild swelling which lasted for about 24 hrs. and did not require any treatment.

Table 1: demographic characteristics

Parameter		PRP	PROLOTHERAPHY	Sig. (p-value)
Age		58.76 ± 4.28	59.00 ± 4.23	0.840
Sex	F	15 (60.00%)	16 (59.30%)	0.957
	M	10 (40.00%)	11 (40.70%)	
BMI		28 ± 2.64	28.00 ± 2.77	0.990
KL Grade	Gr. 2	7 (46.70%)	15 (53.30%)	0.897
	Gr. 3	18 (48.60%)	11 (51.40%)	

Table 2: Comparison of various Scores in between the two groups

Score	PRP (n=25)	Prolotherapy (n=27)
WOMAC Score (0months)	37.84+7.531	35.30+7.824
WOMAC Score (3months)	31.56+8.237	31.56+8.064
WOMAC Score (6months)	33.48+8.771	33.48+8.355
ISK Score (0 months)	11.580+1.0962	11.385+1.1688
ISK Score (3 months)	7.120+0.9713	9.204+1.3248
ISK Score (6 months)	8.080+2.0447	10.630+1.5102
VAS Score (0 months)	6.72+1.173	6.33+1.109
VAS Score (3 months)	4.96+1.485	5.00+1.330
VAS Score (6 months)	5.40+1.472	5.78+1.368
ROM (0 months)	94.12+5.897	92.52+5.323
ROM (3 months)	104.04+6.147	99.74+7.294
ROM (6 months)	96.04+6.757	96.04+6.757

Table 3: Comparison of mean WOMAC scores between the 2 groups at 3 months and 6 months

	Levene's Test for Equality of Variances		t-test for Equality of Means						
	F	Sig.	t	Df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
								Lower	Upper

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Decrease in WOMAC @ 3 Months	Equal variances assumed	11.090	.002	3.539	50	.001	2.53926	.71760	1.09791	3.98061
	Equal variances not assumed			3.445	32.288	.002	2.53926	.73702	1.03853	4.03999
Decrease in WOMAC @ 6 Months	Equal variances assumed	.878	.353	3.708	50	.001	2.54519	.68645	1.16641	3.92396
	Equal variances not assumed			3.662	43.366	.001	2.54519	.69503	1.14386	3.94651

Table 4: Comparison of mean ISK scores between the 2 groups at 3 months and 6 months

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
Decrease in ISK @ 3 Months	Equal variances assumed	3.381	.072	7.559	49	.000	2.17154	.28730	1.59419	2.74888
	Equal variances not assumed			7.508	42.997	.000	2.17154	.28923	1.58824	2.75484
Decrease in ISK @ 6 Months	Equal variances assumed	8.984	.004	5.395	49	.000	2.69231	.49906	1.68942	3.69520
	Equal variances not assumed			5.340	37.682	.000	2.69231	.50421	1.67131	3.71331

Table 5: Comparison of mean VAS scores between the 2 groups at 3 months and 6 months

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	T	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
Decrease in VAS @ 3 Months	Equal variances assumed	.155	.695	1.905	50	.063	.42667	.22398	-.02321	.87654
	Equal variances not assumed			1.901	49.098	.063	.42667	.22448	-.02442	.87776
Decrease in VAS @ 6 Months	Equal variances assumed	.437	.512	2.600	50	.012	.76444	.29402	.17389	1.35499
	Equal variances not assumed			2.613	49.889	.012	.76444	.29258	.17676	1.35213

Table 6: Comparison of mean ROM between the 2 groups at 3 months and 6 months

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	Df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
Increase in ROM @ 3 Months	Equal variances assumed	3.381	.072	-7.559	49	.000	-2.17154	.28730	-2.74888	-1.59419
	Equal variances not assumed			-7.508	42.997	.000	-2.17154	.28923	-2.75484	-1.58824
Increase in ROM @ 6 Months	Equal variances assumed	8.984	.004	-5.395	49	.000	-2.69231	.49906	-3.69520	-1.68942

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	Equal variances not assumed			-5.340	37.682	.000	-2.69231	.50421	-3.71331	-1.67131

DISCUSSION

The conservative treatment of knee osteoarthritis has been well documented in the literature over the past 5 decades. Treatment with PRP restores the natural rheologic and metabolic homeostasis of the joints affected by the arthritic process. The biochemical modifications induced by PRP treatment improve the protective, lubricating, and shock-absorbing effect of the synovial fluid.

