

Clinical evaluation of cissus quadrangularis and moringa oleifera and osteoseal as osteogenic agents in mandibular fracture

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ABSTRACT

Background: Ayurveda the ancient science of medicine describes various herb preparations that achieve the hastening of bone healing. Harjor showed clinical efficacy in the treatment of fractures. **Objectives:** The comparative evaluation of herbal agents as osteogenic agents in mandibular fractures. **Study design:** The patients were divided into four groups. *Group 1:* Osteoseal; *Group 3:* Harjor (Cissus quadrangularis); *Group 2:* Moringa (Moringa Oleifera); *Group 4:* Placebo. **Result and Conclusion:** Pain, Swelling, Tenderness, Mobility reduction is maximum in Osteoseal group and minimum in Placebo. There was an increase in the serum calcium and phosphorus level at different follow-ups in each groups but there was a decrease in the placebo group. Ca, Ca⁺, Phosphorous increase was maximum in the group 1.

Key words: Osteogenic, prana, Asthisanghara

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INTRODUCTION

Fractures of the jaw bones render not only physical trauma but also makes the person miss out on work productivity and other social obligations for a period ranging from four to eight weeks on an average.

Fractures of the jaw bones, like other bones of the body take a reasonably long time to heal. Attempts have been made through the centuries to be able to reduce this period of six to eight weeks, either by means of improved surgical technology or by interfering with the physiological mechanism of bone healing.

Ayurveda the ancient science of medicine describes various herb preparations that achieve the hastening of bone healing.

In Ayurveda most of the names of the plants have been given according to their medicinal values.

The plant is known as Harshankar in Hindi and Asthisanghara in Sanskrit. Harjor means that which joins the bones (har is bone, jor the one which joins).

MATERIALS AND METHODS

Patients with jaw fracture were selected randomly from the outpatient department of the Oral and Maxillofacial Surgery and Trauma center. Patients with mandible fracture and associated undisplaced maxilla, zygomatic complex fracture were also included. Patients on steroid therapy or immunosuppressants and suffering from any other chronic debilitating diseases were not included in this study. The drugs were provided by the

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International Institute of Herbal Medicine in capsule form. The dose was two capsules twice/day with meals.

A total of 44 patients were included in this study and divided into four groups [Tables 1-4].

Group 1: Osteoseal

Group 3: Harjor (Cissus quadrangularis)

Group 2: Moringa (Moringa Oleifera)^[1]

Group 4: Placebo

The capsules were provided by the International Institute of Herbal Medicine and they were certified organic, they were free from any pesticides and chemicals and heavy metals. These were freshly powdered whole herb part dried to low moisture content of 6-7% and then grinded with slow grinders at low temperature. This specific limit of moisture prevents the degradation of the phyto chemicals and also the chemical reaction between different in poly-herbal formulations. This is the only way which can provide at least 90% of the prana of the whole herb intact. In this method most of the active constituents are maintained for a long period and are highly bio-available to the human system through the gastrointestinal tract.

The consent of the patients was obtained after the explaining the nature of the study. Proforma was filled, brief history and clinical examinations were recorded.

Pre- and post-treatment serum calcium, total and ionic,

and phosphorus were also investigated. Radiographs were taken pre- and post-treatment.

Patients were called at the first, fourth, and sixth week for examination—pain, swelling, tenderness, and mobility of the fractured segment were recorded.

Table 2: Moringa olifera (Group 2) analysis of clinical variables at different follow-ups

