

Comparative Efficacy of Open-chain and Close-chain Kinematics on Proprioception, Muscles' Strength and Functional Performances in Individual with Knee Osteoarthritis

Caleb Ademola Gbiri*, Udoka A Chris Okafor and Micheal Taiwo Alade

Department of Physiotherapy, College of Medicine, University of Lagos, Idi-Araba, Lagos, Nigeria

Abstract

This study was designed to compare effects of open-chain and close-chain kinetics on proprioception, muscles' strength and functionality on individual with knee osteoarthritis. Eight-week experimental study was conducted on twenty-five participants. Participants were randomized into two groups. The first group was involved in close-chain exercises (kinesthesia and balance exercises). The second group was involved in open-chain exercises in form strengthening exercises. Their knee proprioception, functional performances, severity of osteoarthritis, muscles' strength and pain were assessed pre-exercise and post-exercise intervention. Twenty-five participants completed this study giving 16.67% attrition rate. Their mean age was 62.7 ± 8.5 years. The close-chain group showed significantly better improvement than the open-chain group in physical function, energy, role limitation, pain and severity of osteoarthritis. The close-chain group performed significantly better in all performances and proprioception after interventions. It was concluded that close-chain kinematics is more effective in improving proprioception functional performances in individuals with knee osteoarthritis.

Keywords: Osteoarthritis; Knee; Kinesthesia; Proprioception; Exercise

Introduction

The great increase in the elderly population worldwide is the most important change in the field of public health in the 21st century. It has been estimated that the number of people over the age of 65 years will be doubled in the first two decades in the 21st century [1]. Consequently, osteoarthritis (OA) and other diseases that are associated with old age will become much more important both medically and economically, posing great demand on the health facilities and caregiver's resources.

Osteoarthritis is the most commonly encountered disease of the musculoskeletal system [2]. Symptoms and disability in individuals with osteoarthritis increase in prevalence with increasing age [3] and they use health-care services at a higher rate than individuals with other chronic diseases [4]. The number of people with OA disability is expected to double by the year 2020 [5], thereby increasing its already significant economic burden. The physical disability arising from knee OA prevents the performance of daily life activities and negatively affects the life quality [2]. Several factors play roles in the occurrence of physical disability in osteoarthritis patient. These include pain, restriction in joint range of movement, muscle weakness, and coordination impairment [6].

The coexistence of knee OA and weakness of the quadriceps muscle groups are well known [7]. Muscle strength measurements are important in the follow-up of outcome of the treatment and the quality of life in individuals with OA [8]. The effect of OA on proprioception has also been established. Decreased proprioception results in predisposition to development of osteoarthritis due to abnormal position of the joint and contributes to functional insufficiency by affecting functional parameters such as decreased walking speed, shortened step and decreased total walking time [9]. However, there is still a big cloud on how to improve proprioception in these individual.

There is significant loss of proprioception and kinesthesia sensation in individuals with osteoarthritis of the knee joint [2,8]. Impaired proprioception adds to functional insufficiency by generating

impairment in walking rhythm, shortening step distance, and a decrease in walking speed and total walking time [6]. Therefore, efforts have been directed towards increasing proprioception in individuals with knee osteoarthritis but the best method of achieving this is still elusive. Therefore this study investigated the comparative effects of close-chain exercises (combined kinaesthesia and balance training) and open-chain exercises (muscle strengthening) on knee proprioception and thigh muscle strength in individuals with osteoarthritis of the knee.

Methods

Prior to the commencement of the study, ethical approval was obtained from a Research and Ethical Committee. All study participants were informed about the procedure of the study and written informed consent was obtained from each patient. The exercise training was carried out in the physiotherapy out-patient department of two tertiary health institutions in Nigeria. Patients who met the inclusion criteria were randomized into two groups (close-chain and open-chain exercises groups) using the one-to-one randomization method by allocating one patient to the study group and the other patient to the control group one by one according to their order in the hospital register. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and the Medical Outcomes Study Short Form Health Survey (SF-36) were used in the assessment of the patients before and after 8 weeks of exercise programme. Isokinetic muscle strength of the quadriceps

*Corresponding author: Caleb Ademola Gbiri, Department of Physiotherapy, College of Medicine, University of Lagos, Idi-Araba, Lagos, Nigeria, Tel: +2348185434054, +2348033598072; E-mail: cgbiri@unilag.edu.ng, calebgbiri@yahoo.com

