COMPARATIVE STUDY ON EFFICACY OF ACECLOFENAC AND ACECLOFENAC PLUS TIZANIDINE IN PATIENTS WITH LOW BACK PAIN AT NEPAL MEDICAL COLLEGE AND TEACHING HOSPITAL

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Abstract

Aim
To compare the efficacy of Aceclofenac and fixed dose combination of Aceclofenac and Tizanidine in the treatment of low back pain.

Methodology
This hospital based randomized, comparative prospective study was conducted with 100 outpatients suffering from LBP who met inclusion and exclusion criteria. The patients were randomized into Group A receiving Aceclofenac (100 mg) and Group B receiving fixed dose combination of Aceclofenac (100mg) and Tizanidine (2mg). Visual analog scale (VAS) was used to measure the pain score on 3rd day and 7th day during treatment.

Results: The baseline mean score for pain in Group A and Group B was 6.37±1.75 and 6.82±1.24 respectively. On 3rd day, the mean pain score of Group A and Group B was reduced to 2.30±1.39 and 1.86±1.01 and on 7th day, the mean pain score was reduced to 1.40±1.19 and 0.75 ±0.872 respectively. There was statistically significant reduction in mean pain score on group B compared to group A at the end of the treatment (P=0.002).

Conclusion
Both the drug regimen (Aceclofenac and Aceclofenac+Tizanidine) were found to be effective while, Aceclofenac+Tizanidine had higher efficacy compared to Aceclofenac only at the end of treatment

Introduction
Low Back Pain (LBP) is the most common complication in day to day life among all people which imposes an enormous social and economic burden on society, and can be seriously disabling associated with high costs of health care, work absenteeism and disablement.1 In general, 60-80% of the world’s population experience LBP during some point in their life.2 World Health Organization study on primary care of persistent pain and well-being, reported that back pain (47.8%) topped the list of most common anatomical pain sites in order of frequency, followed by headache (45.2%), and joint pain (41.7%).3 In the context of Nepal, overall annual prevalence of LBP was 71%, with a prevalence of 67.9% in males and of 74.3% in females and the total duration of back pain in one year was less than 15 days in 73% cases.4 About two thirds of adults suffer from low back pain and is the most frequent reason for visiting a physician5. International guidelines for the management of LBP recommends that the condition should principally be managed in primary care.6 The most common causes of LBP vary from lumbar strain, trauma, degenerative spondylitis, prolapsed disc, osteoporosis, osteomalacia, infection, tumors, ankylosing spondylitis and its prevalence ranges from 8% to 37% with peak prevalence between 45 to 60 years of age.7 Individuals with a history of prior back pain are considered to be at risk of recurrent or persistent back pain and the probability of LBP recurrence within the first year ranges from 60-80%.8
In general, LBP is managed with the short-term use of non-steroidal anti-inflammatory drugs (NSAIDs) and centrally acting skeletal muscle relaxants. Antispasmodic agents (like Tizanidine, Chlorzoxazone, Beclofen) are also effective in the management of nonspecific LBP. Muscle relaxants are also effective in limiting the ensuing disability. Despite of dispute on side effect, 91% of physicians report using muscle relaxants or combination with NSAIDs in LBP due to fast pain relief even if they are conditionally discouraged by guidelines. Aceclofenac stimulates glycosaminoglycan synthesis in human osteoarthritic cartilage and chondroprotective effects by suppressing metalloprotease production and proteoglycan release in human rheumatoid synovial cells and are also used in low back pain with a low gastrointestinal adverse effects. Tizanidine is more effective in the treatment of moderate or severe acute low-back pain than placebo and ibuprofen alone and also possess gastro protective effect. Muscle relaxants in practice could be more useful as an adjunct to other therapeutic modalities, specifically analgesics/NSAIDs.

Hence, these limiting factors demands a need for an ideal fixed dose combination which is devoid of effects on psychomotor performance, free of sedation and higher tolerability. Aceclofenac and Aceclofenac plus Tizanidine are frequently prescribed drug for low back pain in Nepal Medical College and Teaching Hospital (NMCTH). This prospective clinical study was conducted to access and compare the efficacy of aceclofenac with fixed dose combination of aceclofenac and tizanidine in LBP patients.