n = 11	Score Mn ± SD	Change in Score Mn ± SD	't'	'P'	Sig.	
Pain						
Baseline	2.73 ± 0.47	-	-	-	-	
1 week	0.64 ± 0.50	2.09 ± 0.54	12.86	<0.001	Sig.	
1 month	0.0 ± 0.00	2.73 ± 0.47	19.36	<0.001	Sig.	
6 weeks	0.00 ± 0.00	2.73 ± 0.47	19.36	<0.001	Sig.	
Swelling						
Baseline	2.73 ± 0.47	-	-	-	-	
1 week	0.55 ± 0.52	2.18 ± 0.63	12.00	<0.001	Sig.	
1 month	0.0 ± 0.00	2.73 ± 0.47	19.30	<0.001	Sig.	
6 weeks	0.00 ± 0.00	2.73 ± 0.47	19.30	<0.001	Sig.	
Tenderness						
Baseline	2.00 ± 0.45	-	-	-	-	
1 week	0.81 ± 0.40	1.88 ± 0.46	19.68	<0.001	Sig.	
1 month	0.18 ± 0.40	1.82 ± 0.40	14.91	<0.001	Sig.	
6 weeks	0.00 ± 0.00	2.00 ± 0.45	14.83	<0.001	Sig.	
Mobility						
Baseline	1.91 ± 0.30	-	-	-	-	
1 week	0.91 ± 0.30	1.00 ± 0.45	07.42	<0.001	Sig.	
1 month	0.18 ± 0.40	1.73 ± 0.47	12.26	<0.001	Sig.	
6 weeks	0.00 ± 0.00	1.91 ± 0.30	21.00	<0.001	Sig.	
Ca	BT	8.62 ± 0.72	-0.0745 ± 0.97	0.25	0.40	NS
	AT	8.54 ± 0.08				
Ca +	BT	3.58 ± 1.33	+0.2164 ± 0.9375	0.76	0.23	NS
	AT	3.79 ± 0.96				
P	AT	3.68 ± 1.01	-0.02 ± 0.96	0.006	0.50	NS
	BT	3.66 ± 0.94				

There was significant reduction in pain, swelling, tenderness, mobility at different time intervals (follow-ups). Ca, Ca⁺ and P there were non significant changes at AT, Sig. = Significant, NS = Not Significant

Table 1: Osteoseal (Group 1) analysis of clinical variables at different time intervals

n = 11	Mn ± SD	Change Mn ± SD	't'	'P'	Significant	
Pain						
Baseline	2.81 ± 0.41	-	-	-	-	
1 week	0.91 ± 0.54	1.91 ± 0.54	11.74	<0.001	Sig.	
1 month	0.0 ± 0.00	2.81 ± 0.41	23.11	<0.001	Sig.	
6 weeks	0.00 ± 0.00	2.81 ± 0.41	23.11	<0.001	Sig.	
Swelling						
Baseline	2.73 ± 0.46	-	-	-	-	
1 week	0.36 ± 0.51	2.36 ± 0.67	11.63	<0.001	Sig.	
1 month	0.0 ± 0.00	2.73 ± 0.46	19.37	<0.001	Sig.	
6 weeks	0.00 ± 0.00	2.73 ± 0.46	19.37	<0.001	Sig.	
Tenderness						
Baseline	2.36 ± 0.50	-	-	-	-	
1 week	1.00 ± 0.44	1.36 ± 0.50	8.96	<0.001	Sig.	
1 month	0.0 ± 0.00	2.36 ± 0.50	15.54	<0.001	Sig.	
6 weeks	0.00 ± 0.00	2.36 ± 0.50	15.54	<0.001	Sig.	
Mobility						
Baseline	2.36 ± 0.50	-	-	-	-	
1 week	1.00 ± 0.44	0.91 ± 0.30	10.00	<0.001	Sig.	
1 month	0.18 ± 0.40	1.73 ± 0.46	12.26	<0.001	Sig.	
6 weeks	0.00 ± 0.00	1.91 ± 0.30	21.00	<0.001	Sig.	
Ca	BT	8.9545 ± 0.7367	0.4909 ± 0.7436	2.19	0.03	Sig.
	AT	9.4455 ± 0.5027				
Ca +	BT	3.4145 ± 1.3108	0.6664 ± 0.9854	2.24	0.024	Sig.
	AT	4.0809 ± 1.1556				
P	AT	3.5727 ± 0.9127	0.40545 ± 0.4150	3.23	p < 0.01	Sig.
	BT	3.9773 ± 0.7421				

There was significant reduction in severity in pain, swelling, tenderness, mobility at different time intervals (follow-ups). Ca, Ca⁺ P increase significant at AT