Received January 27, 2013; Accepted February 23, 2013; Published February 25, 2013

Citation: Gbiri CA, Okafor UAC, Alade MT (2013) Comparative Efficacy of Open-chain and Close-chain Kinematics on Proprioception, Muscles' Strength and Functional Performances in Individual with Knee Osteoarthritis. *Occup Med Health Aff* 1: 104. doi:10.4172/2329-6879.1000104

Copyright: © 2013 Gbiri CA, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

and hamstring muscles, 10 meter walking time, 10 stairs climbing time, and the sensation of proprioception in the knee were measured on each participant. Proprioception measured was assessed using reproductive test measurements. The subject's ability to reproduce the active and passive knee angles was evaluated at different angles. This procedure was repeated three times at one-day intervals and the averages for every angle were obtained. Care was taken to carry out the testing in a quiet environment in eyes-closed position. The subjects were tested in supine position on a plinth that positioned the subject in different angle of knee flexion. The subjects were asked to reproduce knee flexion from a predetermined angle of passive knee flexion. Using a table tensiometer, the peak torque value of the quadriceps and hamstring muscles group were measured at different angles of the knee joint. Peak torque/body weight (N-m/kg) ratio was used for evaluations. The tensiometer was tied to the legs, at the ankle joint, the subjects were asked to pull the device to a 10 maximum pull.

The close-chain group participated in kinaesthesia and balance exercises while the open-chain group received only strengthening exercises. Prior to the exercises, patients in both groups were informed about knee osteoarthritis and protective recommendations for the knee. The exercises were performed twice a week at duration of thirty minutes at an interval of one day under the researcher's supervision. Isometric and isotonic strengthening exercises were applied to quadriceps and hamstring muscles. Isometric exercises were applied with six seconds contractions with eight repetitions and a rest period of two seconds. Isotonic exercises were started from the third week and the maximum weight that can be lifted 10 times (10 repetition maximum [10 RM]) was determined. The exercises were applied as 10 repetitions with half of this weight, 10 repetitions with three fourths of this weight, and 10 repetitions with the whole 10 RM. 10 RM was determined every week.

The following kinaesthesia and balance exercises were carried out by the participants in the close-chain exercise group:

At week one

1. Standing with feet together in eyes-closed and training balance time without sway.
 - a. On hard ground
 - b. On soft ground (on a mat)
2. Retro walking (25 m)
3. Walking on heels (25 m)
4. Walking on toes (25 m)
5. Walking with eyes closed (25 m)
6. Standing on one extremity for 30 second (repeated in both extremities), leaning forward, backward, and to the sides on one extremity (eyes open), leaning forward, backward, and to the sides on one extremity (eyes closed), and sitting down and standing up from a high chair slowly
7. Stair-up and -down a regular 3 steps staircase (17 cm high and 23 cm wide)
8. Standing with feet approximately shoulder width apart and extend arms out slightly forward and lower than the shoulder. Lift both heels off the floor and try to hold the position for 10 seconds. This was followed by climbing a regular 3 steps staircase (17 cm high and 23 cm wide), up and down

9. Standing with feet side by side, hold arms in the same position as described in the previous exercise. Place one foot on the inside of the opposing ankle and try to hold the position for 10 seconds, followed by climbing a regular three steps staircase (17 cm high and 23 cm wide), up and down

At week two (in addition to exercises during week one)

1. Exercise with wobble board
2. Sitting down and standing up from a low chair slowly
3. Plyometric exercise (crossing a height of 15cm by jumping)
- 4 (a) Walking slowly in a wide circle of 10 meter radius
- (b) Walking quickly in a wide circle of 10 meter radius
- (c) Walking slowly in a narrow circle of 5 meter radius
- (d) Walking quickly in a narrow circle of 5 meter radius

At week three (in addition to exercises during week two)

1. Walk heel-to-toe along a 3m line marked on a medium-density polyfoam mat
2. With the knee straight but not hyperextended, execute single (relatively small) leg raises to the front, then back. This was continued alternating front to back
3. Plyometric exercise (crossing a height of 15 cm by jumping)

The exercises performed on the third day were repeated all through rest of the weeks

