# Iontophoresis Versus Joint Interplay In Relieving Knee Osteoarthritic Pain

Samir A. Sabbahi\* and Foud Ibrahim\*\*

- \* Department of Basic Sciences, Faculty of PT
- \*\*Department of biomechanics

### ABSTRACT

Although there are numerous research studies concerning the treatment of osteo-arthritis (OA). the most effective method of treatment is still undecided. The aim of this current study was to determine the effect of sulicylate iontophoresis and joint interplay in alleviation of primary arthritic knee pain. Eighty male patients suffering from primary unilateral OA of the knee, participated in this study. They were randomly and equally grouped into four groups. Three groups received six treatment sessions of salicylate iontophoresis, joint interplay, and a combination of both respectively. Exercises were added to all investigated groups. The fourth group was a control group in which the patients were under medical treatment. The dependent parameters were pain perception, pain by pressure, functional assessment and muscle strength. The independent parameters were salicylate iontophoresis, joint interplay, and medications. The results of the study indicated that salicylate iontophoresis is the most effective technique for reducing pain, increasing muscle strength and improving functional activities compared to joint interplay. Also, the combination between two techniques, salicylate iontophoresis and joint interplay, in addition to therapeutic exercises is the most beneficial treatment for improving the clinical symptoms of 0.4 knee. Further research into long term effects of these techniques may support their continued use for the management of the clinical symptoms of OA knee.

Key Words: Iontophoresis, Manipulation, Osteo-arthritis

## INTRODUCTION

n the United States of America, an aveage of 37% of the population suffer from osteo-arthritis (OA) which is demonstrable by roentgenography. This percentage increased to 85% when considering only that segment of population aged 75-79 years<sup>6</sup>. The medical approach to the osteo-arthritic patient is aimed at delaying the degenerative process and preventing

disability. The vast amount of research which has been conducted so far has focused mainly on treatment trials which have been ineffective in adressing the main problems. The side effects of the administration of different medications are undesirable and both patients and clinicians are still waiting for an effective solution to the problem. Ion transfer, or iontophoresis, is the introduction of medication by electric current. Iontophoresis can be considered as a safe, non-invasive

technique<sup>11</sup>. It was discovered by LeDuc in 1903. The local application of iontophoresis may prevent the side effects of medications on the systemic circulation in bypassing the liver. The high drug concentration in the target of pathology gives iontophoresis the superiority in treating local pathology. The side effect of aspirin like destruction of normal joint cartilage can be avoided by local administration of iontophoresis.

Joint manipulation or interplay is a manual therapy for joint disorders. Different Chiropractic and Osteopathic schools support the role of manipulation in relieving joint pain and stiffness. Although the scientific bases of manipulation is still questionable, its use in different pathologies is still applicable.

The aim of this study was to compare the effect of salicylate iontophoresis to joint interplay in the elimination of clinical signs (pain) in males with unilateral primary osteoarthritic knee pain.

### METHODS

#### Design

It was a pre-test, post-test research design with repeated measurement. The dependent variables were pain perception( measured by Visual Analogue Scale), pain by pressure (measured by Pressure Threshold Meter), muscle strength (measured by Hydraulic Dynamometer) and functional assessments (measured by Index Severity of OA). The independent variables were salicylate iontophoresis, joint interplay, and exercises. So, this study was a 4x3 research design with repeated measurements. The base line was the pre-test scores compared with the three post-test scores (after 2, 4 and 6 sessions respectively).

## Sample

Eighty male patients, with an age range between 40-60 years-old., suffering from unilateral primary osteo-arthritis participated in this study. They were recruited from Kasr El Ani Hospital, Physical Therapy Clinic, Department of Orthopedics. They were equally and randomly grouped into four groups.

**Group I:** 20 patients received 6 sessions of salicylate iontophoresis and exercises.

**Group II:** 20 patients received 6 sessions of joint interplay and exercises.

**Group III:** 20 patients received 6 sessions of salicylate iontophoresis, joint interplay and exercises.

**Group IV:** (control) 20 patients were under medical treatment.

Every patients was subjected to pre-test evaluation and three post-tests evaluations for the same parameters. Treatment was given every other day.