Table 3: Harjor (Group 3)

n = 11	Mn ± SD	Change in Score Mn ± SD	't'	'P'	Significant
Pain					
Baseline	2.36 ± 0.81	-	-	-	-
1 week	0.27 ± 0.47	2.09 ± 0.70	9.90	<0.001	Sig.
1 month	0.0 ± 0.00	2.36 ± 0.81	9.68	<0.001	Sig.
6 weeks	0.00 ± 0.00	2.36 ± 0.81	9.68	<0.001	Sig.
Swelling					
Baseline	2.36 ± 0.81	-	-	-	-
1 week	0.27 ± 0.47	2.09 ± 0.70	9.90	<0.001	Sig.
1 month	0.0 ± 0.00	2.36 ± 0.81	9.68	<0.001	Sig.
6 weeks	0.00 ± 0.00	2.36 ± 0.81	9.68	<0.001	Sig.
Tenderness					
Baseline	1.91 ± 0.70	-	-	-	-
1 week	0.36 ± 0.50	1.54 ± 0.52	9.82	<0.001	Sig.
1 month	0.00 ± 0.00	1.91 ± 0.70	9.04	<0.001	Sig.
6 weeks	0.00 ± 0.00	1.91 ± 0.70	9.04	<0.001	Sig.
Mobility					
Baseline	1.73 ± 0.47	-	-	-	-
1 week	0.64 ± 0.50	1.09 ± 0.30	12.00	<0.001	Sig.
1 month	0.00 ± 0.00	1.73 ± 0.47	12.26	<0.001	Sig.
6 weeks	0.00 ± 0.00	1.73 ± 0.47	12.26	<0.001	Sig.
Ca					
BT	8.76 ± 1.15	0.46 ± 1.03	1.47	0.18	NS
AT	9.21 ± 0.74				
Ca +					
BT	3.24 ± 1.45	0.41 ± 0.76	1.77	0.10	NS
AT	3.65 ± 1.09				
P					
AT	3.43 ± 0.47	0.38 ± 0.42	2.96	<0.01	Sig.
BT	3.81 ± 0.55				

There was significant reduction in pain, swelling, tenderness, and mobility. There were non-significant Ca, Ca⁺ and P increase in at AT, Sig. = Significant, NS = Not Significant

Radiographic interpretation was done which showed there was significant radiographic evidence of the early healing of the fracture in the cases treated with Osteoseal, Harjor followed by Moringa and at last Placebo [Tables 1-5].

OBSERVATION and RESULTS

1. Result

Osteoseal is Best group and Placebo is worst.

Pain, swelling, tenderness, mobility reduction in maximum in osteoseal group and minimum in placebo at different follow-ups Ca, Ca⁺, P increase is maximum.

2. Result

The most common cause of trauma was found to be RTA, followed by fall from height as described in Table 1.

The most common site of fracture was parasymphysis (45.4%) followed by body fracture (34.9%), and the least common site was ramus fracture [Table 2].

The increased number of automobiles on the road and lack of traffic sense, coupled with high speed are the main causes of RTAs.

Table 4: Placebo (Group 4) comparison of clinical variables at different follow-up