The lower extremity isometric and isotonic strengthening programmes were carried out as follows:

At week one:

1. 5-min fixed bike exercise without resistance
2. Range-of-motion and active stretching exercises applied to hamstring and quadriceps muscles
3. Quadriceps isometric strengthening exercise
4. Hamstring muscles isometric exercise

At week two: (in addition to exercises during week one)

1. Short-arc terminal extension exercise for the knee joint
2. Isometric exercise for the abductor and adductor muscles of the hip joint

At week three: (in addition to exercises in week two)

1. Short-arc terminal extension exercise with resistance for the knee joint
2. Isometric strengthening exercise with resistance for the hamstring muscles

The exercises performed on the third day was repeated all through rest of the weeks

Data was summarized using descriptive statistics and standard deviation, frequency and percentiles. Independent *t*-test was used to compare the proprioception and functional performance in the two groups. Pearson's correlation coefficient was used to find the relationship between proprioception and functional performance.

Results

Twenty-five out of the 30 participants completed this study giving 16.67% attrition rate. Their age ranged between 47 and 74 years with a mean of 62.7 ± 8.5 years, (Table 1). Their mean height, weight and BMI

Variables	Kinaesthesia group		Strengthening group	
	Mean	SD	Mean	SD
Age (years)	60.2	8.3	65.9	8.1
Height (cm)	1.53	0.1	1.57	0.1
Weight (kg)	70	12.8	74.2	20.6
Body Mass Index (kg/m ²)	30	5.1	31.8	14.3

Table 1: Physical characteristics of the participants.

Parameter		Experimental Group		Control Group		p-Value
		Mean	SD	Mean	SD	
10 m walk-time	Pre-exercise	13.3	2.3	11.9	3.8	0.20 (Seconds)
	Post-exercise	19.2	3.4	21.1	4.2	0.23
	p-Value	0.00		0.00		
4-stair climbing	Pre-exercise	12.5	2.1	14.3	5.9	0.01
	Post-exercise	17.5	5.7	19.9	7.6	0.35
	p-Value	0.00		0.00		
Physical function	Pre-exercise	18.2	14.1	16.3	9.3	0.3
	Post-exercise	39.3	9.5	35.1	8.3	0.79
	p-Value	0.00		0.00		
Pain	Pre-exercise	21.3	5	18.2	4.5	0.73
	Post-exercise	10	7.9	8.5	4.3	0.09
	p-Value	0.00		0.00		
Osteoarthritis severity	Pre-exercise	75.4	17.9	67.4	16.2	0.82
	Post-exercise	35.6	26.1	33	15.3	0.23
	p-Value	0.00		0.00		
Role limitation	Pre-exercise	59.2	19.3	65.9	20.1	0.84
	Post-exercise	37.9	12.8	35.5	15.7	0.95
	p-Value	0.00		0.00		
Energy	Pre-exercise	58.2	14.4	55.4	18.6	0.45
	Post-exercise	70.6	12.9	74.1	9.4	0.59
	p-Value					
40° Knee flexion (N-m/ kg)	Pre-exercise	40.2	7.2	44.3	4.6	0.04
	Post-exercise	40.1	1.3	40.9	1.7	0.1
	p-Value	0.05		0.03		
60° Knee flexion (N-m/ kg)	Pre-exercise	64.6	5.7	64.5	6.5	0.8
	Post-exercise	61.2	1.3	60.5	2	0.21
	p-Value	0.03		0.03		
80° Knee flexion s	Pre-exercise	84.1	5.6	82.9	6.5	0.61
	Post-exercise	82.1	1.4	80.9	1.1	0.26
	p-Value	0.04		0.04		
Hamstring muscle strength	Pre-exercise	5.9	2.1	4.9	2	0.33
	Post-exercise	8.6	1.3	9.1	2.3	0.02
	p-Value	0.00		0.00		
Quadriceps muscle strength	Pre-exercise	12	4	10.3	3.7	0.73
	Post-exercise	16.8	2.8	16.8	4.4	0.88
	p-Value	0.00		0.00		
p<0.00						

Table 2: Pre and post-intervention comparison of the performances of the two groups of the participants.