## MATERIALS AND EQUIPMENT

- Iontophore 611 OPM (Life Tech. Inc.)
- Trans Q1 polymer gel electrode with 3 cc pouch
- Three cc of 3% salicylate solution for treatment with iontophoresis.
- Visual Analogue Scale (VAS).
- Index Severity of Osteo-arthritis (ISOA) Questionnaire.
- Hydraulic Dynamometer
- Pressure Threshold Meter
- Treatment couch
- Knee support

### **Procedure**

1. The investigators selected the sample of the study among the referred patients.

- 2. A complete explanation about the procedure was given to each patient after signing a consent form to participate in the study.
- 3. Every participant was subjected to a complete evaluation of the following four research parameters. The scores were documented as pre-test for each patient.
- I. Visual Analogue Scale (VAS).

Participant was instructed to mark along a 10 cm horizontal line the point which reflected the degree of pain he felt. The range was from no pain to unbearable pain.

II. Index Severity of Osteo-arthritis (ISOA)

Participant was asked to complete a questionnaire related to pain during certain activities and functional abilities. Points from 0-6 were allocated for each response and summated to give an overall handicap score ranging from minor handicap to extremely severe handicap.

## III. Hydraulic Dynamometer

The participant was instructed to extend the knee from the sitting position. The dynamometer was placed on the lower end of the leg just above the joint line of the ankle and the maximal isometric contraction of quadriceps muscle was measured in Kgs. The score of three successive trials with rest periods in between were recorded and the mean was calculated.

### IV. Pressure Threshold Meter

Pressure was applied at a constantly increasing rate of 1kg/second to the medial and lateral joint lines of the knee respectively, just anterior to the medial and lateral collateral ligaments of the knee. Readings were taken when the participant indicated that he was begining to feel pain. The scores of three successive trials with

- rest periods in between were recorded and the mean calculated.
- 4. Participants were randomly assigned to one of four groups. The 1<sup>st</sup> participant to the group I, and the 2<sup>nd</sup> to the group II, and so on until all four groups were complete.
- 5. Within groups 1-3 the participants received salicylate iontophoresis and exercises alone(GI), joint interplay and exercises alone (GII) and a combination of the above (GIII).
- 6. Iontophoresis parameters were 3 mA x 15 minutes. The active electrode was a negative electrode. The skin under both active and inactive electrode was cleansed by alcohol to improve the conductive property of the skin. Salicylate solution was taken by a 5 cc plastic syringe and gradually saturated the active electrode. The active electrode was applied onto the medial side of the knee joint.
- 7. For joint interplay procedures a treatment couch was used and participants positioned in either supine lying or sitting on the edge of the couch. A combination of long axis traction, posterior and anterior glide techniques were used.
- 8. Each participant performed a specific exercise program consisting of six exercises with a set number of repetitions and holding times (seconds). Exercises focused mainly on quadriceps strengthening.
- 9. After the completion of two, four and six treatment sessions re-evaluation of the four research parameters (as in pre-test) were undertaken and documented.

## **Data Analysis**

The data was analysed to ascertain if there was any significant difference between the groups. Anova was used for comparative

analysis between the groups and Scheffet F test to identify differences between two sets of data i.e. pre-set, post-test.

## RESULTS

# The results of this study presented in tables 1-3, and figure 1 indicated the following:

1. After six treatment sessions salicylate iontophoresis was shown to be the most effective technique for reducing pain, increasing strength and improving functional activities compared to joint interplay (see fig. 2).

- 2. After six treatment sessions, the combination between two techniques, salicylate iontophoresis and joint interplay, in addition to exercise was shown to be superior to all other combination for reducing pain, increasing strength and improving functional activities (fig.2).
- 3. After six treatment sessions all groups have demonstrated significant difference in relation to improvement of clinical symptoms from a greater to a lesser degree as follow: Group 3 (iontophoresis + joint interplay + exercise), Group 1 (iontophoresis + exercise), Group 2 (joint interplay + exercise) and Group 4 (control).

Table (1): Analysis of the measured parameters between all groups before treatment and 2nd session