n = 15	Mn ± SD	Change Mn ± SD	't'	'P'	Significant
Pain					
Baseline	2.37 ± 0.50	-	-	-	-
1 week	0.91 ± 0.70	1.45 ± 0.69	7.02	<0.001	Sig.
1 month	0.18 ± 0.40	2.18 ± 0.44	17.89	<0.001	Sig.
6 weeks	0.00 ± 0.00	2.37 ± 0.50	15.54	<0.001	Sig.
Swelling					
Baseline	2.27 ± 0.46	-	-	-	-
1 week	0.82 ± 0.60	1.45 ± 0.68	7.02	<0.001	Sig.
1 month	0.0 ± 0.00	2.27 ± 0.47	17.89	<0.001	Sig.
6 weeks	0.00 ± 0.00	2.37 ± 0.50	15.54	<0.001	Sig.
Tenderness					
Baseline	1.81 ± 0.41	-	-	-	-
1 week	1.00 ± 0.00	0.82 ± 0.40	6.70	<0.001	Sig.
1 month	0.45 ± 0.52	1.36 ± 0.50	8.96	<0.001	Sig.
6 weeks	0.00 ± 0.00	1.81 ± 0.41	14.91	<0.001	Sig.
Mobility					
Baseline	1.73 ± 0.47	-	-	-	-
1 week	1.09 ± 0.30	0.64 ± 0.50	4.18	<0.001	Sig.
1 month	0.91 ± 0.30	0.81 ± 0.60	4.50	<0.001	Sig.
6 weeks	0.00 ± 0.00	1.73 ± 0.47	12.26	<0.001	Sig.
Ca					
BT	8.82 ± 0.87	-0.65 ± 0.68	3.18	<0.001	Sig.
AT	8.16 ± 0.80				
Ca +					
BT	4.23 ± 0.26	-0.27 ± 0.39	2.31	<0.05	Sig.
AT	3.96 ± 0.35				
P					
AT	3.47 ± 0.66	-0.28 ± 0.38	2.45	<0.05	Sig.
BT	3.19 ± 0.53				

There was significant reduction in pain, swelling, tenderness, and mobility at different follow-ups. Ca, Ca⁺ and P decreased significantly at AT, Sig. = Significant, NS = Not Significant

3. Result

Osteoseal is best group and Placebo is worst.

Pain, swelling, tenderness, mobility reduction is maximum in osteoseal group and minimum in Placebo. There was an increase in the serum calcium and phosphorus level at different follow-ups in each groups but there was a decrease in the placebo group. Ca, Ca⁺, phosphorus increase was maximum in the osteoseal group.

Suitable, antibiotic, analgesic, and anti-inflammatory drugs were given for five days [Tables 6 and 7].

DISCUSSION

Cissus quadrangularis contains vitamins and steroid which are found to have a specific effect on bone fracture healing. The anabolic steroidal principle from Cissus quadrangularis shows a marked influence on the rate of fracture healing by influencing early regeneration of all connective tissues involved in the healing and quicker mineralization of callus. There was shortening of about two weeks in the duration of bone healing.^[2]

The hastening in the fracture healing was attributed to the stimulation of all cells of mesenchymal origin, namely, the fibroblasts, chondroblasts and osteoblasts, by Cissus quadrangularis.

