Clinical Evaluation of the Efficacy of Arthocare Forte, A Chondro-Protective and Anti-Arthritic Drug in the Management of Bacterial Plaque-Induced Chronic Periodontitis

Anyanechi CE, Chukwuneke FN¹, Ngim N²

Departments of Dental Surgery and ²Orthopedics and Trauma, University of Calabar Teaching Hospital, Calabar, ¹Department of Oral and Maxillofacial Surgery, University of Nigeria Teaching Hospital, Enugu State, Nigeria

Abstract

Background: Arthocare forte medication is made up of different constituents and the advantages offered by this disposition have not been explored in the management of chronic periodontitis. Aim: The aim was to assess the clinical response of bacterial plaque-induced generalized chronic periodontitis to arthocare medication, and the relationship of age and gender to the prevalence of chronic periodontal disease. Subjects and Methods: This study was done at the Dental Surgery Clinic of the University of Calabar Teaching Hospital, Nigeria. It was a Prospective randomized controlled trial evaluating the effect of arthocare treatment on 81/162 patients with teeth mobility over a period of 5 years. All the patients (162) underwent root planing, and 81/162 (50%) were treated with arthocare for comparative analysis. The variables recorded were patient’s age, gender, and degree of tooth mobility, periodontal pocket, and bleeding from the pocket after treatment. Statistical analysis was done using EPI INFO 7. Results: Majority of the patients were between 46 and 75 years in both control (n = 59/81, 72.8%) and experimental groups (n = 52/81, 64.2%). There were 86/162 (53.1%) males and 76/162 (46.9%) females, giving a male-to-female ratio of 1.1:1. Seventy-seven patients (95.1%) in the experimental group had total remission in comparison to 32/81 (39.5%) in control group which was statistically significant (P < 0.001). Conclusion: The arthocare administered to patients in the experimental group speeds up the regenerative capacity and stability of the periodontium when compared with the control. Multicentre clinical trials are recommended to validate the use of arthocare forte in the treatment of generalized chronic periodontitis.

Keywords: Arthocare, Bacterial plaque, Chronic periodontitis

Introduction

Chronic periodontitis is the inflammation of the periodontal tissues and is characterized by loss of connective tissue attachment and alveolar bone.[1,2] This condition commonly induced by bacterial plaque, is endemic in all civilized societies, and after 40 years of age is the most important reason for loss or extraction of teeth, and sometimes predisposing to the development of squamous cell carcinoma of the head and neck region.[3,4] From the available literature, the therapeutic approaches for the treatment of chronic periodontitis are categorized into three: Anti-infective treatment designed to stop the progression of periodontal tissue loss by the causative agent(s); regenerative therapy, which tend to restore structures destroyed by the disease, and periodontal tissue maintenance therapy, to maintain periodontal stability that is relevant after all forms of treatment.[6,7] Consequently, over the years, the focus of treatment has been debridement-based treatments such as scaling and root planing, flap surgeries, adjunctive use of antibiotics systemically (e.g., amoxicillin, metronidazole, ciprofloxacin) or locally (e.g., tetracycline, doxycycline, minocycline, chlorhexidine, metronidazole), guided tissue regeneration using polytetrafluoroethylene membranes, enamel matrix derivative, and laser.[8-15] These treatment methods when used in isolation
or in combination have their shortcomings in clinical dental practice but have shown improvement in the patient’s condition by reducing clinical attachment loss (CAL) and periodontal pocket depths, absence or decreased bleeding on probing the periodontal pockets, reduction in tooth mobility and migration, and sometimes, this mobility is completely halted due to the reattachment of the periodontal tissue fibers to the teeth. Apart from halting disease progression and resolving inflammation which most of these treatment methods offer, the optimal goal of therapy for patients who have lost a significant amount of periodontium resulting in teeth mobility and migration is regeneration of the lost tissues in order to prevent eventual teeth loss is not achieved. However, from the existing literature, many variables responsible for complete regeneration of the periodontium are unknown.