Parameter	Group	Mean Diff test	Scheffe F. test	Mean Diff test	Scheffe F. test	P value
V.A.S.	Gl vs G2	0.125↓	0.229	1.175 ↓	17.117	< 0.05
(Score)	G1 vs G3	0.150↓	0.330	1.100 ↑	15.002	< 0.05
	G1 vs G4	0.075↑	0.830	1.425 ↓	25.176	< 0.05
	G2 vs G3	0.025↓	9.170	2.275 ↑	64.168	< 0.05
	G2 vs G4	0.200↑	0.587	0.250 ↓	0.775	> 0.05
	G3 vs G4	0.225↑	0.743	2.525 ↓	79.045	< 0.05
I.S.O.A.	G1 vs G2	0.100 ↑	0.023	0.650 ↓	1.837	> 0.05
(Score)	G1 vs G3	0.150 ↑	0.052	0.150 ↑	0.098	> 0.05
	G1 vs G4	0.000 ↑	0.000	1.900 ↓	15.696	< 0.05
	G2 vs G3	0.050 ↑	5.799	0.800 ↑	2.783	< 0.05
	G2 vs G4	0.100 ↓	0.023	1.250 ↓	6.793	< 0.05
	G3 vs G4	- 0.150 ↓	0.052	2.050 ↓	18.272	< 0.05
Dynamometer	GI vs G2	0.300 ↑	0.060	0.900 ↑	0.589	> 0.05
(kg)	G1 vs G3	0.100 ↑	6.665	1.550 ↓	1.746	> 0.05
muscle	GI vs G4	0.100 ↑	6.665	1.850 ↑	2.487	> 0.05
strength	G2 vs G3	0.200 ↓	0.027	2.450 ↓	4.361	> 0.05
	G2 vs G4	0.200 ↓	0.027	0.950 ↑	<b>Q</b> 656	< 0.05
	G3 vs G4	0.000 ↓	0.000	3.400 ↑	<b>8.399</b>	> 0.05
Pre. Thr.	G1 vs G2	0.000 ↑	0.000	0.350 ↑	1.203	> 0.05
(kg)	Gl vs G3	0.050 ↑	0.028	0.100 ↓	0.098	> 0.05
	G1 vs G4	0.050 ↑	0.028	1.250 ↑	15.342	< 0.05
	G2 vs G3	0.050 ↑	0.028	0.450 ↓	1.988	> 0.05
	G2 vs G4	0.050 ↑	0.028	1.900 ↑	7.953	< 0.05
	G3 vs G4	0.000 ↑	0.000	1.350 ↑	7.953	< 0.05

VAS: Visual Analogue Scale

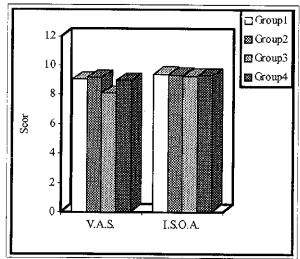
IOSA:

PTM:

Index Severity of Osteo-arthritis Pressure Threshold Meter G1 = group 1G2 = group 2

G3 = group 3 & G4 = group 4

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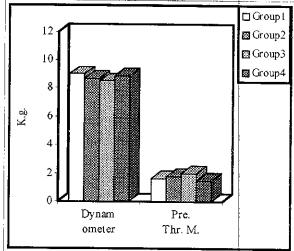


Fig. (1) shows the mean and SD for all groups before treatment VAS: Visual Analogue Scale

ISOA: Index Severity Of Osteo-arthritis

PT : Pressure Threshold

This Figure shows no difference between groups

Comparison between the measured parameters in group I using one way ANOVA showed a significant differences as follows:

For VAS. (score): The mean difference between pre-test &  $2^{nd}$ ,  $4^{th}$  &  $6^{th}$  session respectively were 2.075, 3.85 & 4.9 which is significant at P<0.05.

For ISOA. (score): The mean difference between pre-test &  $2^{nd}$ ,  $4^{th}$  &  $6^{th}$  session respectively were 2.3, 3.85 & 5.5 which is significant at P<0.05.

For Dynamometer (kg): The mean difference between pre-test & 2<sup>nd</sup>, 4<sup>th</sup> & 6<sup>th</sup> session respectively were 1.8, 3.8 & 5.95 which is significant at P<0.05.

For PTM. (kg): The mean difference between pre-test &  $2^{nd}$ ,  $4^{th}$  &  $6^{th}$  session respectively were 1.8, 3.8 & 5.95 which is significant at P<0.05.

Comparison between the measured parameters in group II (joint interplay) using one way ANOVA showed a significant differences as follows:

For VAS. The mean difference between pretest &  $2^{nd}$ ,  $4^{th}$  &  $6^{th}$  session respectively were 1.025, 2.0 & 3.025 at P<0.05 which is significant.

For ISOA. The mean difference between pretest &  $2^{nd}$ ,  $4^{th}$  &  $6^{th}$  session respectively were 1.55, 2.95 & 3.9 at P<0.05 which is significant.

Bull. Fac. Ph. Th. Cairo Univ.,: Vol 2. No (1) Jan. 1997 For record of dynamometer. The mean difference between pre-test and  $2^{nd}$ ,  $4^{th} \& 6^{th}$  session respectively were 1.2, 2.35 &3.6 at P<0.05 which is significant.

