

A COMPARATIVE STUDY ON THE SAFETY AND EFFECTIVENESS OF GLUCOSAMINE-DIACEREIN AND UNIVESTIN – CHONDROITIN IN KNEE OSTEOARTHRITIC PATIENTS IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Background: Knee Osteoarthritis is a progressive disease showing increasing trend of occurrence in a population .It has lead to great morbidity and disability. Combinations which showed anti-inflammatory property and suppression of cartilage degeneration are better options for management of knee osteoarthritis. According to medical practice, quick relief within short period of exposure to drug therapy is preferred. This study was an attempt to compare the safety and effectiveness of diacerein-glucosamine and univestin-chondroitin combinations in knee osteoarthritic patients in a tertiary care hospital. These drugs are now prescribed by Indian physicians in the current scenario.

Patients and Method: The study began only after getting the approval from Institutional Ethics Committee and obtaining Inform Consent from subjects. The study was conducted in the department of orthopedics in Pushpagiri Medical College hospital, Kerala. From 140 patients who arrived at the Orthopedics OPD Pushpagiri medical college hospital, we sorted and selected only 64 patients based on the study criteria. We divided into two groups (32 each) one receiving diacerein-glucosamine and another receiving univestin chondroitin combinations. From these groups grade 1 and 2 patients are subdivided. They were assessed by WOMAC, KOOS, VAS, 6 minute walk test, and Standard ADR questionnaires (Naranjo's) for measuring safety and effectiveness of drug combinations. Change in the short term effectiveness for both drugs measure was assessed before the start of treatment, and after 30 days of treatment.

Conclusion: For Grade 1 patients both drugs were equally effective. But for Grade 2 Patients diacerein-glucosamine combination therapy shows more benefit than univestin-chondroitin. However, semi-synthetic drug combination showed more safety profile than synthetic drug combination in the short term treatment of knee osteoarthritis.

Keywords : univestin –chondroitin , diacerein-glucosamine , OA , WOMAC , KOOS , VAS

INTRODUCTION

OA (Osteoarthritis) may be defined as a heterogeneous group of conditions that lead to joint symptoms and signs which are associated with defective integrity of articular cartilage in addition to related changes in the underlying bone and at the joint margins. OA is usually a progressive disease of synovial joints that represents failed repair of joint damage that results from stresses that may be initiated by an abnormality in any of the synovial joint tissues including articular cartilage, subchondral bone, ligament mensci, periarticular muscles,

peripheral nerves or synovium. This ultimately results in the breakdown of cartilage and bone leading to the symptoms of pain, stiffness and functional disability. Abnormal intra-articular stress and failure of repair may rise as a result of biochemical, biomechanical and genetic factors. This process may be localized to as single joint, a few joint or generalized and the factors that initiate OA likely varying depending on the joint site.⁽¹⁾

MATERIALS AND METHODS

STUDY DESIGN: Prospective Observational Study

STUDY SETTING: Tertiary care setting; Department of Orthopedics; Pushpagiri Medical College Hospital, Thiruvalla.

STUDY POPULATION: All patients with Kellgren-Lawrance Osteoarthritic (knee) Grade 1,2 reported to Department of Orthopedics, Pushpagiri Medical College Hospital, Thiruvalla

STUDY PERIOD: 6 months

SAMPLE SIZE: As per the following equation,

$$n = [(Z_{1-\alpha/2} + Z_{1-\beta}) \sigma]^2 / d^2, \quad n=64$$

$Z_{1-\alpha/2}$: value of z at significance level 5%

$Z_{1-\beta}$: value of z at power 95%

σ : standard deviation of population

d : difference of the means

INCLUSION CRITERIA

- OP patients in orthopedics department.
- Both female and male patients.
- Those who give consent voluntarily to participate in the study.
- Patients receiving diacerein-glucosamine and univestin – chondroitin combinations.
- Patients sorted for grade 1, 2 osteoarthritis (knee).
- Patients between the age of 35-70. Patients with primary knee OA.
- Patients having comorbidities of hypertension or diabetes can be included.
- Patients receiving NSAIDs for one week.

EXCLUSION CRITERIA:

- Patients who are not willing to give consent.
- Patients taking steroid medications.
- Patients who were advised or had undergone knee replacement surgery.
- Patients having Pre-existing deformities of knee.
- Patients having rheumatoid arthritis, seronegative arthritis, gouty arthritis and secondary osteoarthritis.

- Patients having previous history of fracture and trauma. Patients with renal insufficiency.
- Patients receiving anticoagulants.

BRIEF PROCEDURE OF THE STUDY

➤ A prospective, observational study was conducted in Department of orthopedics at Pushpagiri Medical College Hospital on the topic comparative study on the safety and effectiveness of glucosamine-diacerein and univestin – chondroitin in knee osteoarthritis patients in a tertiary care hospital.

➤ The entire study was carried out only after getting approval from Institutional Ethics Committee.

➤ The selection of patients was based upon the inclusion and exclusion criteria. All patients were provided with a brief introduction regarding the study and the confidentiality of the data. A written Informed Consent was obtained from the patient or care-giver. Patients who met inclusion criteria were first divided into two groups.

➤ Demographic details of the patients were collected and recorded.

➤ One set of patients received Glucosamine (750mg)-diacerein (50mg) and others received Univestin (250mg) Chondroitin (200mg), for a period of 1 month.

➤ The patients were also prescribed with NSAID for 1 week along with the medication.

➤ The patients were further divided into 2 groups based on the Kellgren-Lawrence grade 1, 2.

➤ We used the standard questionnaire including WOMAC, KOOS, VAS, 6 minute walk test, and Standard ADR questionnaires.

➤ Between the two groups, change in the short term efficacy measure was assessed before the start of treatment, and after 30 days of treatment.

RESULT:

In the prospective observational study 64 patients with grade 1 and 2 knee OA were selected. Among them 32 were received Univestin – chondroitin (DRUG 1) and others received Diacerein - Glucosamine (DRUG 2) combinations respectively.

1. WOMACQUESTIONNAIRE

Table 1: Distribution of patients according to gender by WOMAC index

Gender	Frequency	Percentage
Male	12	18.8
Female	52	81.3
Total	64	100

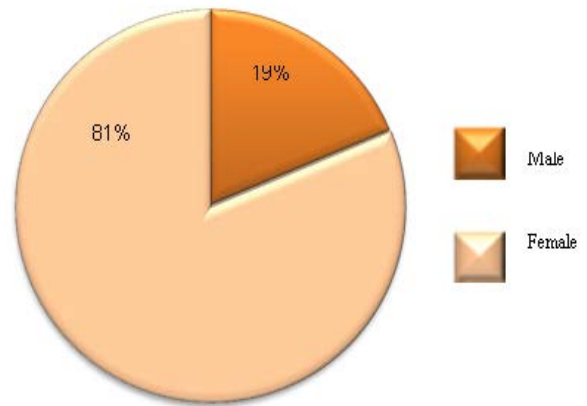


Figure 1: Graphical representation for Distribution of patients according to Gender

Table 2: Distribution of patients according to age by WOMAC index

DRUG	No: of patients	Minimum	Maximum	Mean	Std.deviation
1	32	36	80	59.969	11.9069
2	32	36	72	53.313	11.0262