Materials and methods
It is a hospital based randomized comparative prospective study with 100 patients was conducted in Department of Orthopaedics, Nepal Medical College and Teaching Hospital, atterkhel, Kathmandu from December 2014- June 2015. Both male and female patients having age between 16-70 years with low back pain, uncomplicated acute lumbarosacral pain, association with degenerative spinal disorders and with pain intensity at rest of at least 3 on a 10-point VAS were included in this study. Where as patients having definite organic cause of LBP, with a history of hypersensitivity to NSAIDs or Tizanidine, receiving muscle relaxants or analgesic therapy in the past 1 week before inclusion in the study and pregnant and lactating women were excluded from this study. Data was collected using pretested proforma and VAS. Patients were included in the study after obtaining informed consent. Pain grading on VAS before and after the drug therapy was recorded.

Patients were randomized into group A and group B. Odd number patients were included in group A and even number patients in group B. Group A patients received Aceclofenac (100 mg) alone twice a day for 7 days and group B patients received fixed dose combination tablets of aceclofenac (100 mg) and tizanidine (2 mg) twice a day for 7 days. Patients were explained about the VAS. The efficacy was compared on the basis of pain relief using VAS. Each case was followed up on day 3 and day 7 during their treatment to access their pain on VAS. Clinical efficacy of drugs under study was evaluated by using pain scores. VAS consists of 5 items for pain on 0 to 10 points while no pain at point 0. These itemswere the questions about the severity of pain, patients were currently experiencing in their lower back during study. The pain on VAS offers five response options ranging from ‘mild pain’ to ‘worst possible pain’ at 1 to 10 points. A response of ‘none’ is scored as ‘0’, mild as 1-2, moderate as 3-4, severe as 5-6, very severe as 7-8 and worst possible pain as 9-10. Scores of pain before treatment, after treatment on day 3 and day 7 were accessed. A decrease in pain score, leading to ‘0’ on VAS will be considered clinical cure.

Statistical analysis carried out using Statistical Package for Social Sciences (SPSS) version 16. The findings were summarized by using tables and bar diagrams. Results were expressed as mean ± standard deviation. Descriptive statistics like Chi-square test were used to analyze socio-demographic data. Different statistical test of significance like paired t test and independent sample t test were applied. The P value less than 0.05 were considered statistically significant. The Ethical clearance was taken from the Ethical Review Board/ Ethical Clearance Committee of Nepal Medical College and Teaching Hospital (NMCTH).
Result
Out of 100 patients, 57 (57%) were female and 43 (43%) were male. The mean age of the patients was 43.05±15.07 years. The most commonly involved age group was 36-45 years (24 patients). In Aceclofenac group, 24 (24%) were female and 19 (19%) were male while in Aceclofenac+Tizanidine group, 33 (33%) were female and 24 (24%) were male. There was no statistically significant difference (P=0.82) in gender wise distribution of low back pain in the two drug groups.

The baseline mean score for pain in Aceclofenac group was 6.37±1.75 and on 3rd day, the mean pain score was reduced to 2.30±1.39. While on 7th day, the mean pain score was reduced to 1.40±1.19, there was statistically significant difference in pain reduction (p=0.000).

Similarly, in Aceclofenac+Tizanidine group, the baseline mean pain score of LBP was 6.82±1.24 and on 3rd day, the mean pain score was reduced to 1.86±1.01. While on 7th day, the mean pain score was reduced to 0.75 ±0.87. Hence, there was statistically significant difference in pain reduction (P=0.000).
Though there was highly statistically significant reduction in visual analog scale (VAS) pain score by both drug group on their follow up, but at the end of treatment on 7th day, good response on pain reduction in Aceclofenac+Tizanidine, with statistically significant difference in pain reduction (P=0.02) was observed. The result obtained with Aceclofenac and Aceclofenac+Tizanidine on mean pain score on VAS in two groups are summarized in table below