Parameter	Close-chain		Open-chain		p-Value
	Mean Difference	SE	Mean Difference	SE	
Hamstring strength	4.181	0.084	3.500	0.054	0.002
Quadriceps strength	4.367	0.063	5.208	0.07	0.031
40° angle of proprioception	3.431	0.860	2.114	0.923	0.012
60° angle of proprioception	4.001	1.431	4.000	0.843	0.512
80° angle of proprioception	2.000	1.826	1.909	0.980	0.807
10 meter walk	9.157	0.143	7.645	0.125	0.002
4-stair climbing	5.670	0.496	5.532	0.466	0.034
Osteoarthritis symptom	4.273	0.452	5.279	0.196	0.047
Knee stiffness	1.182	0.189	2.250	0.003	0.045
Pain	9.745	0.075	10.596	0.306	0.022
ADL	18.746	0.298	20.021	0.590	0.008
Severity	34.409	0.282	37.467	0.837	0.005
General Health	12.341	0.137	11.542	0.087	0.007
Physical Health	47.728	5.135	39.583	4.522	0.002
Emotional Health	54.555	0.477	47.225	1.083	0.007
Energy	18.727	2.758	15.875	0.988	0.012

Table 3: Comparison of the effect of close-chain and open-chain kinematics of the symptoms and severity of osteo-arthritis in the participants.

were 71.8 ± 16.4 kg, 1.55 ± 0.1 meters, 30.8 ± 10.0 kg/m² respectively (Table 1). Ten (40%) were married while 15 (60%) were widows (Table 1). There were significant improvement in the pre-exercise and post-exercise training values of 4-stair climbing and physical function in both groups (Table 2). The close-chain group's scored significantly lower than those in open-chain group in 4-stair climbing at post-exercise training period (Table 2). The close-chain group showed significantly better improvement than the open-chain in physical function, energy, role limitation, pain and severity of osteoarthritis at post-exercise stage. The post-exercise value of the close-chain group was lower and but closer to the predetermined angle than those of the strengthening group. There was significant improvement between the pre-exercise and post-exercise periods in the two groups (Table 2). The mean values of the quadriceps and hamstrings muscles were significantly higher in the open-chain group than the close-chain group at post-exercise training period (Table 2). There was significant inverse relationship between each of walking-time and stair-climbing and ability to perform the activity of daily living and the health-related quality of life. There was no significant difference in the pre-exercise and post-exercise measures of proprioception at 400 and 800 of knee flexion in the open-chain group (Table 2). The close-chain group performed significantly better in all performances except in quadriceps muscle strength, symptoms of osteoarthritis, knee stiffness and pain severity (Table 3). There was no significant difference in performances in the proprioception in the two groups except in the 400 proprioception where the close-chain group performed significantly better (Table 3).

Discussion

The study investigated the comparative effects of combined kinaesthesia and balance training, and muscle strengthening on knee proprioception and thigh muscle strength in individuals with osteoarthritis of the knee. The mean age of the participants for this study shows that knee osteoarthritis is more common at elderly age. The fact that more than four-fifth (84) of the participants were female shows the higher prevalence of osteoarthritis of the knee among women than men at older age. This may be attributed to the hormonal changes that occur in post-menopausal women. Women have been shown to demonstrate increase in body adiposity and body weight after menopause. Increase

in weight has also been shown to significantly predispose an individual to early and severe knee osteoarthritis. The significant increase in 10 m walk-time between the pre-exercise and post-exercise stages in both groups shows that combined kinaesthesia and balance training is as effective as strengthening exercise in improving functional performance in terms of walking speed in individuals with knee osteoarthritis. So also, the fact that none of the groups demonstrated better significant improvement in the walking time shows that both techniques are effective in improving functionality in individuals who is undergoing rehabilitation from knee osteoarthritis. This finding agrees with those of Skinner et al. [10] and Sharma et al. [11] who concluded that combined kinaesthesia and balance training had no superior advantage over strengthening in improving walking-time in people with knee osteoarthritis. However, it disagrees with that of Diracoglu et al. [2] who despite record of effectiveness of strengthening concluded that combined kinaesthesia and balance training programmes had superiors advantage in improving walking time in individuals with knee osteoarthritis.

