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EFFECTIVENESS OF PROTEOLYTIC ENZYMES (PAPAIN AND BROMELAIN) IN COMPARISON WITH PHYSICAL THERAPY (EXERCISE AND THERAPEUTIC ULTRASOUND) IN OSTEOARTHRITIS OF KNEE JOINT

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ABSTRACT

The present research is intended to explore a new dimension for the management of knee joint osteoarthritis. This study resulted in encouraging results for the administration of enzymes (bromelain & papain) supplementation along with physical therapy measures for the management of knee joint arthritis. As therapeutic exercises are effective but slow in commencement, therefore such remedy is required which can accelerate the recovery period. These two methods of alternative medicine fulfill the need particularly in associations between pain and disability (functional status).

Key-words: Osteoarthritis, enzymes, supplementation, physical therapy, disability

INTRODUCTION

Osteoarthritis (OA) is one of the most common causes of functional loss and disability in the old age people (Blackburn 1996). It is the most well-known condition influencing synovial joints as well (Lopez and Murray, 1998). It is a degenerative joint disease in which the cartilage degeneration is the fundamental feature and has got the highest incidence of all diseases (Deyle *et al.,* 2005). It is commonly associated with hypertrophic alterations in the bone (Goodman, 2005) and can cause remarkable pain and loss of functional status (Bruyere *et al.,* 2010). Growing age is the strongest risk factor for practically all types of osteoarthritis. Obesity is one of the common risk factors in many types of arthritis, particularly in the weight-bearing joints like knee joint (Chao and Kalunian, 2010). General physical training appears to be beneficial to patients with OA of the knee joint (Rogind *et al.,* 1998). Studies have been undertaken to investigate the effects of different exercises like aerobic and anaerobic training on serum lipid per oxidation levels and on antioxidant enzyme activities (Turgay and Kayatekin, 2000). The focus of physical therapy treatment for osteoarthritis is to develop awareness for self-management, increase strength and range of motion, decrease in pain, and improve functional daily living activities (Corriveau and Pelland, 2001; Walsh and Hurley, 2009). Along with conventional treatments, the supplements or neutraceuticals are regularly administered to the patients of arthritis like chondrotin and Glucoseamine (Huskisson, 2009). Usually management is progressed pharmacologically with acetaminophen and when acetaminophen is unsuccessful to overcome the symptom then NSAID therapy is the next option (Towheed *et al.,* 2006). A study showed that hyaluronidase and collagenase treatment of cartilage wounds increases histological integration and improves biomechanical bonding strength (Bravenboer and Caroline, 2004).

Enzyme supplementation can be an effective non-surgical preference for those suffering from osteoarthritis. Efficacy of enzymes has been a topic of discussion in different research studies. Proteolytic enzymes have analgesic effect, besides the well known anti-inflammatory and edema-reducing properties (Klein and Kullich, 1999).

Bromelain is a basic, aqueous extract obtained from both the plant stems and unripe pineapple (*Ananas comosus* Merr, var Cayenne of the Family Bromeliaceae) fruit, which contains various proteolytic enzymes. *Bromelain* is usually recommended due to its anti-inflammatory, analgesic, antithrombic, and fibrinolytic properties. The reported research studies specify that the utilization of bromelain, at different doses and duration, have constructive clinical results in form of reduced soft tissue swelling, pain and joint inflexibility (Cohen and Goldman, 1964).

Enzymes like pancreatin, bromelain, and papain are vital for relieving inflammation and arthritis pain, as well as quickening time of recovery from injuries and essential for the efficient absorption of carbohydrates and proteins as well. Alongwith conventional treatments, the supplements or neutraceuticals like chondrotin and Glucoseamine are regularly administered to the patients of osteoarthritis (Huskisson, 2009). Increasing the production of hayaluronic acid (HA) by means of glucoseamine administration might be a way to explain the pain relieving effect of glucoseamine. HA is synthesized by hyaluronic acid synthases HAS (Uitterlinden *et al.,* 2008). A short-term evaluation study has indicated that oral enzymes could be considered as an effective and safe alternative to NSAIDs such as diclofenac in the treatment of painful osteo-arthritis (Klein and Kullich, 2000). Another study gave initial

evidence that the protease supplement may be useful for reducing strength loss immediately after eccentric exercise and for aiding in short-term strength recovery.