<table>
<thead>
<tr>
<th>Visit day</th>
<th>Drug groups</th>
<th>Aceclofenac</th>
<th>Aceclofenac+Tizanidine</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td></td>
<td>6.37±1.75</td>
<td>6.82±1.24</td>
<td></td>
</tr>
<tr>
<td>Day 3</td>
<td></td>
<td>2.30±1.39</td>
<td>1.86±1.01</td>
<td>0.82</td>
</tr>
<tr>
<td>Day 7</td>
<td></td>
<td>1.40±1.19</td>
<td>0.75 ±0.87</td>
<td>0.02</td>
</tr>
</tbody>
</table>

**Discussion**

In the present study, numbers of female patients were 1.33 times higher than male patients. The number of female patients and male patients suffering from LBP were 57 and 43, respectively. The results obtained in the present study are in agreement with the study of Pareek et al. However, male patients with LBP were 1.5 times higher than female patients in his study. Another study by Desai et al had supporting result to present study with female patients 1.66 times more than male. While, Lavsky found that men reported more low back pain at the time of the interview than women. Therefore, though the result obtained in present study is supported by numerous earlier studies, there was no relationship between sex and diagnosis.

The incidence of LBP increases with age. The results of present study revealed, the number of patients was higher in age group 36-45 years (24 patients). The mean age of the patients was 43.05±15.07 years (range 16-70). The result obtained was somewhat similar to the study done by Bierring-Sorensen reporting (highest frequency of symptoms in the age range of 35 to 55) while sickness, absence, and symptom duration increase with increasing age. Crook et al reported that persistent pain has an incidence of 14%, while there was variation in age dependent estimation from 8% for patients between 10 and 30 years to 40% over 81 years of age. Study conducted by Bressler et al showed that persons over 65 years have greater frequency with low back pain. Therefore, the results of this study are in correlation with numerous workers who reported that the incidence of LBP is higher in elderly individuals.

The result for the efficacy of Aceclofenac in this study are in accordance with the preliminary findings of Schattenkirchner et al and Agrifoglio et al who demonstrated that patients of LBP treated with Aceclofenac had significantly greater reduction in pain score from baseline at the end of treatment, compared with Diclofenac. In another study conducted by Pasero et al reported that efficacy of Aceclofenac was superior to that of naproxen in the terms of mean change in pain score, leading to good pain relief. Hence, the findings of earlier studies confirmed the result in the present study that Aceclofenac is effective in treatment of LBP.

The Superiority of Aceclofenac+Tizanidine over Aceclofenac was in accordance to the result in the efficacy of fixed dose combination of Aceclofenac+Tizanidine which was similar to the findings of Pareek et al, who demonstrated that the patient of low back pain (LBP) treated with Aceclofenac+Tizanidine had significantly greater reduction in pain score from baseline at the end of treatment due to combined effect of two drugs.

The result of this study indicated that LBP is common in age group 36-45. Female are more prone to LBP than male. Both study drug group are effective in the treatment of LBP but Aceclofenac+Tizanidine appears to be more efficacious than Aceclofenac in one week treatment period.

**Conclusion**

NSAIDs and skeletal muscle relaxants are the treatment of choice for LBP. Either NSAIDs or the combination of NSAIDs and muscle relaxants are frequently used drug for LBP. Aceclofenac has comparatively fewer side-effects
Tizanidine and ibuprofen in acute persistent pain and well-being. My sincere thanks to all the friends and staffs of Department of Orthopedics. My sincere thanks to Prof. Dr. T. N. Pradhan, Department of Pharmacology, Prof. Dr. Ram Kewal Shah, Head of Department of Orthopedics, Prof. Dr. Ravikant Chhaidial Gupta, Head of Department of Community Medicine, Nepal Medical College and Teaching Hospital (NMC) and to Ms. Anushruti Shrestha for their guidance and suggestions throughout the research. My sincere thanks to all the friends and staffs of Department of Pharmacology and Department of Orthopedics for their valuable comments and moral support.

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References

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