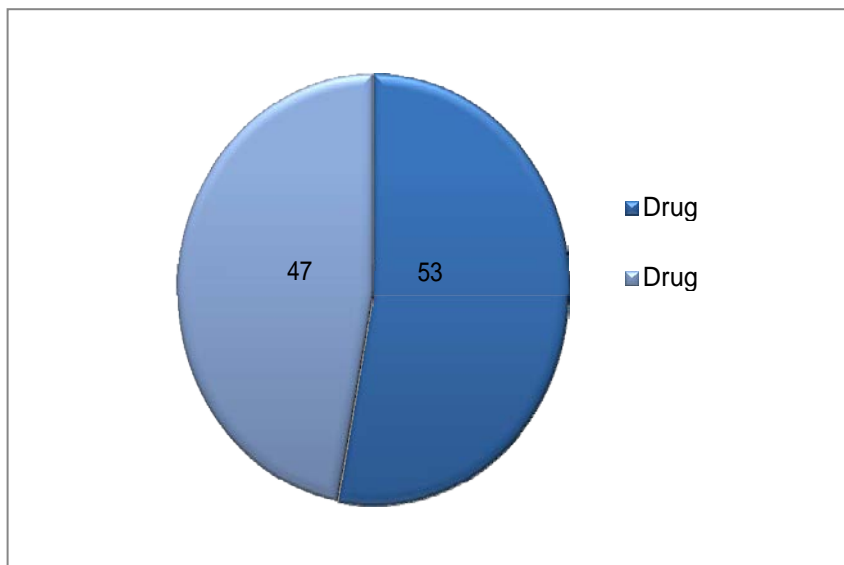
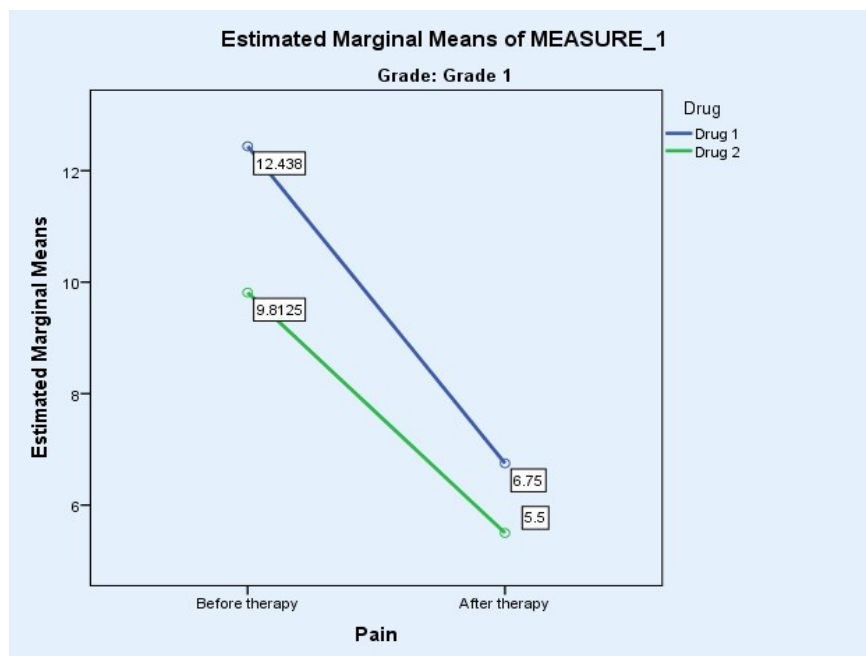


Figure 2: Graphical representation for Distribution of patients according to age by WOMAC index

Table 3: Table representing the statistical analysis of difference in pain in study subjects by WOMAC index

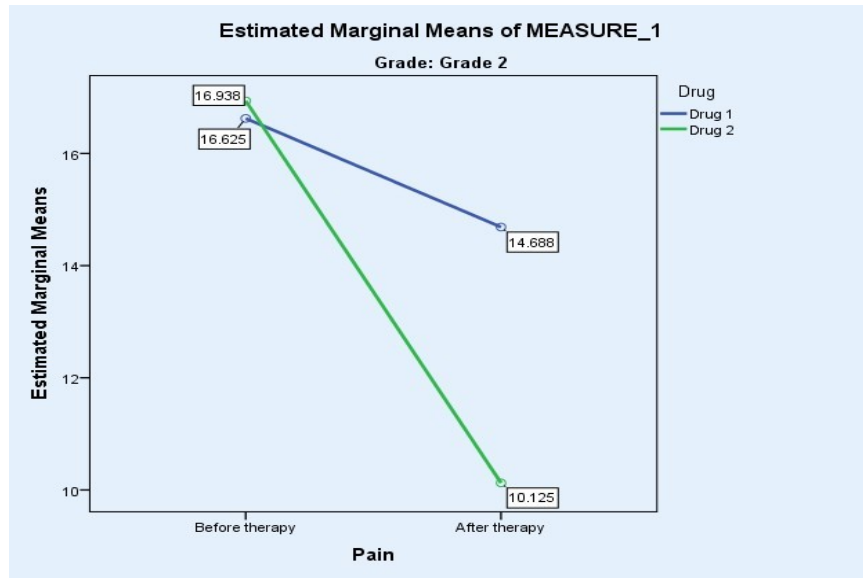
Patients		Mean square	F-value	Significance
Grade 1	Before and After therapy	400	208.923	0.000
	Before and after therapy against both drugs	7.653	3.950	0.056
Grade 2	Before and After therapy	306.250	87.761	0.000
	Before and after therapy against both drugs	95.063	27.242	0.000

Figure: 3(a)



There is no considerable change of effect in pain by the use of drug 1 and 2 in grade 1 patients

Figure: 3(b)



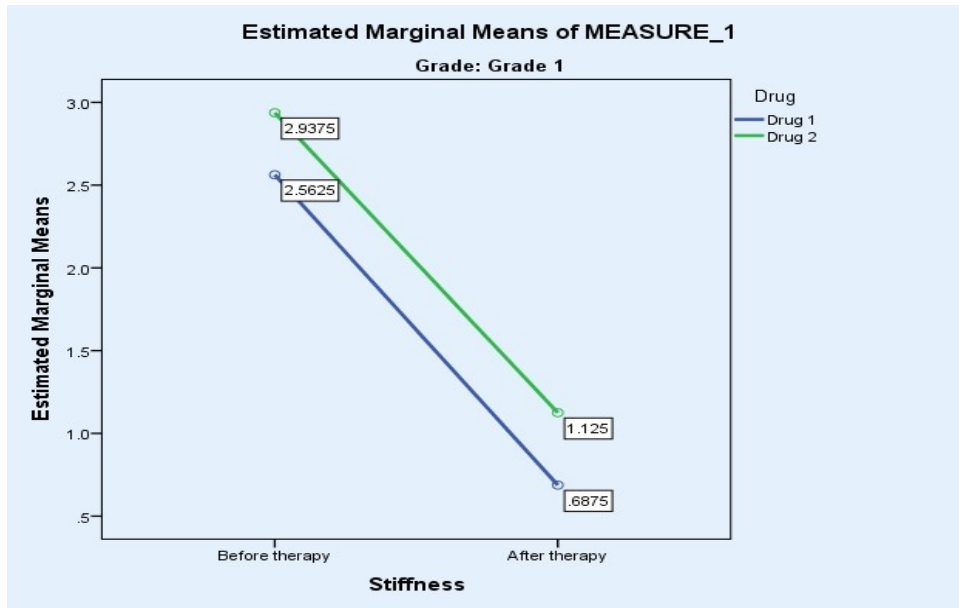
In grade 2 patients there is decrease in pain by the use of drug 2 compared to drug 1. Thus drug 2 is more effective in case of grade 2 patients.

Figure 3: Graphical Representation for estimated marginal measure of pain using WOMAC index score.

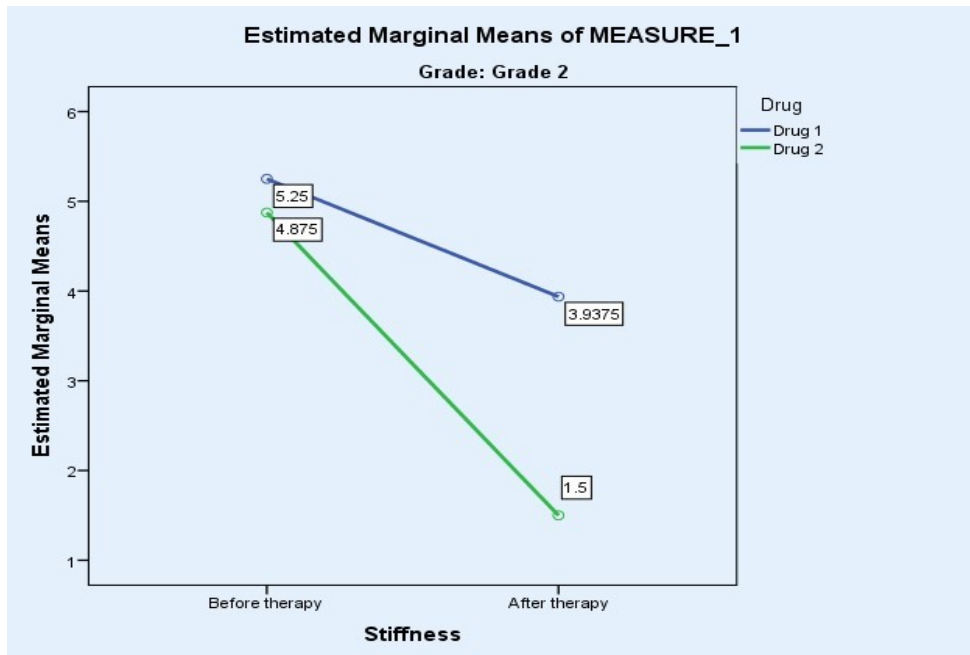
Table 4: Table representing the statistical analysis of difference in stiffness in study subjects by WOMAC index

Patients		Mean square	F-value	Significance
Grade 1	Before and After therapy	54.391	34.648	0.000
	Before and after therapy against both drugs	0.016	0.010	0.921
Grade 2	Before and After therapy	87.891	47.428	0.000
	Before and after therapy against both drugs	17.016	9.180	0.005

Figure4(a)



There is no considerable change of effect in stiffness by the use of drug 1 and 2 in grade 1 patients. Figure:4(b)