The analysis of the above given two therapeutic features, their interaction and effects on arthritic joint was investigated. Prospective randomized controlled clinical trials in a homogeneous patient group with Knee osteoarthritis (OA) were conducted and following groups were formulated and classified as:

Group A (n=20) performed exercises (Isometric quard), drilling exercises 15 x 3 sets each)
Group B (n=20) performed exercises and received ultrasound Therapy (0.5 W/cm^2 X 3 mints)
Group C (n=20) received therapeutic ultrasound therapy, and was given oral enzymes supplements (Bromelain & Papain tablets 2 x BD for 3 Weeks).

Written informed consents were obtained from all patients.

MATERIALS AND METHODS

Population dynamics:

Human samples were collected from physiotherapy department of Fatima hospital, Baqai Medical University (BMU) and Baqai Institute of Diabetology and Endocrinology (BIDE). In sampling following aspects were taken into consideration i.e. gender, age, grade of osteoarthritis, cause of osteoarthritis, environmental and occupational conditions etc. The method used for processing of samples depended on the objective of the study and on the intended use of data obtained.

Inclusion Criteria

Patients of either sex, aged 50–80 years, fulfilling the American College of Rheumatology clinical and radiological criteria for knee osteoarthritis, were enrolled. Also if they had a history of symptoms for at least 6 months and insufficient/failed response to analgesics and/or regular non-steroidal anti-inflammatory drugs (NSAID), or were intolerant to regular NSAID. The diagnosis of OA is based on clinical signs and symptoms and radiological features but most often based on radiographic study (Rousseau and Delman, 2007).Osteoarthritis patients samples were distributed across grade II, III and grade IV arthritis according to Kellgren and Lawrence index KL (Kellgren and Lawrence, 1957) and (Menkes, 1991). After a series of sampling different sub groups were formulated and classified as:

Group A: n=20 performed exercises only
Group B: n=20 performed exercises and given ultrasound therapy treatment
Group C: n=20 performed ultrasound therapy, and received enzymes supplement.

Kellgren and Lawrence index (KL)

Patients were assessed by a detailed physical assessment form based on Kellgren and Lawrence index (KL) (Peterson *et al*., 1997), for the level of osteoarthritis. X-Rays to show Kellgren and Lawrence stage II, III & IV radiological evidence of unilateral or bilateral knee osteoarthritis was accepted. The Kellgren-Lawrence scorings were from 0 to 4, where:

0 = Normal radiograph
1 = Doubtful pathology
2 = Minimal osteophytes, possible narrowing, cysts, and sclerosis
3 = Moderate, as in definite osteophytes with moderate joint space narrowing
4 = Severe, with large osteophytes and definite joint space narrowing.

Exclusion Criteria

The exclusion criteria ensured that no subject/patient had inflammatory knee disorders, other arthropathies, metabolic bone disease, serious systemic diseases, neoplasms, history of knee trauma or knee surgery, and previous intra-articular injections, knee joint replacement, rheumatoid arthritis, Paget's disease, joint fractures, hyperparathyroidism, hyperthyroidism and hypothyroidism clinical joint effusion, varus or valgus knee deformity (at physical examination, as confirmed by standard radiograph).

Out Come Measures

Physical Markers/Parameters:

To check out the difference in physical parameters and functional status of the patients suffering from osteoarthritis, a visual analogue scale (For Pain Analysis), Quadriceps strength (MMT) and to determine the functional status (6 minute walk test MWT) and goniometry (ROM) was performed after 6 sessions of treatment interventions in all groups.

RESULTS AND DISCUSSION

GROUP: 1 (Exercise Interventions)

Patients participated in 20 out of 20 assessments (100%). With mean age (58.50) male (50%) female (50%).

GROUP: 2 (Exercise and Therapeutic Ultrasound)

Patients participated in 20 out of 20 assessments (100%). With mean age (57.00) male (50%) female (50%).

