Louthrenoo et al.[8] found that diacerein was as effective as piroxicam in the treatment of symptomatic knee OA and concluded that diacerein had a better safety profile and an added advantage of carry-over effect.

Baliga et al.,[9] reported that there was a statistically significant early reduction in the mean VAS scores in knee OA patients given diacerein Modified-Release (MR) 100 mg and conventional diacerein 50 mg for 8 weeks.

Singh et al. [10] concluded that the use of diacerein and diclofenac sodium together decreased pain and improved function significantly more than diclofenac sodium alone in knee OA. The pain relieving effect of diacerein plus diclofenac (group III) of the present study is consistent with the finding of Singh et al.[10] However, diacerein alone appeared as effective as diclofenac plus diacerein in the present study.

Zheng et al. [11] concluded that diacerein was as effective as diclofenac sodium in treating patients with knee OA. This agrees with inter-group comparisons in this study. However, intra-group changes following treatment in this study suggest that diacerein alone might be better than diclofenac alone when assessment was done two months after therapy.

In the present study, diacerein alone (but not diclofenac alone or diacerein combined with diclofenac) improved the walking time two months after therapy. The finding that diacerein alone was better than diacerein plus diclofenac sodium in improving the walking time two months after therapy; might suggest that diclofenac sodium might have interfered with the structure modifying effect of diacerein, if they were taken together for two continuous months.

Furthermore, it should be noted that the lack of efficacy of diclofenac sodium in improving the walking time might have been also due to the low dose of diclofenac sodium (75 mg per day, which is half the maximum daily dose) and/or the low number of patients in this group. It should be noted that the effect of diacerein on the walking time was not previously addressed.

Regarding the observed adverse reactions during the two-month period, it was generally mild. But combined intake of diacerein and diclofenac sodium might increase side effects. Diarrhea was seen in 40% of patients who were taking diacerein (groups I and III). This does not contradict the findings of others.[12] However; the risk of diacerein intake for > 2 months was not investigated in this study.

In conclusion, diacerein appeared as effective as diclofenac sodium in improving pain severity. Diacerein, unlike diclofenac sodium, was effective in improving the walking time. Either diacerein or diclofenac sodium showed little side effects. However, it seemed that the addition of diclofenac to diacerein might increase side effects. In light of this study, it may be recommended to give diacerein (osteocerein) for patients with knee OA to control their knee pain for up to 2 months without serious or intolerable side effect, especially in those who have contraindication to NSAIDs.

Recommendations: Further studies are needed to investigate the long term effects of diacerein with and without NSAIDs on a large number of patients with OA. Also, it is recommended to reassess patients every 2 weeks during the first month (i.e. before diacerein exerts its effect).

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Table 1: Demographic and clinical data of the studied patients.

		Group I	Group II	Group III	Test (*p* value)
		n= 20	n=10	n= 20	
Age (years)	Median (Min- Max)	55 (51- 73)	55 (51- 64)	56.5 (51- 70)	H= *0.519* (*p*=.771)
Onset *n (%)*	Gradual	14(70)	10(100)	13(65)	MCp= .341
	Sudden	2(10)	0(0)	2(10)	
	Acute	4(20)	0(0)	5(25)	
Disease duration (Months)	Median (Min- Max)	12 (1- 180)	12 (1- 60)	15 (1- 240)	H= 0.532
Course n (%)	Progressive	18(90)	10(100)	20(100)	FEp= .350
	Intermittent	2(10)	0(0)	0(0)	
Side involved n (%)	Bilateral	15(75)	8(80)	15(75)	MCp=.967
	Right	2(10)	1(10)	1(5)	
	Left	3(15)	1(10)	4(20)	
Mild effusion n (%)	Yes	10(50)	0(0)	10(50)	FEp=.016*
	No	10(50)	10(100)	10(50)	
Tenderness n (%)	Yes	17(85)	10(100)	18(90)	FEp= .61
	No	3(15)	0(0)	2(10)	
Crepitus n (%)	Palpable	13(65)	3(30)	13(65)	MCp= .24
	Audible	6(30)	6(60)	4(20)	
	Rt audible/ Lt palpable	1(5)	0(0)	2(10)	
	Rt palpable/ Lt audible	0(0)	1(10)	1(5)	
Knee Alignment n (%)	Normal	13(65)	7(70)	7(35)	MCp= .23
	Genu varum	6(30)	2(20)	9(45)	
	Genu valgum	1(5)	1(10)	4(20)	

H: Kruskal Wallis test; MCp: Monte Carlo test; FEp: Fisher Exact test. *Significant

Table 2: Pain visual analogue scale and the 20 meters fast walking time in the studied groups before and after treatment (intra-group comparison).

	Groups	Before treatment	After Treatment		Friedman $\chi 2$	*P*
			After 1 month	After 2 months		
Pain (VAS, in mm)	Group I(n=20)	70_a(30-100)	$50_{a,b}$(0-100)	50_b(10-90)	11.742	.033*
	Group II(n=10)	90(50-100)	85(20-100)	70 (10-100)	5.586	.061
	Group III (n=20)	70_a (50-100)	55_a(0-90)	60_a (20-100)	6.083	.048*
Walking time (sec)	Group I (n=20)	20_a (13-34)	$18_{a,b}$ (11-33)	17_b (12-23)	14.147	.001*
	Group II (n=10)	20.5 (17-36)	20.5 (16-43)	21 (16-30)	1. 967	.393
	Group III (n=20)	19.5 (10-59)	20 (10-56)	26 (10-63)	3.647	.161

Note: Minimum and maximum appear in parentheses below the medians. Medians with differing subscripts within rows are significantly different at the adjusted $p < 0.05$ based on post hoc paired comparisons. *p Significant.

Table 3: Comparison between the three studied groups regarding pain VAS and the 20 meters fast walking time (inter-group comparison).

Assessment		Studied Groups			H	*p*	Adjusted *p**
		G I	G II	G III			
		n= 20	n=10	n= 20			
Pain (VAS, in mm)	Before treatment versus After 1 month	10 (-40- 90)	0 (-20- 40)	20 (-20- 90)	1.419	.492	.159
	After 1 month versus After 2 month	0 (-40- 50)	5 (-10- 50)	0 (-60- 40)	1.650	.438	.924
	Before treatment versus After 2 months	30 (-40- 70)	10 (0- 40)	25 (-20- 40)	2.247	.325	.263
Walking time (sec)	Before treatment versus After 1 month	1.5 (-13- 6)	0 (-7- 4)	1 (-20- 7)	3.497	.174	.290
	After 1 month versus After 2 month	1_a (-2- 17)	5_a (-3- 13)	-1_a (-21- 8)	7.207	.027	.006†
	Before treatment versus After 2 months	2.5_a (-2- 16)	$5_{a,b}$ (-3- 6)	0_b (-21- 13)	8.454	.015	.008†

Note: Minimum and maximum appear in parentheses below medians. Medians with differing subscripts within rows are significantly different at the adjusted p <0.05 based on post hoc paired comparisons.*: p value after adjustment for height, occupation and effusion by linear regression model. †: Significant.

Table 4: The frequency of adverse reactions.

Adverse reaction	Patient's groups		
	G I (n=20)	G II (n=10)	G III (n=20)
	n (%)	n (%)	n (%)
Heartburn	-	2(20%)	5(25%)
Nausea	-	2(20%)	4(20%)
Mild Diarrhea	8(40%)	-	8(40%)
Urine discoloration	20(100%)	-	20(100%)