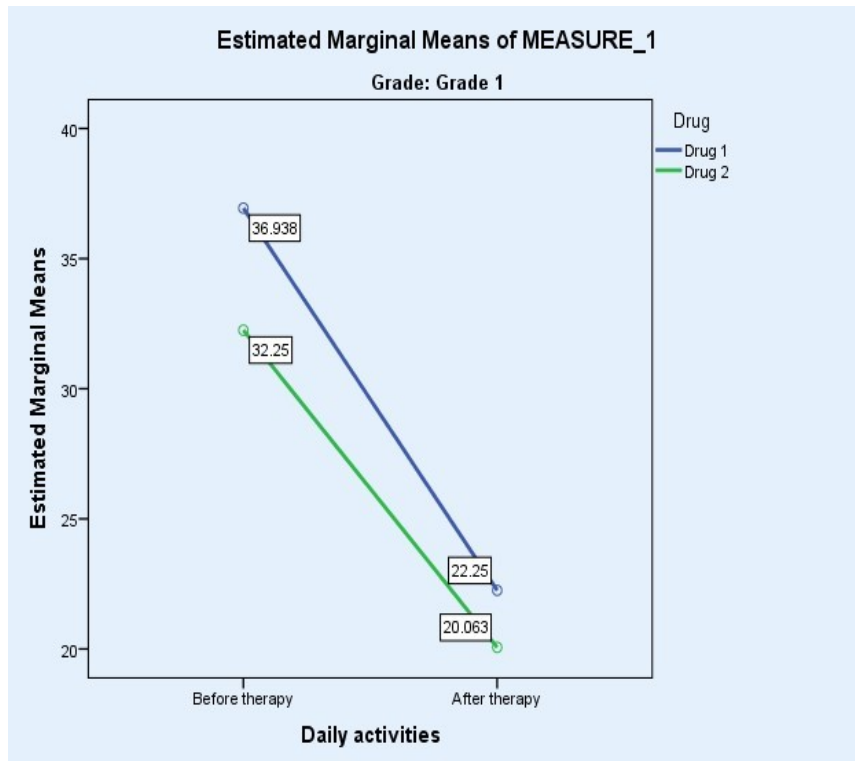
In grade 2 patients there is decrease in stiffness by the use of drug 2 compared to drug 1. Thus drug 2 is more effective in case of grade 2 patients.

Figure 4 (a,b): Graphical Representation for estimated marginal measure of stiffness by WOMAC index score.

Table 5: Table representing the statistical analysis of variability in daily activities of study subjects by using WOMAC index.

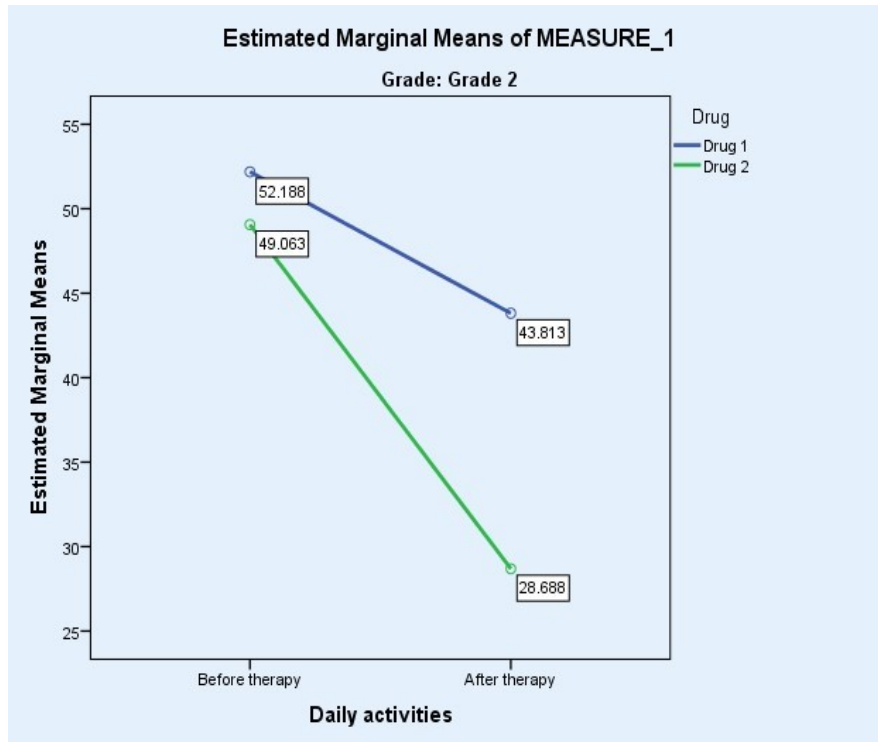
Patients		Mean square	F-value	Significance
Grade 1	Before and After therapy	2889.063	258.770	0.000
	Before and after therapy against both drugs	25.000	2.239	0.145
Grade 2	Before and After therapy	3306.25	128.357	0.000
	Before and after therapy against both drugs	576.000	22.362	0.000

Figure 5(a)



There is no considerable change of effect in daily activities by the use of drug 1 and 2 in grade 1 patients.

Figure5(b)



In grade 2 patients there is better changes in daily activities by the use of drug 2 compared to drug 1. Thus drug 2 is more effective in case of grade 2 patients.

Figure 5 (a,b): Graphical Representation for estimated marginal measure of daily activities by WOMAC index score.

1. KOOSQUESTIONNAIRE

Table 6: Table for Distribution of patients according to age by KOOS index

DRUG	GRADE	Minimum	Maximum	Mean	Std.deviation
1	Grade1	36	80	59.94	13.359
	Grade2	38	80	60.00	10.702
2	Grade1	36	66	53.81	9.446
	Grade2	37	72	52.81	12.708

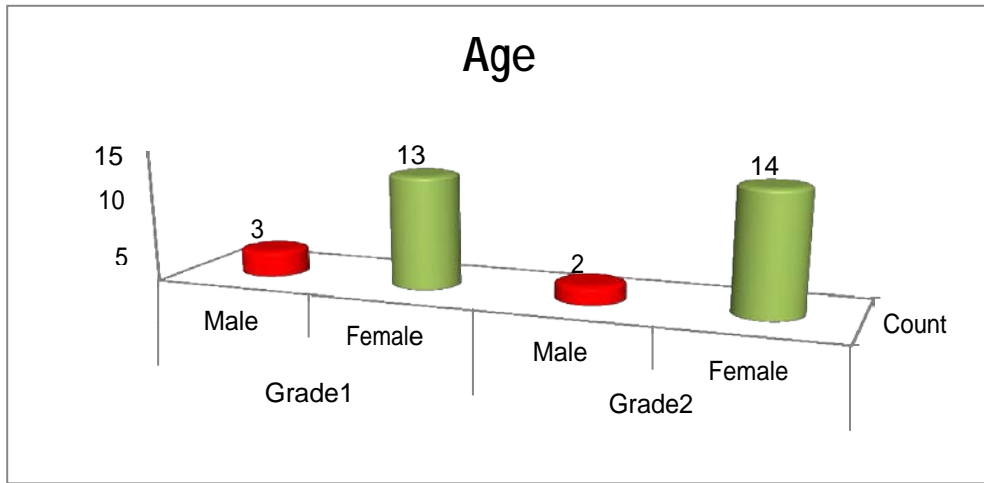


Figure 6: Graphical representation for Distribution of age according to KOOS score

Table 7: Table for Distribution of patients according to gender by KOOS index

Drug	Grade	Sex	Count	Percent
Drug 1	Grade 1	Male	3	18.8
		Female	13	81.3
	Grade 2	Male Female	2	12.5
			14	87.5
Drug 2	Grade 1	Male	4	25.0
		Female	12	75.0
	Grade 2	Male Female	1	6.3
			15	93.8