Two recent innovative treatment methods which have been promised to improve cartilage repair and soft tissue healing are PRP and prolotherapy.[17] Some,[16,18-22] prospective studies have been designed to evaluate the effectiveness of PRP, Prolotherapy and Genicular neurolysis separately on knee OA and have obtained statistically significant improvements in all the clinical scores at the end of therapy.

Chemical neurolysis techniques are more effective method to accomplish a larger, complete and thorough lesioning as compared to an RFN needle. In our cases, we used 1 mL of 99% alcohol with 0.25% Bupivacaine to maintain about a 50% concentration of alcohol in the tissues. The usual concentration of ethyl alcohol used for chemical neurolysis varies from 30% to 100% solution.[23] We believe that chemical neurolysis is cheaper alternative than RFN and its significance should be investigated further.

Results of present study indicated that PRP along with Genicular neurolysis can significantly decrease pain, joint stiffness and improve quality of life. There was significant improvement of pain at one month but not as much at 6 months. So there was weaning of beneficial effects gained earlier but also at 6 months follow up, these improvements were significantly better when compared to baseline. Weaning was faster in prolotherapy group which showed that PRP is better therapeutic agent for cartilage repair than dextrose prolotherapy. We used many scoring systems like WOMAC score, ISK score, VAS score which added advantage to our study. By adding genicular nerve neurolysis, there was more improvement in all scores like study by Jean-Lon Chen et al,[24] which also showed that the application of perineural genicular nerve blocks by injecting 5% dextrose water further augments the treatment effectiveness of platelet rich plasma, offering long-lasting pain and functional improvements of the knee joints lasting up to a period of 6 months. Rushin maria das et al,[16] performed chemical neurolysis (by alcohol) of genicular nerves and found good outcome with >50% improvement in in their NRS scores like our study.

Our study like Alireza Pishgahi et al,[20] Rayegani S M et al,[25] found the effectiveness of PRP over dextrose Prolotherapy in knee osteoarthritis patient using VAS and WOMAC score for outcome measurementOur study is comparable to Shu-Fen Sun et al,[26] which reported significant ISK reduction after PRP injection in patients with knee OA. In our study, there was mean improvement in range of flexion(9.92 degrees) at knee joint which was more than Adel H. Hegaze et al (7 degrees).

Limitations of study: Several limitations existed in this study. First, it was a single center study with small sample size, and we recruited patients with K-L grade 2 and 3 OA Knee only. The result cannot be generalized to all the OA populations with different radiographic severity. Second, the injector and the patients were not blinded in this study. However, the injector was not involved in outcome assessments and data analysis and the evaluator remained blinded to the study groups and treatment. Third, the combination of Genicular neurolysis with PRPor Prolotherapy in our study was done by sequential neurolysis of genicular nerves followed by PRP or Prolotherapy. Whether PRP or Prolotherapy should be given first, followed by Alcoholic neurolysis, vice versa or by new technology, remains unclear. Fourth, we did not investigate the effect of study on the cartilage and joint structure that needed Advanced imaging such as MRI, that cant be included due to higher cost. Fifth, Short period of follow-up of only 6 month, which is relatively short for a chronic disease like osteoarthritis of knee.

As our study is conducted at single center with limited small number of patients so for better analysis, we recommend study to be conducted at multi-center with large number of sample size.

CONCLUSION

Hence we conclude that alcoholic neurolysis of genicular nerves with PRP was better than alcoholic neurolysis of genicular nerves with 25%-dextrose. However,prolotherapy with alcoholic neurolysis can be used for pain relief and functional improvement in patients of KL Grade 2 and 3 primary osteoarthritis of knee.

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