Table 5: Comparison of change in severity in clinical variables among the groups

	(A)	(B)	(C)	(D)	AVB		AVC		AVD		BVC		BVD		CVD	
	Osteoseal Mn±SD	Moringa Mn±SD	Harjor	Placebo	t	p	t	p	t	p	t	p	t	p	t	p
Pain																
1 W	1.91±0.54	2.09±0.54	2.09±0.70	1.45±0.69	0.78	NS	0.68	NS	1.74	NS	0	NS	2.42	<0.05	2.16	<0.05
1 M	2.81±0.41	2.73±0.47	2.36±0.81	2.18±0.44	0.42	NS	1.65	NS	3.48	<0.01	1.31	NS	2.84	<0.01	0.65	NS
6 W	2.81±0.41	2.73±0.47	2.36±0.81	2.37±0.50	0.42	NS	1.65	NS	2.25	<0.05	1.31	NS	1.74	NS	0.02	NS
Swelling																
1 W	2.36±0.67	2.18±0.63	2.09±0.70	1.45±0.68	0.64	NS	0.93	NS	3.16	<0.01	0.32	NS	2.61	<0.05	2.18*	NS
1 M	2.73±0.46	2.73±0.47	2.36±0.81	2.27±0.47	0.0	NS	1.31	NS	2.32	<0.05	1.31	NS	2.29	<0.05	0.31	NS
6 W	2.73±0.46	2.73±0.47	2.36±0.81	2.27±0.47	0.0	NS	1.31	NS	2.32	<0.05	1.31	NS	2.29	<0.05	0.32	NS
Tenderness																
1 W	1.36±0.50	1.18±0.40	1.54±0.52	0.82±0.40	0.93	NS	0.82	NS	2.80	<0.01	1.82	NS	2.11	NS	3.64 ^(C)	NS
1 M	2.36±0.50	1.82±0.40	1.91±0.70	1.36±0.50	2.80	<0.01	1.74	NS	4.70	<0.001	0.37	NS	2.39	NS	2.12*	NS
6 W	2.36±0.50	2.00±0.45	1.91±0.70	1.81±0.41	1.78	NS	1.73	NS	2.82	<0.01	0.35	NS	1.04	NS	0.41	NS
Mobility																
1 W	0.91±0.30	1.00±0.45	1.09±0.30	0.64±0.50	0.56	NS	1.42	NS	1.53	NS	0.55	NS	1.78	NS	2.56*	NS
1 M	1.73±0.47	1.73±0.47	1.73±0.47	0.81±0.60	0.04	NS	0.04	NS	3.99	<0.001	0.0	NS	4.01	<0.001	4.01 ^(C)	NS
6 W	1.91±0.30	1.91±0.30	1.73±0.47	1.73±0.47	0.07	NS	1.06	NS	1.06	NS	1.06	NS	1.07	NS	1.07	NS
Ca	0.49±0.74	0.08±0.97	0.46±1.03	-0.65±0.68	1.12	NS	1.80	NS	3.75	<0.001	0.90	NS	2.04*	NS	2.99 ^(B)	NS
Ca+	0.67±0.98	0.21±0.94	0.41±0.70	-0.27±0.39	1.11	NS	0.63	NS	2.91	<0.01	0.55	NS	1.60	NS	2.66	NS
P	0.40±0.42	0.02±0.96	0.38±0.47	-0.28±0.38	1.21	NS	0.14	NS	3.96	<0.001	1.14	NS	1.77	NS	4.73 ^(C)	NS

–ve sign shows decrease from baseline* $P<0.05$, sig., (B) $P<0.01$ sig. (C) $P<0.001$ sig., NS = not significant, W = Week, M = Month

Table 6: Etiology

Etiology N-44	%
Road traffic accident (RTA)	79.3
Fall from height	11.5
Interpersonal violence	9.09
Animal bite	1.4

Table 7: Site of fractures

Sites	%
Symphysis	9.04
Parasymphysis	45.4
Body	34.9
Angle	25
Ramus	4.5
Subcondyle	18.4
Maxilla	4.5
Zygoma	4.5

Thus *Cissus quadrangularis* builds up the chemical composition of the fractured bone namely mucopolysachrides, collagen calcium phosphorus and others as well as its functional efficiency.^[2]

In our study intermaxillary fixation was removed at the third or fourth week in cases which were treated by Harjor and Osteoseal, there was no mobility no tenderness. At the sixth week there was a significance rise in serum calcium both ionic and total, and serum phosphorus also. In another study there was no significance alternation in the serum calcium level at the third week.^[3] Radioactive Ca64 bone uptake decreased in the first week, followed by a gradual increase in subsequent weeks, and came to normal in six to eight weeks. It seems that Harjor increases the efficacy of the fracture healing mechanism which functions under the rule of maximum economy deposition of calcium is just enough safe joining of the broken parts of bone

and entire remodeling process comes to end faster.^[4-6]

In another study the early radiographic evidence of periosteal reactin and bony dissolution in the Harjor-treated group indicates a faster healing process.^[2] Active constituents of *Cissus quadrangularis* may stimulate the proliferation and differentiation of mesenchymal cells (MSCs) and promote new bone formation through the WntLRP5-B-Creatnin signaling pathway of pre-osteoblast formation. It can be used to treat various bone disorders and can also be used as a preventive measure for disorders that lead to decreased bone mineral density.^[7]

The role of nutrition in bone healing is the most important factor which influences bone healing, Calcium is effective but cannot be utilized just by increasing the uptake—the ability of absorption of the calcium also has to be increased. Lysine is an amino acid that helps in the absorption of calcium, Vitamin C is essential nutritionally to make the collagen that helps the body form healthy bones. It also promotes bone healing. Aspirin and anti-inflammatory drugs can retard bone healing. The damaged cells in the fractured area release a large amount of prostaglandin these are important in first stage of tissue repair, and as so causes pain, and if blocked by pain killers for longer duration can affect n bone healing. The antioxidant and antimicrobial activities are also reported by Murthy *et al.*^[8,9]