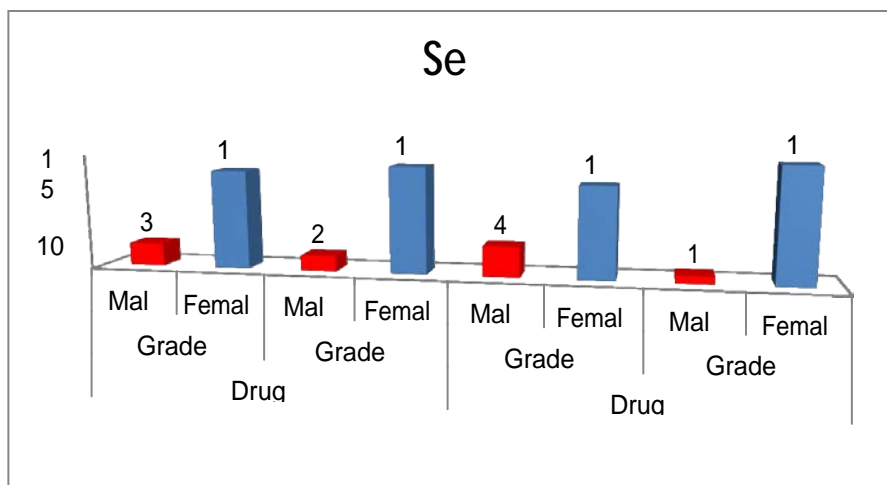
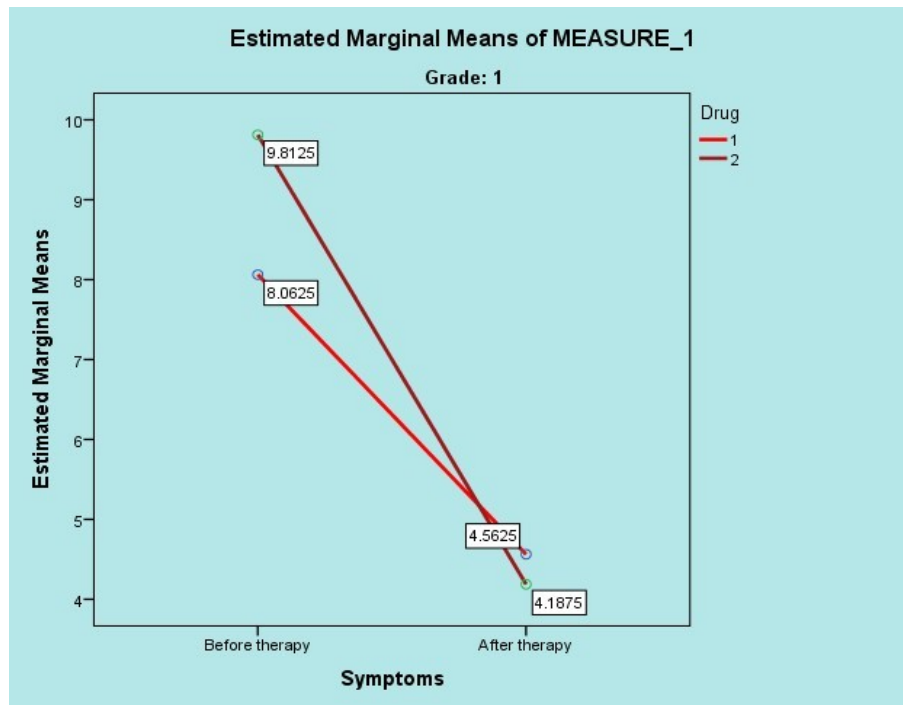


Figure 7: Graphical Representation for Distribution of gender by KOOS index

Table 8: Table representing the statistical analysis of difference in symptoms in study subjects by KOOS index

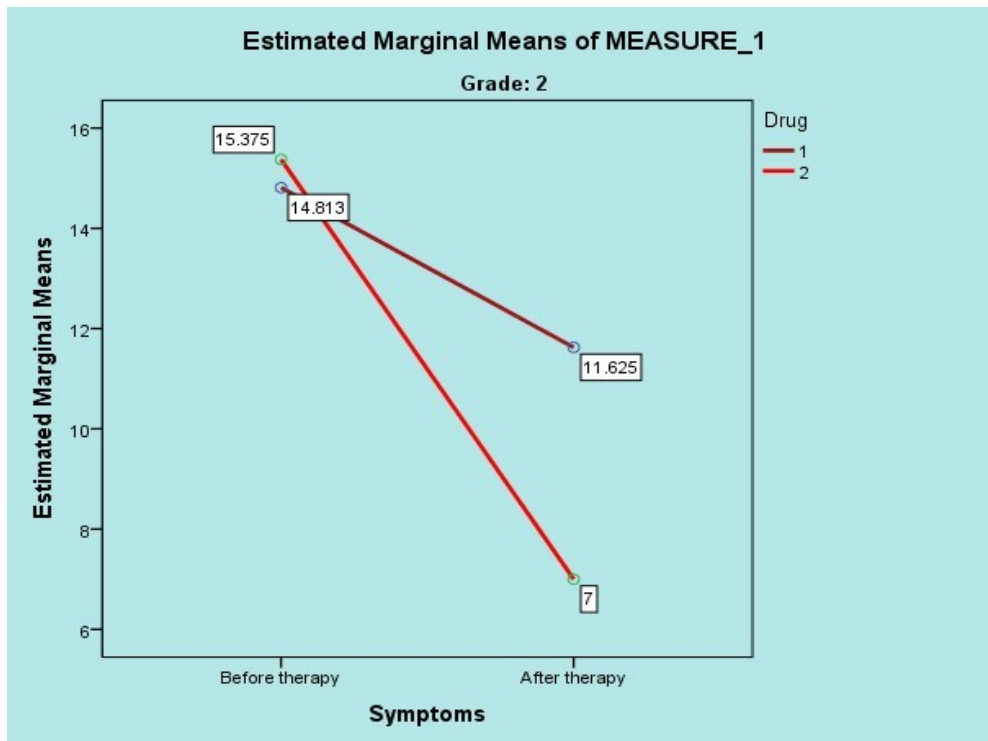
Patients		Mean square	F-value	Significance
Grade 1	Before and After therapy	2889.063	213.160	0.000
	Before and after therapy against both drugs	18.063	11.560	0.002
Grade 2	Before and After therapy	534.766	119.640	0.000
	Before and after therapy against both drugs	107.641	24.082	0.000

Figure 8(a)



In grade 1 patients there is change of effect in symptoms by the use of drug 1 and 2 in grade 1 patients. Here the drug 2 is more effective compared to drug 1.

Figure8(b)



In grade 2 patients there is effective change in symptoms by the use of drug 1 and 2 in grade 1 patients. Here the drug 2 is more effective compared to drug1.

Figure 8: Graphical Representation for estimated marginal measure of symptoms by KOOS index

Table 9: Table representing the statistical analysis of difference in stiffness in study subjects by KOOS index

Patients		Mean square	F-value	Significance
Grade 1	Before and After therapy	54.391	34.648	0.000
	Before and after therapy against both drugs	0.016	0.010	0.921
Grade 2	Before and After therapy	87.891	47.428	0.000
	Before and after therapy against both drugs	17.016	9.180	0.005

Figure 9(a)

. There is no considerable change or effect in stiffness by the use of drug 1 and 2 in grade 1 patients

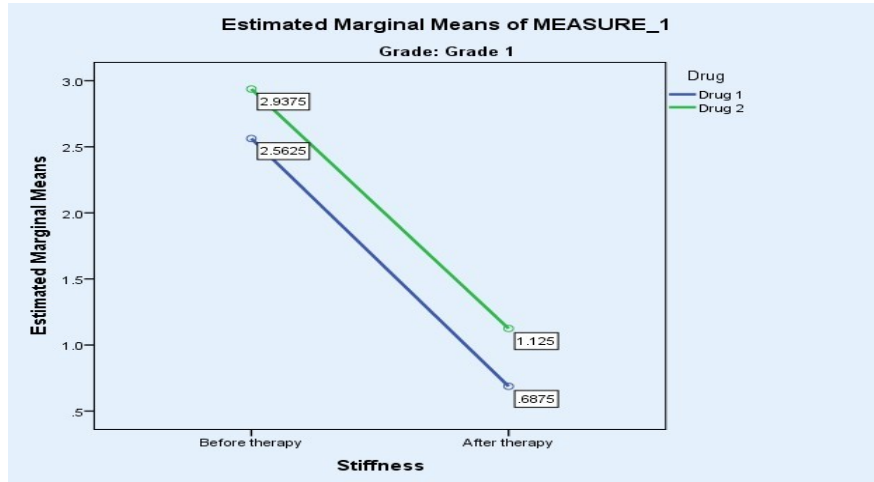
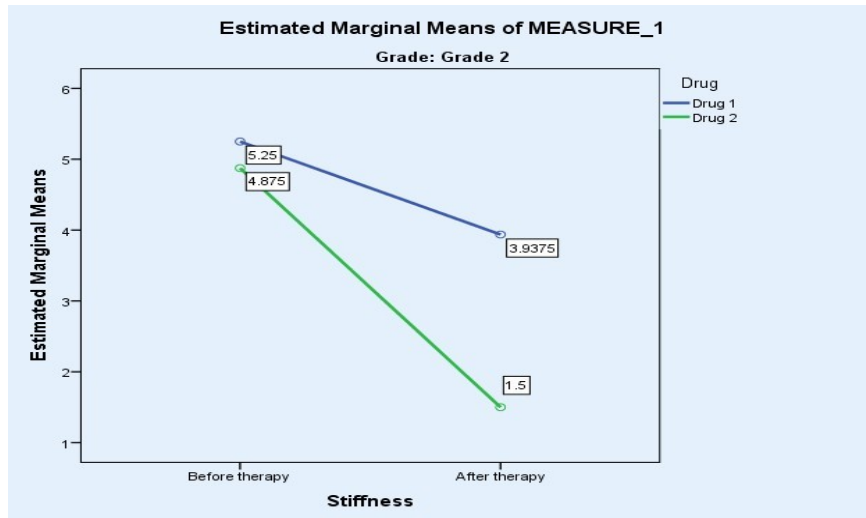


Figure 9(b)



In grade 2 patients there is effective change in stiffness by the use of drug 2 compared to drug 1. Thus drug 2 is more effective in case of grade 2 patients.