For PTM. The mean difference between pretest &  $2^{nd}$ ,  $4^{th}$  &  $6^{th}$  were 0.9, 1.85 & 2.45 at P<0.05 which is significant.

Comparison between the measured parameters in group III using one-way ANOVA showed a significant differences as follows:

For VAS. The mean difference between pretest &  $2^{nd}$ ,  $4^{th}$  &  $6^{th}$  session were 3.325, 5.875 & 7.775 at P<0.05 which is significant.

For ISOA. The mean difference between pretest &  $2^{\text{nd}}$ ,  $4^{\text{th}}$  &  $6^{\text{th}}$  session were 2.3, 4.35 & 6.9 at P<0.05 which is significant.

For Dynamometer record: The mean difference were 3.45, 7.15 & 10.9 between pretest and  $2^{nd}$ ,  $4^{th}$  &  $6^{th}$  session respectively at P<0.05.

**For PTM.** The mean difference between pretest &  $2^{nd}$ ,  $4^{th}$  &  $6^{th}$  session were 1.4, 2.9 & 5.45 at P<0.05 which is significant.

Comparison between the measured parameters in group IV using one-way ANOVA showed a significant differences as follows:

**For VAS.** The mean difference between pretest &  $2^{nd}$ ,  $4^{th}$  &  $6^{th}$  session were 0.575, 1.125 & 2.00 at P<0.05 which is significant.

**For ISOA.** The mean difference between pretest &  $2^{nd}$ ,  $4^{th}$  &  $6^{th}$  session were 4.0, 1.4 & 1.75 at P<0.05 which is significant.

For record of Dynamometer. significant difference was seen between the record of pretest and 4<sup>th</sup> session and pre-test and 6<sup>th</sup> sessionj. The mean difference were respectively 0.05, 1.05, & 135.

**For PTM.** The mean difference between pretest &  $2^{nd}$ ,  $4^{th}$  &  $6^{th}$  session were 0.05, 0.75 & 1.05 . The difference is significant between pre-tes &  $4^{th}$  session and between pre-test and  $6^{th}$  session at P<0.05.

Table (2): Analysis of difference of the measured parameters between all groups at 4th & 6th session

Parameter	Group	Mean Diff test	Scheffe F. test	Mean Diff test	Scheffe F. test	P value
V.A.S.	G1 vs G2	1.975 ↓	44.478	2.000 ↓	43.305	< 0.05
(Score)	G1 vs G3	1.875 †	40.088	2.725 ↑	80.391	< 0.05
	G1 vs G4	2.650 ↑	80.077	2.825 ↓	86.400	< 0.05
	G2 vs G3	3.850 ↓	169.019	4.725 ↑	241.702	< 0.05
	G2 vs G4	0.675 ↑	5.195	0.825 ↓	7,369	< 0.05
	G3 vs G4	4.525 ↑	233.48	5.550 ↓	333.474	< 0.05
I.S.O.A.	G1 vs G2	1.100 ↑	6.239	1.500 ↓	14.179	< 0.05
(Score)	Gl vs G3	0.650 ↑	2.178	1.550 ↑	15.140	< 0.05
	G1 vs G4	2.450 ↑	30.949	3.750 ↓	88.619	< 0.05
	G2 vs G3	1.750 ↑	15.790	3.050 ↑	58.623	< 0.05
·	G2 vs G4	1.350 ↓	9.397	2.250 ↓	31.903	< 0.05
	G3 vs G4	3.100 ↓	49.550	5.300 ↓	177.018	< 0.05
Dynamometer	G1 vs G2	1.750 ↑	2.570	2.650 ↑	6.670	< 0.05
(kg)	GI vs G3	3.250 ↑	<b>8.</b> 864	4.850 ↓	22.341	< 0.05
muscle	G1 vs G4	2.850 ↑	6.816	4.700 1	20.980	< 0.05
strength	G2 vs G3	0.500 ↓	8.858	7.500 ↓	53.424	< 0.05
	G2 vs G4	1.100 ↓	1.015	2.050 ↑	3.991	< 0.05
	G3 vs G4	6.100 ↓	31.226	9.550 ↑	86.621	< 0.05
Pre. Thr.	G1 vs G2	0.450 ↑	1.794	0.800 ↑	4.874	< 0.05
(kg)	G1 vs G3	0.550 ↑	2.679	2.350 ↓	42.055	< 0.05
	G1 vs G4	1.600 ↑	22.676	2.250 ↑	38.552	< 0.05
	G2 vs G3	1.000 ↑	20.979	3.150 ↓	75.562	< 0.05
	G2 vs G4	1.150 ↑	11.714	1.450 ↑	16.011	< 0.05
	G3 vs G4	2.150 ↑	40.945	4.600 ↑	161.138	< 0.05