The plant extract serves as a rich source of calcium ion, when reacted with CO₂ lead to formation of calcite crystals of highly irregular morphology indicating that bioorganic molecules present in extract modulate the crystals morphology.^[10]

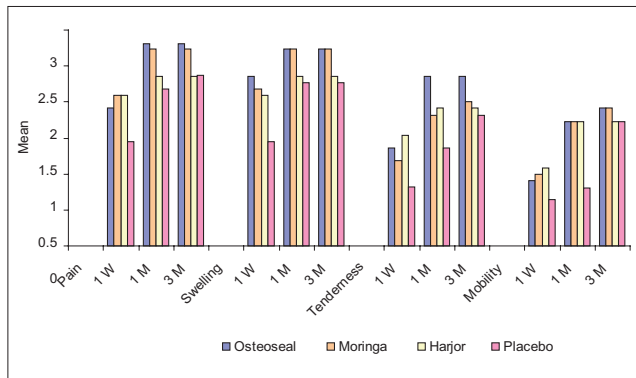


Figure 1: Comparative clinical evaluation

The leaves and stems of *Moringa olifera* are known to have a large amount of their calcium bound in calcium oxalate crystals more vitamin than carrot, more calcium than milk more iron than spinach more vitamin c than orange and more potassium than in Banana.^[9]

One tablespoon of (8 g) of leaf powder will satisfy about 14% of protein, 40% of calcium, 23% of iron, and all the vitamin A needs of a child aged one to three years. Six teaspoons full of powder will satisfy nearly all the women, daily need of iron and calcium needs during pregnancy and breast feeding.^[4]

It also has potent antibacterial, antifungal, antiviral, and anti-inflammatory activity analgesic antipyretic and muscle relaxant actions.^[11,12]

Osteoseal is a formula with the highest natural bioavailable calcium, phosphorus, vitamins and amino acids. It helps prevent bone density loss, supplies natural, herbal calcium and minerals for strong bones and teeth, speeds healing of fractured bones, promotes healthy bone growth and increases bone mineral density in osteoporosis. It is a combination of Harjor, Shajan and Neem.^[4]

Osteoseal should be avoided during the first three months of pregnancy and should not be recommended in higher doses for the rest of the pregnancy due to its neem content which has some anti-fertility and abortive properties.

Neem is to prevent infection in the fractured bone joint and surrounding tissues as well as to support the analgesic anti-inflammatory action of these two herbs.

Harjor showed clinical efficacy in the treatment of fractures,^[5] our study also showed reduction in intermaxillary fixation time from six weeks to three to four weeks with Osteoseal, followed by Harjor, followed by Moringa, and in cases of placebo there was no reduction in time of intermaxillary fixation

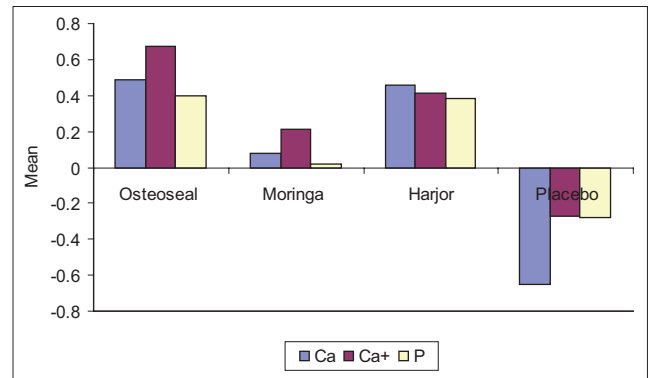


Figure 2: Comparative biochemical evaluation

[Figure 1]. Serum Ca level, both ionic and total, and serum phosphorus level were significantly increased in the other three groups but decreased in the placebo group [Figure 2].

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