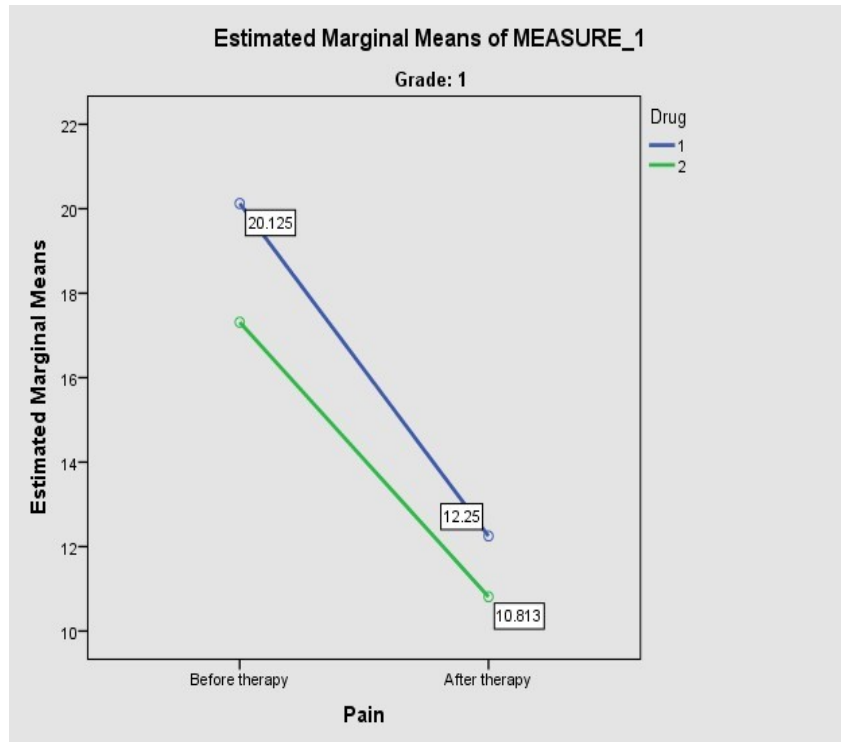
Figure 9: Graphical Representation for estimated marginal measure of stiffness by KOOS index

Table 10: Table representing the statistical analysis of difference in pain in study subjects by KOOS index

Patients		Mean square	F-value	Significance
Grade 1	Before and After therapy	826.563	255.968	.000
	Before and after therapy against both drugs	7.562	2.342	0.136
Grade 2	Before and After therapy	798.063	63.182	.000
	Before and after therapy against both drugs	196.000	15.517	.000

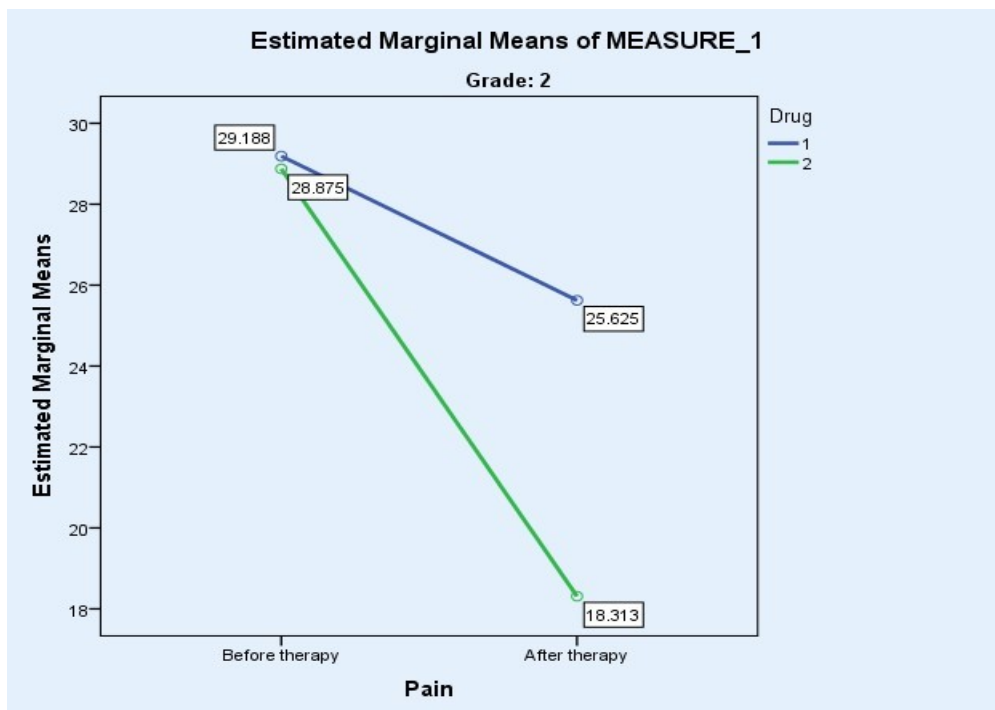
Figure 10: Graphical Representation for estimated marginal measure of pain KOOS index

Figure 10(a)



There is no considerable change or effect in pain by the use of drug 1 and 2 in grade 1 patients.

Figure10(b)



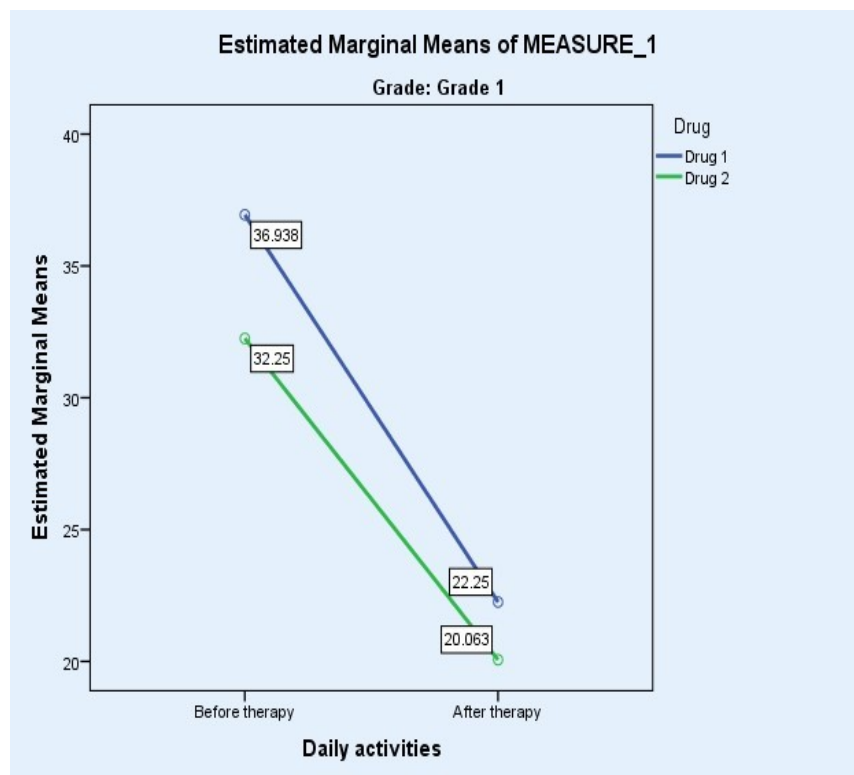
In grade 2 patients there is decrease in pain by the use of drug 2 compared to drug 1. Thus drug 2 is more effective in case of grade 2 patients.

Table 11: Table representing the statistical analysis of variability in daily activities in study subjects by KOOS index

Patients		Mean square	F-value	Significance
Grade 1	Before and After therapy	2889.063	258.770	0.000
	Before and after therapy against both drugs	25.000	2.239	0.145
Grade 2	Before and After therapy	3306.250	128.357	0.000
	Before and after therapy against both drugs	576.000	22.362	0.000

Figure 11: Graphical Representation for estimated marginal measure of daily activities KOOS index

Figure11(a)



There is no considerable change or effect in daily activities by the use of drug 1 and 2 in grade 1 patients.