Exercise and Therapeutic Ultrasound Group

As it is evident from the above statistics that in this group, the combined interventions (Exercise and Therapeutic Ultrasound) effects significantly in improving pain (VAS = 0.007) and functional status (6MWT = 0.010) of knee joint arthritis patients as compared to exercise group.

As exercises and ultrasound therapy is useful in decreasing pain, therefore it is evident from the above graphical representation that these two interventions made significant difference not only physiologically but statistically too.

Exercises are helpful in maintaining physical and functional status of patients. Therefore, its efficacy is an integral part in osteoarthritis of knee joint in which the physical activities of patients get compromised.

GROUP: 3
(Received ultrasound therapy & Enzymes Supplement)

Therapeutic Ultrasound and enzymes supplementation Group

Therapeutic interventions (Enzymes supplementation and Ultrasound therapy) made considerable and marked difference in all aspects i.e. in diminishing pain (VAS = 0.000), improving range of motion (ROM = 0.006) and above all in improving functional status (6 MWT = 0.015). As limited functional independence is the core issue in knee osteoarthritic patients.

Enzymes supplementation made a drastic change in the pain and functional management of patients with knee joint arthritis. Physical evaluation designate that oral enzymes can be administered as an efficient and secure adjunct to therapeutic exercises, therapeutic ultrasound and other pharmaceutical treatment such as NSAIDs or diclofenac in the management of painful osteoarthritis of knee joint.

As decrease of pain make patient to move is pain free range which help patient to use muscle power effectively, hence helped in improving muscle strength or upgrading of muscle grade.

As therapeutic ultrasound is well-known for its mechanical properties and smashing of adhesions therefore along with enzymes supplementation therapeutic ultrasound helped in decrease adhesions. In other words, we can say that their combined effects helped in restoration of range of motion (ROM).As above graph shows that clearly.

Functional independence is one of the chief complaints of knee arthritic patients. Non pharmacologic measures were evaluated to improve the activities of patients with knee joint osteoarthritis. The results provided by the combined interventions of therapeutic ultrasound and enzyme supplementation to patients can be recommendation to improve the functional status of patients with knee joint arthritis.

The object of this study was to explore a new dimension for the management of knee joint osteoarthritis. As far as our knowledge is apprehended, this study encouraging results. Particularly associations between pain, disability (functional status), and muscle strengthening consequences in patients with osteoarthritis of knee joint. Based on the evidences, patients who were treated with therapeutic exercises only showed mild and short term improvement (decrease pain and improve muscle strength) on the visual analogue scale (VAS) and manual muscle testing criteria (MMT). Those patients who were treated with the physical therapy exercises and therapeutic ultrasound, showed comparatively reasonable improvement or beneficial effects on pain and mild beneficial effects on disability outcome measures (6MWT). Ultrasound demonstrated the capability to generate therapeutically effects which may offer secure and efficient application in the management of knee joint arthritis. On the other hand, those patients who were treated with physical therapy exercise and enzymes supplementation reported significantly pain and

stiffness than the other group of patients. The efficacy of oral enzyme therapy (supplementation) along with therapeutic ultrasound, in patients with moderate to severe knee joint osteoarthritis was analyzed in group 3. The enzymes supplements papain and Bromelain can be recommended for moderate to severe knee osteoarthritis when taken in combination with physiotherapeutic treatment options. Productive result for enzyme supplementation group in osteoarthritis patients were found out and these results incorporated with significant pain reduction, improve functional status and to some extent enhanced cartilage repair. No adverse events associated with the medication were reported in any of these case reports.

Table 1. Case Summary Group 1 (Pre-Treatment) (N = 20).