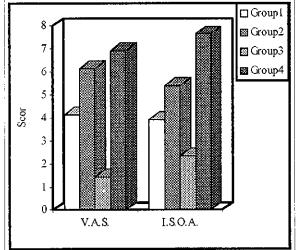
VAS: Visual Analogue Scale

IOSA: Index Severity of Osteo-arthritis

PTM: Pressure Threshold Meter

G1 = group 1G2 = group 2

G3 = group 3 & G4 = group 4



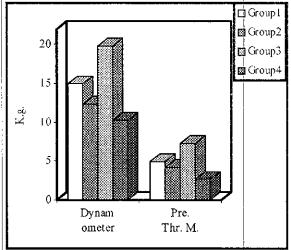


Fig. (2) Show the mean and SD for all groups after treatment.

Bull, Fac. Ph. Th. Cairo Univ.,: Vol 2. No (1) Jan. 1997 Table (3) Mean and standard deviation of all parameters for all groups after 6 sessions

14010 (5) 112000 450	Group 1	Group 2	Group 3	Group 4
V.A.S. (Score)	$4.125 \pm (0.559)$	$6.125 \pm (0.455)$	$1.400 \pm (0.447)$	$6.920 \pm (0.605)$
I.S.O.A. (Score)	$3.900 \pm (0.788)$	$5.400 \pm (0.754)$	$2.350 \pm (0.745)$	7.650 = (0.813)
Dynamometer (kg) muscle strength	$14.950 \pm (0.788)$	12.300 ± (1.593)	19.800 ± (2.067)	10.25 ± (2.314)
Pre. Thr. (kg)	$4.900 \pm (0.641)$	$4.100 \pm (0.553)$	$7.250 \pm (0.851)$	$2.65 \pm (0.671)$

VAS: Visual Analogue Scale

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G1 = group 1

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## DISCUSSION

The main purpose of this study was to examine the efficacy of salicylate iontophoresis as compared to joint interplay in the treatment of The results Osteo-arthritis of the knee. indicated that salicylate iontophoresis is the most effective technique in reducing pain, increasing muscle strength and improving compared to joint functional activities interplay. Also, the combination between two techniques, salicylate iontophoresis and joint interplay, in addition to therapeutic exercises, is the most beneficial of all the combination of clinical the for improving techniques symptoms of OA knee.

## Effect of Salicylate Iontophoresis on Relieving Primary Arthritic Knee Pain

The significant clinical improvement in patients who receive salicylate iontophoresis could be attributed to the efficiency of the technique in delivering non-steroidal anti-inflammatory drug (salicylate) to the structure of the knee joint. Similar results to those of the present study were reported by other authors who used non-steroidal anti-inflammatory drug

via iontophoresis in the treatment of joint pathology underlying The pain<sup>3</sup>. inflammation in OA of the knee may highlight the role and the therapeutic effect of salicylate in the management of the clinical symptoms. It is reported<sup>13</sup> that many forms of tissue injury are followed by release of prostaglandin and bradykinin which are irritating hormones that give rise to sign of inflammation. The effect of asprin and related drugs may inhibit the synthesis and production of these chemically irritating substances<sup>13</sup>. It has been claimed that daily administration of asprin orally markedly breakdown of articular the accelerated cartilage9. This effect might be avoided by the local application of salicylate by iontophoresis. It may also be assumed that a change in ions concentration in the extra-articular fluids had an effect which resulted in an improvement of clinical symptoms observed in this study.

Although, it is beyond the scope of this research to prove the depth of penetration of iontophoresis, improvement of the clinical symptoms indicated that salicylate may reach the structures of the knee joint. Salicylate has been shown to have a sedative effect on

mechano-receptors of the joint capsule and inhibits the formation of the more irritating chemical sustances, bradykinin and prostaglandin in the joint cavity<sup>13</sup>. It has been reported in various animal studies that the depth of penetration by iontophoresis using radio-labeled Lidocaine and Dexamethasone may reach up to 3 cm in different tissue concentrations (10 & 2). This penetration should be sufficient to reach the knee joint capsule and cavity.