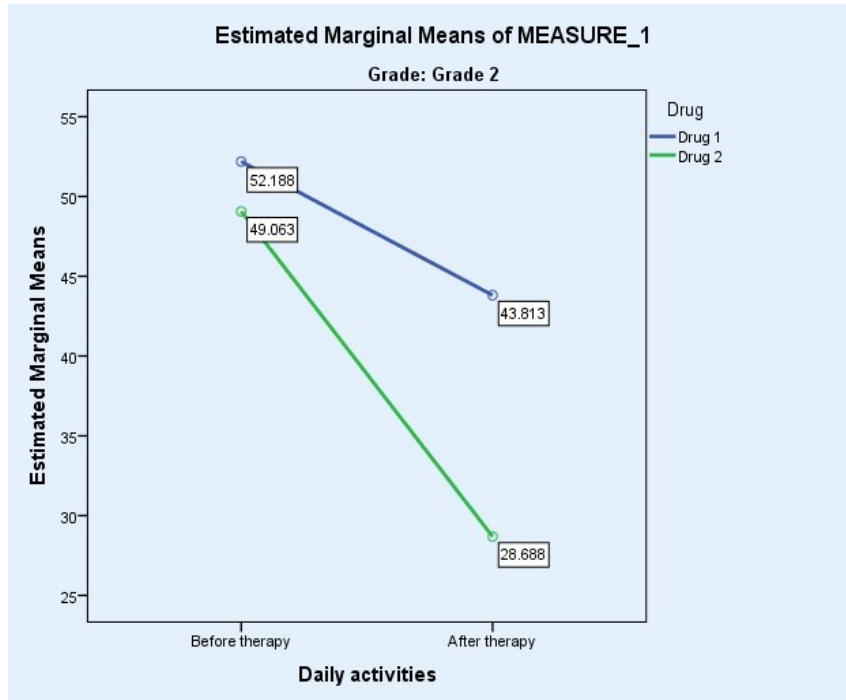


Figure11(b)

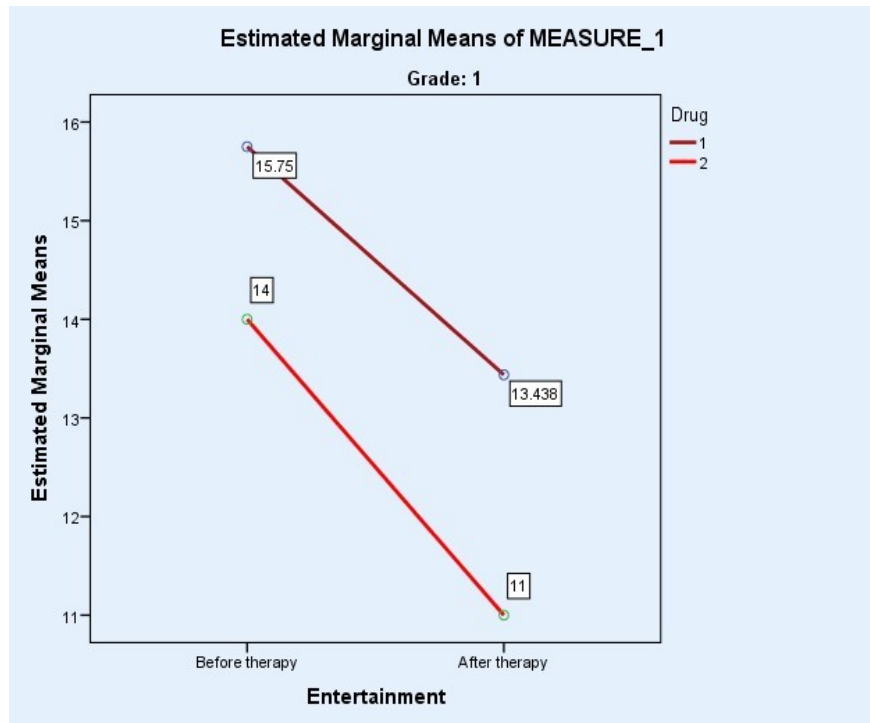
In grade 2 patients there is decrease in daily activities by the use of drug 2 compared to drug1
Thus drug 2 is more effective in case of grade 2 patients.

Table 12: Table representing the statistical analysis of variability in entertainment activities in study subjects by KOOS index

Patients		Mean square	F-value	Significance
Grade 1	Before and After therapy	112.891	89.789	0.000
	Before and after therapy against both drugs	1.891	1.504	0.230
Grade 2	Before and After therapy	172.266	76.456	0.000
	Before and after therapy against both drugs	40.641	18.037	0.000

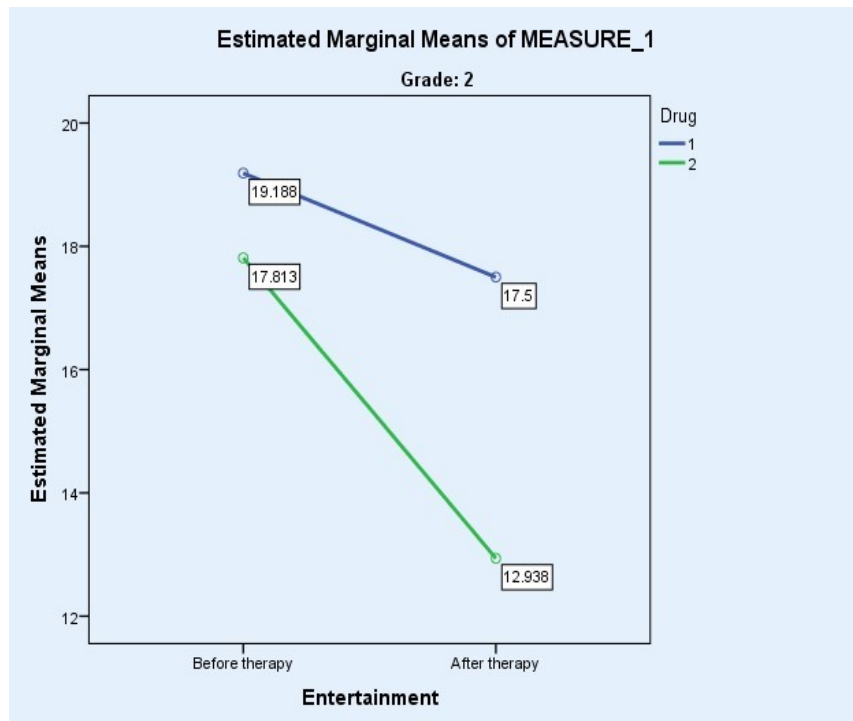
Figure 12: Graphical Representation for estimated marginal measure of entertainment activity by KOOS index

Figure 12(a)



There is no considerable change of effect in entertainment by the use of drug 1 and 2 in grade 1 patients.

Figure 12(b)



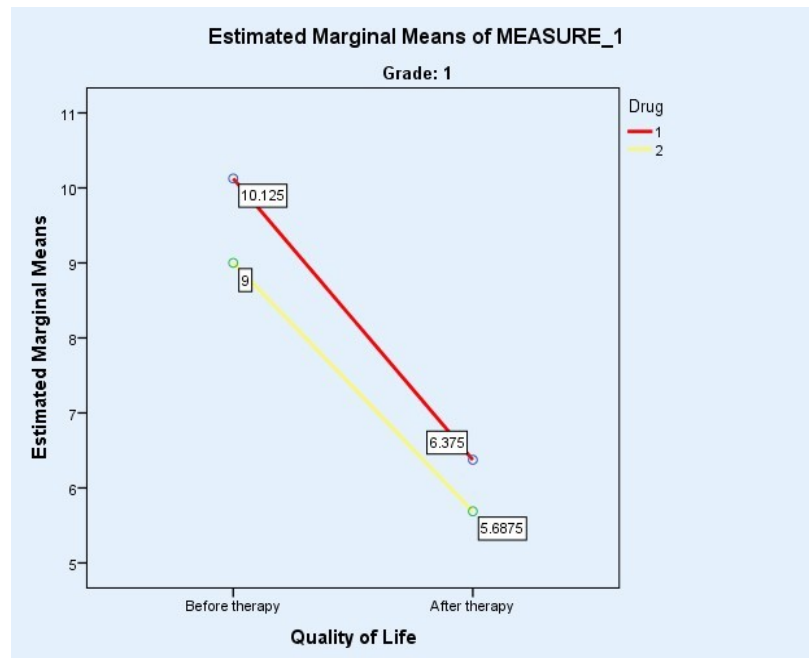
In grade 2 patients there is effective change in entertainment by the use of drug 2 compared to drug 1. Thus drug 2 is more effective in case of grade 2 patients.

Table 13: Table representing the statistical analysis of difference in Quality Of Life in study subjects by KOOS index.