The finding that both combined kinaesthesia and balance training, and strengthening exercise improved stair-climbing in individuals with knee osteoarthritis also shows the effectiveness of these programmes in the rehabilitation of individuals with knee osteoarthritis. The fact that there was no significant difference in the post-rehabilitation outcome in terms of stair-climbing shows that clinicians have the choice of choosing either of these programmes to improve stair-climbing function in individuals with osteoarthritis of the knee. This result disagrees that of Diracoglu et al. [2] that there was better improvement in the 4-stair-climbing at post-exercise in people who have undergone combined kinaesthesia and balance than those who underwent strengthening.

This result of this study showed significant improvement in physical function, energy, role limitation, pain and severity of osteoarthritis at the post-rehabilitation period. This shows that both combined kinaesthesia and balance training, and strengthening rehabilitation programmes are effective in improving participation and functionality as well as severity of symptoms in individuals with knee osteoarthritis. This result agrees with that of Van der Esch et al. [12] who stated that the interaction between muscle strength and proprioception contributed significantly to the variance in functional ability and an increase of muscle strength would result in a bigger improvement in functional ability. The outcome of this study also revealed that patient with poor proprioception and weak muscle strength can benefit from the exercise performed in form of either combined kinaesthesia with balance training or muscle strengthening programmes. It also shows that combined proprioception and balance training will significantly improve muscle strength in individuals with knee osteoarthritis. This shows that muscle performance can be effectively improved in patients with muscle weakness if kinaesthesia and balance training programme is utilized. This will reduce the cumbersomeness that characterized the use of weight in strengthening of weak muscles. Therefore, Physiotherapists will have alternative source of muscle strengthening programme rather than over-reliance on weight for strengthening programme. This improvement may have been due to the inter-relationship between improved proprioception and increase muscle strength [12,13]. The remarkable improvement in the level of proprioception in the two groups showed that a good kinaesthesia and balance training coupled with strength training as well as a standard strength training programme is effective in improving proprioception in individuals with knee osteoarthritis. This finding corroborates previous studies who opined that poor proprioception can be compensated by adequate muscle strength [2,13-16]. This study showed that poor

proprioception is association with knee osteoarthritis. This finding corroborates findings of previous studies that osteoarthritis impairs proprioception [17-19]. This impaired proprioception has been said to be a general problem and not a local phenomenon in knee OA patients [19-21]. This functional status and motor control improvement might have been due to improvement in dynamic stabilization, synergistic and synchronous working of the muscle groups resulting from repetitive movements that that characterize activities of daily living [2,22,23].

Conclusion

This study showed that proprioceptive perception is impaired in individuals with knee osteoarthritis and that this impairment is large enough as it affects their functional performance. Both open-chain and close-chain kinematics improve functional performance and reduce symptoms and severity in individuals with knee osteoarthritis. Close-chain kinematics is more effective in improving proprioception functional performances in individuals with knee osteoarthritis.