S.NO.	Age of subject	Gender of subject	VAS Before Treatment	MMT Before Treatment	ROM before Treatment	Functional Status
1	50	Female	7	3	Decrease/Limited ROM	Decrease
2	70	Female	8	4	Normal/Complete	Normal
3	60	Male	5	3	Decrease/Limited ROM	Decrease
4	50	Female	8	3	Decrease/Limited ROM	Decrease
5	60	Female	7	3	Decrease/Limited ROM	Decrease
6	55	Female	8	4	Normal/Complete	Normal
7	50	Female	10	3	Decrease/Limited ROM	Decrease
8	50	Female	8	4	Decrease/Limited ROM	Decrease
9	60	Male	6	4	Normal/Complete	Normal
10	60	Male	8	4	Decrease/Limited ROM	Decrease
11	60	Male	7	3	Decrease/Limited ROM	Normal
12	55	Male	9	3	Decrease/Limited ROM	Decrease
13	70	Male	5	4	Normal/Complete	Normal
14	50	Male	6	4	Normal/Complete	Decrease
15	50	Male	7	3	Decrease/Limited ROM	Decrease
16	65	Female	5	4	Normal/Complete	Normal
17	50	Female	8	4	Normal/Complete	Decrease
18	50	Female	9	3	Decrease/Limited ROM	Decrease
19	65	Male	9	3	Decrease/Limited ROM	Decrease
20	60	Male	8	3	Decrease/Limited ROM	Decrease

Table 2. Case Summary Group 1 (Post Treatment) (N = 20).

S.No.	Age Of subject	Gender of subject	VAS Before Treatment	MMT Strength Before Treatment	ROM before Treatment	Functional Status
1	50	Female	5	3	Improve	Improve
2	70	Female	5	4	Normal/Complete	Normal

3	60	Male	4	4	Improve	Improve
4	50	Female	7	4	Improve	No change
5	60	Female	5	4	Improve	Improve
6	55	Female	5	4	Normal/Complete	Normal
7	50	Female	6	3	Improve	No change
8	50	Female	8	4	Improve	No change
9	60	Male	6	4	Normal/Complete	Normal
10	60	Male	4	4	No change	Improve
11	60	Male	4	4	Improve	Normal
12	55	Male	6	4	No change	No change
13	70	Male	4	5	Normal/Complete	Normal
14	50	Male	3	4	Normal/Complete	Improve
15	50	Male	4	5	No change	No change
16	65	Female	2	4	Normal/Complete	Normal
17	50	Female	3	4	Improve	Improve
18	50	Female	5	3	No change	No change
19	65	Male	4	4	Improve	No change
20	60	Male	7	4	Improve	No change

Table 3. Case Summary Group 2 (Pre-Treatment) (N=20).

S.NO.	Age of subject	Gender of subject	VAS Before Treatment	MMT Strength Before Treatment	ROM before Treatment	Functional Status
1	60	Female	8	grade 4	Decrease/Limited ROM	Decrease
2	70	Male	7	grade 4	Normal/complete ROM	Decrease
3	57	Male	8	grade 3	Decrease/Limited ROM	Decrease
4	60	Male	6	grade 3	Normal/complete ROM	Normal
5	63	Female	9	grade 3	Decrease/Limited ROM	Decrease
6	50	Female	9	grade 3	Decrease/Limited ROM	Decrease
7	80	Female	8	grade 4	Decrease/Limited ROM	Decrease
8	55	Male	7	grade 3	Decrease/Limited ROM	Decrease
9	50	Female	6	grade 4	Normal/complete ROM	Normal
10	50	Male	5	grade 5	Normal/complete ROM	Normal
11	60	Female	7	grade 4	Decrease/Limited ROM	Decrease
12	50	Male	9	grade 3	Decrease/Limited ROM	Decrease
13	52.00	Male	8	grade 3	Decrease/Limited ROM	Decrease

14	64.00	Female	7	grade 4	Decrease/Limited ROM	Decrease
15	60	Male	7	grade 4	Decrease/Limited ROM	Decrease
16	50	Female	6	grade 4	Normal/complete ROM	Normal
17	59.00	Male	8	grade 3	Decrease/Limited ROM	Decrease
18	55	Female	9	grade 3	Decrease/Limited ROM	Decrease
19	70	Male	9	grade 3	Decrease/Limited ROM	Decrease
20	55	Female	7	grade 4	Normal/complete ROM	Decrease

Table 4. Case Summary Group 2 (Post-Treatment) (N=20).