Patients		Mean square	F-value	Significance
Grade 1	Before and After therapy	199.516	204.850	0.000
	Before and after therapy against both drugs	0.766	0.786	0.382
Grade 2	Before and After therapy	297.563	111.065	0.000
	Before and after therapy against both drugs	33.063	12.341	0.001

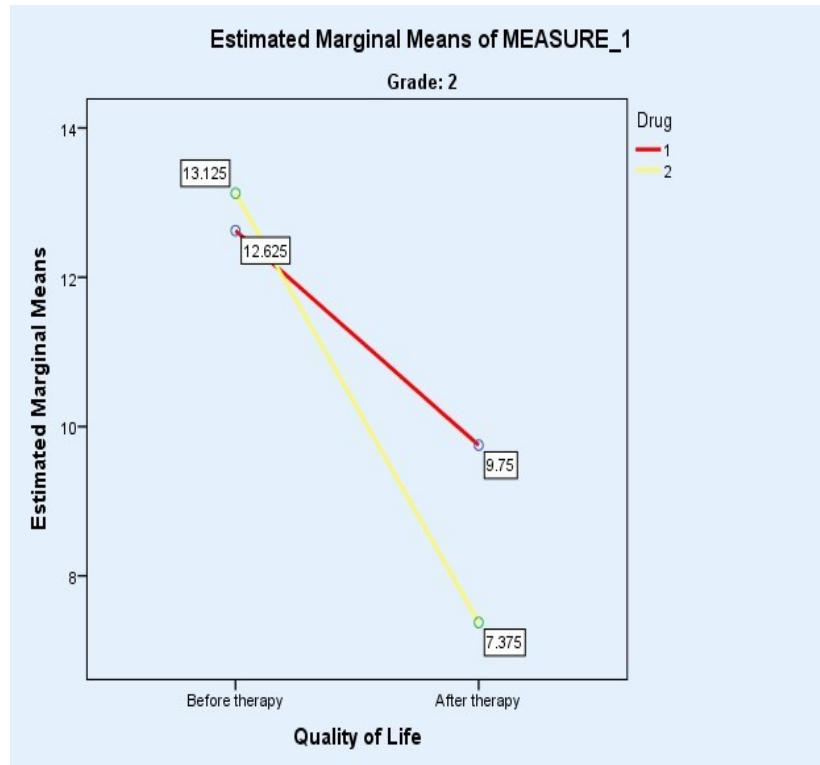
Figure 13: Graphical Representation for estimated marginal measure for Quality Of Life using KOOS score.

Figure 13(a)



There is no considerable change or effect in the use of drug 1 and drug 2.

Figure 13(b)



In grade 2 patients there is effective change in quality of life by the use of drug 2 compared to drug 1. Thus drug 2 is more effective in case of grade 2 patients.

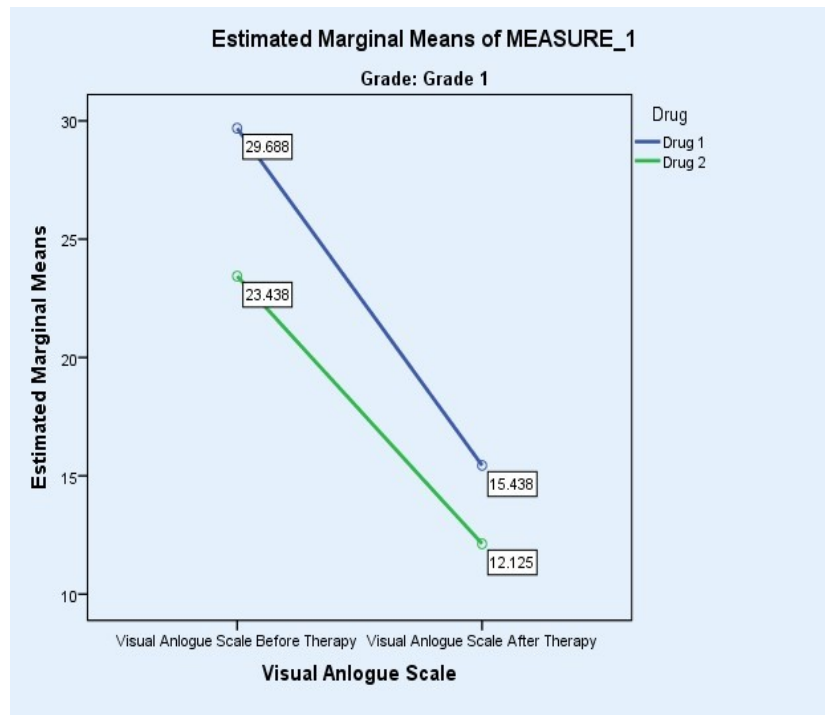
3. VAS SCORE

Table 14: Table representing the statistical analysis of difference in pain in study subjects by VAS score.

Patients		Mean square	F-value	Significance
Grade 1	Before and After therapy			
		2613.766	152.490	0.000
	Before and after therapy against both drugs	34.516	2.014	0.166
Grade 2	Before and After therapy	3206.391	106.528	0.000
	Before and after therapy against both drugs	1048.141	34.823	0.000

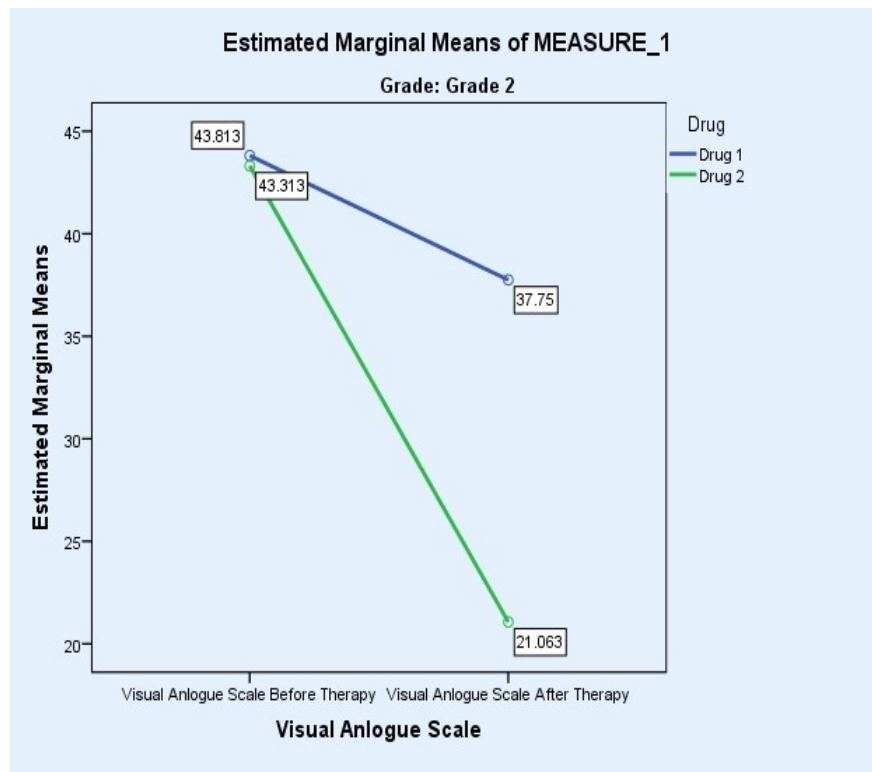
Figure 14: Graphical Representation for estimated marginal measure of pain by VAS score

Figure 14(a)



By the use of drug 1 and 2 in grade 1 patients there is no considerable change or effect in pain which measured by visual analogue scale.

Figure 14(b)



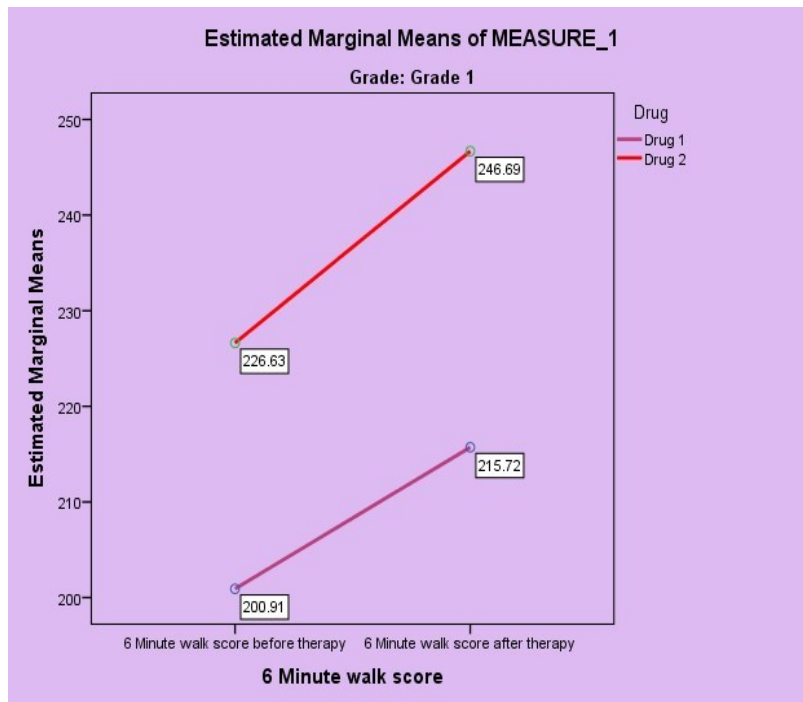
In grade 2 patients there is decrease in pain by the use of drug 2 compared to drug 1. Thus drug 2 is more effective in case of grade 2 patients.