References

1. Adelman AM, Daly MP (2001) Twenty common problems in geriatrics. International McGraw-Hill Medical Publishing Division.
2. Diracoglu D, Aydin R, Baskent A, Celik A (2005) Effects of kinesthesia and balance exercises in knee osteoarthritis. *J Clin Rheumatol* 11: 303-310.
3. Hawker GA, Wright JG, Coyte PC, Williams JI, Harvey B, et al. (2001) Determining the need for hip and knee arthroplasty: the role of clinical severity and patients' preferences. *Med Care* 39: 206-216.
4. Gabriel SE, Crowson CS, Campion ME, O'Fallon WM (1997) Direct medical costs unique to people with arthritis. *J Rheumatol* 24: 719-725.
5. Elders MJ (2000) The increasing impact of arthritis on public health. *J Rheumatol Suppl* 60: 6-8.
6. Sharma L, Cahue S, Song J, Hayes K, Pai YC, et al. (2003) Physical functioning over three years in knee osteoarthritis: role of psychosocial, local mechanical, and neuromuscular factors. *Arthritis Rheum* 48: 3359-3370.
7. Messier SP, Glasser JL, Ettinger WH Jr, Craven TE, Miller ME (2002) Declines in strength and balance in older adults with chronic knee pain: a 30-month longitudinal, observational study. *Arthritis Rheum* 47: 141-148.
8. Hassan BS, Doherty SA, Mockett S, Doherty M (2002) Effect of pain reduction on postural sway, proprioception, and quadriceps strength in subjects with knee osteoarthritis. *Ann Rheum Dis* 61: 422-428.
9. KeerR, Grahame R (2003) Hypermobility syndrome: Recognition and management for therapists. New York, Edinburg, Butterworth-Heinemann.
10. Skinner HB, Barrack RL, Cook SD, Haddad RJ Jr (1984) Joint position sense in total knee arthroplasty. *J Orthop Res* 1: 276-283.
11. Sharma L, Pai YC, Holtkamp K, Rymer WZ (1997) Is knee joint proprioception worse in the arthritic knee versus the unaffected knee in unilateral knee osteoarthritis? *Arthritis Rheum* 40: 1518-1525.
12. Van der Esch M, Steultjens PM, Knol D, Dinant H, Dekker J (2006) Joint laxity and the relationship between muscle strength and functional ability in patients with osteoarthritis of the knee. *Arthritis Rheum* 55: 953-959.
13. Fransen M, McConnell S, Bell M (2002) Therapeutic exercise for people with osteoarthritis of the hip or knee. A systematic review. *J Rheumatol* 29: 1737-1745.
14. Grob KR, Kuster MS, Higgins SA, Lloyd DG, Yata H (2002) Lack of correlation between different measurements of proprioception in the knee. *J Bone Joint Surg Br* 84: 614-618.
15. Riemann BL, Lephart SM (2002) The Sensorimotor System, Part II: The Role of Proprioception in Motor Control and Functional Joint Stability. *J Athl Train* 37: 80-84.
16. Verhagen E, van der Beek A, Twisk J, Bouter L, Bahr R, et al. (2004) The effect of a proprioceptive balance training program for the prevention of ankle sprains: a prospective controlled trial. *Am J Sports Med* 32: 1385-1393.

17. Garsden LR, Bullock-Saxton JE (1999) Joint reposition sense in subjects with unilateral osteoarthritis of the knee. *Clin Rehabil* 13: 148-155.
18. Koralewicz LM, Engh GA (2000) Comparison of proprioception in arthritic and age-matched normal knees. *J Bone Joint Surg Am* 82: 1582-1588.
19. Lund H, Juul-Kristensen B, Christensen H (2004) Impaired proprioception of both knees and elbows in patient with knee osteoarthritis compared to healthy participants. *Osteoarthritis and Cartilage*. 12 (Suppl B, 9th World Congress of the Osteoarthritis Research Society International).
20. Prentice WE, Reestablishing proprioception, kinesthesia, neuromuscular control in rehabilitation. *Rehabilitation Techniques in Sport Medicine*, (2nd edn) pp118 –125 McGraw Hill.
21. Shakoor N, Furmanov S, Nelson DE, Li Y, Block JA (2008) Pain and its relationship with muscle strength and proprioception in knee OA: Results of an 8-week home exercise pilot study. *J Musculoskelet Neuronal Interact* 1: 35-42.
22. Lesmes GR, Costill DL, Coyle EF, Fink WJ (1978) Muscle strength and power changes during maximal isokinetic training. *Med Sci Sports* 10: 266-269.
23. Brinkmann JR, Perry J (1985) Rate and range of knee motion during ambulation in healthy and arthritic subjects. *Phys Ther* 65: 1055-1060.

Citation: Gbiri CA, Okafor UAC, Alade MT (2013) Comparative Efficacy of Open-chain and Close-chain Kinematics on Proprioception, Muscles' Strength and Functional Performances in Individual with Knee Osteoarthritis. *Occup Med Health Aff* 1: 104. doi:[10.4172/2329-6879.1000104](https://doi.org/10.4172/2329-6879.1000104)

Submit your next manuscript and get advantages of OMICS Group submissions

Unique features:

- User friendly/feasible website-translation of your paper to 50 world's leading languages
- Audio Version of published paper
- Digital articles to share and explore

Special features:

- 250 Open Access Journals
- 20,000 editorial team
- 21 days rapid review process
- Quality and quick editorial, review and publication processing
- Indexing at PubMed (partial), Scopus, DOAJ, EBSCO, Index Copernicus and Google Scholar etc
- Sharing Option: Social Networking Enabled
- Authors, Reviewers and Editors rewarded with online Scientific Credits
- Better discount for your subsequent articles

Submit your manuscript at: www.omicsonline.org/submission/