S.NO.	Age of subject	Gender of subject	VAS After Treatment	MMT Strength After Treatment	ROM After Treatment	Functional Status
1	60	Female	7	Grade-3	Improve	Improve
2	70	Male	6	Grade-3	Normal	No change
3	57	Male	8	Grade-3	Improve	No change
4	60	Male	5	Grade-3	Normal	Normal
5	63	Female	7	Grade-4	No change	No change
6	50	Female	7	Grade-3	No change	No change
7	80	Female	7	Grade-3	Improve	No change
8	55	Male	5	Grade-3	Improve	Improve
9	50	Female	6	Grade-4	Normal	Normal
10	50	Male	5	Grade-4	Normal	Normal
11	60	Female	6	Grade-3	Improve	No change
12	50	Male	7	Grade-3	Improve	Improve
13	52	Male	8	Grade-3	No change	No change
14	64	Female	6	Grade-3	No change	No change
15	60	Male	5	Grade-3	Improve	No change
16	50	Female	6	Grade-4	Normal	Normal
17	59	Male	7	Grade-3	Improve	No change
18	55	Female	8	Grade-3	Improve	Improve
19	70	Male	7	Grade-3	Improve	No change
20	55	Female	7	Grade-4	Normal	Normal

Table 5. Case Summary Group 3 (Pre-Treatment) (N=20).

S.No.	Age of Subject	VAS Before Treatment	MMT Strength Before Treatment	ROM before Treatment	Functional Status
1	70	6	3	Decrease/Limited	Decrease/Limited

2	55	5	4	Normal/Complete	Normal/Complete
3	75	8	4	Decrease/Limited	Decrease/Limited
4	50	6	3	Decrease/Limited	Decrease/Limited
5	55	8	3	Decrease/Limited	Decrease/Limited
6	55	9	3	Decrease/Limited	Decrease/Limited
7	50	6	4	Normal/Complete	Normal/Complete
8	50	7	3	Decrease/Limited	Decrease/Limited
9	55	8	3	Decrease/Limited	Normal/Complete
10	75	5	4	Normal/Complete	Normal/Complete
11	60	9	3	Decrease/Limited	Decrease/Limited
12	50	6	3	Decrease/Limited	Decrease/Limited
13	60	9	3	Decrease/Limited	Decrease/Limited
14	60	9	3	Decrease/Limited	Decrease/Limited
15	60	8	4	Decrease/Limited	Decrease/Limited
16	65	9	3	Decrease/Limited	Decrease/Limited
17	65	8	3	Decrease/Limited	Decrease/Limited
18	55	8	3	Decrease/Limited	Decrease/Limited
19	60	8	4	Decrease/Limited	Decrease/Limited
20	65	7	3	Decrease/Limited	Decrease/Limited

Table 6. Case Summary Group 3(Post-Treatment) (N=20).

S.NO.	Age of subject	VAS After Treatment	MMT Strength After Treatment	ROM After Treatment	Functional Status
1	70	5	4	Improve	Improve
2	55	3	4	Normal/Complete	Normal
3	75	6	5	Improve	Improve
4	50	4	4	Improve	Improve
5	55	5	4	Improve	Improve
6	55	4	5	Improve	Improve
7	50	3	5	Normal/Complete	Normal
8	50	5	4	Improve	No change
9	55	3	5	Improve	Improve
10	75	4	5	Normal/Complete	Normal
11	60	4	4	No change	Improve
12	50	3	4	Improve	Improve
13	60	5	4	Improve	Improve
14	60	5	4	Improve	Improve
15	60	6	4	Improve	Improve
16	65	5	5	Improve	No change
17	65	6	4	Improve	Improve
18	55	4	4	Improve	Improve
19	60	6	5	No change	Improve
20	65	4	5	Improve	Improve

CONCLUSION

Dealing with osteoarthritis necessitates a many-sided and comprehensive approach like combination of pharmacological (enzymes supplementation) and non- pharmacological (exercise and therapeutic ultrasound) therapies. Bromelain and papain have together revealed steady effectiveness in diminishing knee arthritis pain and improving joint functional status related with osteoarthritis. These supplements can be securely undertaken as primary remedy in osteoarthritis patients prior to initiating treatment with acetaminophen, NSAIDs, physical therapy treatment and other conventional medication. However, there are definite indications to recommend that these enzymatic agents combined with therapeutic exercises possibly will help not only in prevention of radiographic succession of disease but also in improving the functional status of the patients.

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