# Effect of Joint Interplay (Manipulation) on Relieving Primary Arthritic Joint Pain

The rationale for the reduction of joint pain following manipulation is still under scientific review. It has been postulated that this reduction in joint pain occurs because of the neuromuscular effect on the mechanoreceptors<sup>7</sup>. Often reflex muscle spasm and pain prevent the patient from performing active exercise. The therapist can passively guide the limb further into range without eliciting spasm or pain and may be the treatment of choice when the patient is psychologically reluctant to perform active exercise8.

Manipulation results in elastic deformation of connective tissue. According Kalternborn<sup>4</sup> this deformation becomes plastic exercise within the gained with applied painless range of motion. Kalternborn also stated that slow capsular stretch can result in plastic elongation of connective tissue and therefore reduction of soft tissue contractures4. The statistically significant difference between the control group and the joint interplay plus exercise group in this study may lend support to the advantages of manipulation over the use of non-steroidal anti-inflammatory drugs for treating the symptoms of OA. Other clinical

studies have supported joint manipulation over the administration of steroids which could produce faster effects but with the risk of secondary side effects<sup>12</sup>.

# Effect of Therapeutic Exercises

The effect of a therapeutic exercise program may be toincrease the functional capacity and muscle strength by reducing pain. One clinical study investigated the effect of a specific exercise program in conjunction with a physical therapy program for subjects with OA of the knees. The results were positive indicating less pain and an increase in muscle strength and endurance. In addition, it was reported that a significant increase in walking distance and reduced pain on activities occured.

# Double Effect of Iontophoresis, Manipulation and Exercise on Relieving Primary Knee arthritic Pain

The results of this study indicate that the most effective plan of treatment for unilateral primary O.A. knee is salicylate iontophoresis, joint interplay in addition to therapeutic exercises. This may be due to the double effect of salicylate iontophoresis and joint interplay on resolution of inflammatory processes. The cumulative effect of both techniques may result in pain reduction and increased ROM. These may also be neural modulation through therapeutic exercise.

### Conclusion

Although OA is a common disease, there is no definite treatment to control the symptoms and prevent progress of the disease.

The results of this study demonstrated the superiority of a combination of salicylate iontophoresis, joint interplay plus exercise to alleviate the clinical symptoms of the disease. In addition, salicylate iontophoresis and

exercise proved to be more effective than joint interplay plus exercise for controlling symptoms.

Although the findings of this study are significant, further research is required to examine the long term effectiveness of these techniques before their use can be advocated with any degree of confidence. Without further research their use remains emperical.

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# الملتعر العربي

# مور عملية التأين ضم التحريك السلبي في تخفيف ألآم غشونة الركبة

الهدف الأساسى لهذه الدراسة هو مقارنة تأثير دور عملية التأين ضد التحريك السلبى في تخفيف الأم خشونة الركبة . وقد أجريت هذه الدراسة على ثمانين مريضا تم أختيارهم من العيادة الخارجية للعظام بالقصر العيني ممن يعانون من الأم خشونة الركبة ، بدون إصابات أو أمراض أخرى في الركبة وتتراوح أعمارهم بين ٤٠ - ٢٠ عاما وتم تقسيمهم إلى أربع مجموعات متساوية . وقد أستخدم في علاج المرضى عملية تأيين السلسيلات والعلاج اليدوى للمفصل ، عملية التأين بالإضافة اللى العلاج اليدوى للمفصل بالإضافة إلى التمريضات العلاجية الثلاثة بالترتيب . أما المجموعة الضابطة فكانت تحت إشراف علاج طبى .

العلاجية لكل من الملجموعات العلاجية الثلاثة بالعربيب . أما المجموعة الصابحة قنائك لحث إسراف فادع كبين . وقد تم علاج كل مريض في كل مجموعة من المجموعات الثلاثة الأولى في ثلاث جلسات أسبوعيا لمدة أسبوعين . وقد استخدم في عملية النقرة ما دلي :-

خط لتقييم الآلم - مراجع لتقييم الأم الركبة - قياس شدة العضلة - قياس الأم بالضغط.

وقد أوضحت نتيجة هذه الدراسة أن نسبة الألم أنخفضت انخفاضا وأضحا في المجموعة الثالثة حيث تم تطبيق التمرينات العلاجية والجهاز الأيوني والعلاج اليدوي للمفصل وكانت المجموعة التالية لها من حيث انخفاض الألم هي المجموعة الأولى ثم المجموعة الثالثة . وكمان الانخفاض في نسبة الألم غير ملحوظ في المجموعة الرابعة (المجموعة الضابطة).