4.6-MINUTE WALK SCORE

Table 15: Table representing the statistical analysis of walking capability in subjects by 6-min walk score

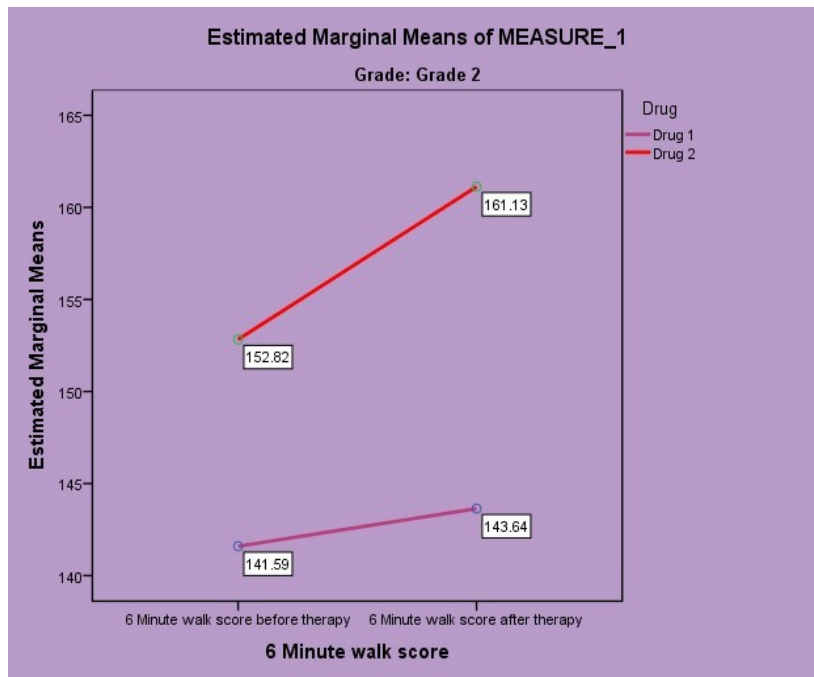
Patients		Mean square	F-value	Significance
Grade 1	Before and After therapy	4863.319	213.160	0.000
	Before and after therapy against both drugs	110.513	11.560	0.345
Grade 2	Before and After therapy	427.973	43.592	0
	Before and after therapy against both drugs	156.563	15.947	0

Figure 15: Graphical Representation for estimated marginal measure of 6-minute walking score
Figure 15(a)



By the use of drug 1 and 2 in grade 1 patients there is no considerable change or effect in six minute walk score of patients before and after therapy.

Figure:15(b)



In grade 2 patients there is effective change in six minute walk of patients by the use of drug 2 compared to drug 1. Thus drug 2 is more effective in case of grade 2 patients.

5. NARANJO’S SCALE

Table 16: Table representing statistical analysis of Adverse Drug Reactions.

Side Effects (ADR)	Frequency	Percent
Doubtful ADR	61	95.3
Possible ADR	3	4.7
Probable ADR	0	0
Definite ADR	0	0
Total	64	100.0

Side effects	No of patients
Gastritis	1
Yellow discoloration of urine	2

From the table we can conclude that 95.3% were doubtful ADR and remaining 4.7% is possible chance of ADR. Among 64 patients 3 of them reported the side effects especially gastritis, yellow discoloration of urine and abdominal discomfort.

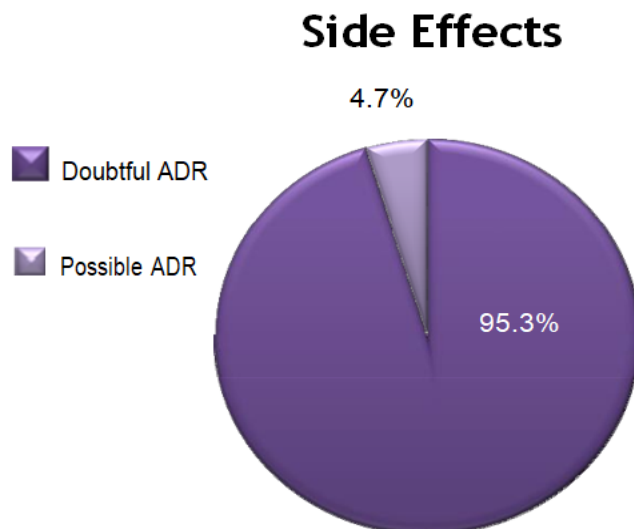


Figure 16: Graphical representation of Adverse Drug Reactions

SUMMARY

A prospective, observational study was conducted in Department of orthopedics at Pushpagiri Medical College Hospital to compare the safety and effectiveness of glucosamine- diacerein and univestin – chondroitin in knee osteoarthritis patients. From 140 patients who arrived at the orthopedics OPD Pushpagiri medical college hospital , we sorted and selected only 64 patients based on the study criteria. Demographic details of the patients were collected, recorded and analyzed. We used the standard questionnaire including WOMAC, KOOS, VAS, 6 minute walk test, and Standard ADR questionnaires (Naranjo's) for measuring safety and effectiveness of drug

combinations. Change in the short term effectiveness for both drugs measure was

assessed before the start of treatment, and after 30 days of treatment. Collected data was organized, tabulated and analyzed using statistical method and described with the help of tables and graphs.

- The majority of patients belong to 35-80 age groups. Among the patients there is no significant relationship between drug

effectiveness with respect to their age proportion. The age of population only have a relationship with occurrence of disease. Possibility of disease occurrence increase with aging.

- Female are more prone to knee osteoarthritis than males. Gender has no direct relationship with effectiveness of drugs.
- Diarrhoea, gastritis and dark yellow coloured urine are adverse drug reactions that are reported by 3 of the patients within one month of therapy using diacerein-glucosamine combination. There are no observed adverse drug reactions reported for univestin-chondroitin for short period of time.
- Both drug combinations showed reduction in WOMAC AND KOOS pain scores. Both the drugs showed anti-nociceptive property by reducing pain within short period of therapy. In grade 1 patients there is no considerable change in anti-nociceptive effect for both drugs. In grade 2 patients there is significant reduction in pain by use of drug 2 as compared todrug1.
- Both drug combinations showed reduction in

WOMAC AND KOOS stiffness scores. Both the drugs showed anti-inflammatory property by reducing stiffness within short period of therapy. In grade 1 patients there is no considerable change in anti-inflammatory effect for both drugs. In grade 2 patients there is significant reduction in stiffness by use of drug 2 as compared to drug 1.

- The difficulty in performing daily activities and entertainment activities decreased with use of both drugs. In grade 1, both drugs showed similar effect. However Diacerein-glucosamine combination is more beneficial for grade 2.
- The 6-min walking score increased for those taking diacerein-glucosamine than those patients taking univestin-chondroitin combination.
- The Quality of Life was found to be more improved for patients taking diacerein-glucosamine than univestin; chondroitin combinations.
- Among 64 populations, diacerein-glucosamine combination was found to be more effective in knee osteoarthritis patients of grade 1 and 2. However univestin-chondroitin was found to have more safety profile in short term therapy.

CONCLUSION

Knee Osteoarthritis is a progressive disease showing increasing trend of occurrence in a population. Females are more prone to this disease than male. This study is an attempt to compare the safety and effectiveness of diacerein-glucosamine and univestin chondroitin combinations which are prescribed by physicians in the current scenario. The current study was conducted in the department of orthopaedics in Pushpagiri medical college hospital. 64 patients having knee OA were selected for the study and they were divided into two groups (32 each), one receiving diacerein-glucosamine and another receiving univestin chondroitin combinations.

We can conclude that both drugs are equally effective for grade 1 and grade 2 patients. The study reveals that among these two drugs diacerein-glucosamine combination therapy shows more

benefit for grade 2 patients than univestin-chondroitin. As per AAOS (17), ARA (18), NHS (19) guidelines there are no combination of medication that shows anti-inflammatory property and that suppress cartilage degeneration. In this study we found that both the combination therapies showed anti-inflammatory property and that suppress cartilage degeneration. Apart from this, there is 4.7% of possible chance of ADR for diacerein – glucosamine combination. However, there are no ADRs reported for the other combination. Hence semi-synthetic drug combination showed more safety profile than synthetic drug combination in the treatment of knee

osteoarthritis. Since Univestin is a newer drug for knee OA in the current scenario, supporting studies on its combination therapy was not yet conducted. According to medical practice, quick relief within short period of exposure to drug therapy is preferred. Therefore further studies to reveal the short term effectiveness of univestin is needed.

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