Arthocare forte with each capsule partly containing chondroitin (400 mg) and glucosamine (500 mg) sulfates, is a chondro-protective and anti-arthritis drug that is effective in controlling degenerative joint diseases such as rheumatoid arthritis, osteoarthritis, osteoporosis, ankylosing spondylitis, and other conditions such as fractures, low back pain, and arthritis due to sport injury/active lifestyle. There is paucity of literature on the use of this drug in the management of these conditions apart from that provided by the manufacturer. However, in these circumstances, it is designed to ease articular pain, rebuild and rehabilitate damaged cartilage, reduce inflammation, and improve patients’ mobility. On the contrary, the documented side effects are gastralgia, swollen stomach, loose stool, diarrhea, nausea, insomnia, headache, and drowsiness. In addition, glucosamine may affect glucose homeostasis, and therefore, have to be used with caution in diabetic patients. Furthermore, individuals with active peptic ulcer and those on diuretics should use glucosamine cautiously as they exhibit lower response.

The basis for this attempt at using arthocare forte medication in the management of chronic periodontitis was the positive therapeutic effects of its various constituents such as glucosamine sulfate potassium, methyl sulfonyl methane (MSM), chondroitin sulfate sodium, in the treatment of chronic periodontitis and degenerative joint diseases in humans.[16-21] To the best of the authors’ knowledge, no study has been carried out in the past to determine the effect(s) of this drug on the damaged periodontium of the dentition. The purpose of this study was to determine whether arthocare forte had hoped-for effects on generalized chronic periodontitis, and the relationship of age and gender to the prevalence of chronic periodontal disease over a period of 5 years.

Subjects and Methods

We carried out a prospective randomized controlled trial that clinically evaluated the effect of arthocare forte treatment on 81 out of 162 patients with teeth mobility as a result of generalized chronic periodontitis between July 2008 and June 2013. These are consecutive patients at the Dental Surgery Clinic of our Tertiary Health Institution who gave informed consent. The sample size was calculated using two-arm sample size determination formula for statistical superiority design. Ethical approval was obtained from the Research Ethics Committee of this institution and the study conducted in accordance with the Helsinki Declaration of 1975, as revised in 2000. All the patients underwent root planing initially out of which 81/162 (50%) were treated with arthocare for comparative analysis. The variables recorded were patient’s age, gender, and degree of tooth mobility, periodontal pocket, and bleeding from the pocket after treatment.

Inclusion criteria

- Patients above the age of 15 years with one tooth diagnosed in their oral cavity as having generalized chronic periodontitis with true periodontal pockets induced by bacterial plaque and which did not show evidence of clinical or radiological involvement of the furcation area in the molar teeth
- No discharge of pus from the periodontal pockets
- Absence of occlusal trauma associated with malocclusion
- Those who kept three post treatment appointments.

Exclusion criteria

- Patients with conditions such as diabetes mellitus, peptic ulcer, blood dyscrasias, malnutrition, human immunodeficiency virus infection or acquired immunodeficiency syndrome
- Pregnant or lactating mothers
- Those on diuretics, steroid, and oral contraceptive therapy
- Admission to usage of tobacco
- Generalized chronic periodontitis due to trauma, and multiple teeth involvement
- Those generalized chronic periodontitis associated with pseudo-periodontal pockets, and lesions such as tumors, cysts, and other allied conditions.

The diagnosis of chronic periodontitis, made by the full-mouth examination and recording, was based on the presence of tooth mobility, true periodontal pockets, and bleeding of the periodontal pockets on probing. The assessment of the severity of chronic periodontitis was based on the American Academy of Periodontology classification,[22] as revised in 1999.[23,24] Tooth mobility was scored as M1, M2, and M3 in the ascending order depending on the severity, whereas periodontal pocket was also recorded depending on the CAL that was estimated from the bottom of the periodontal pocket to the cement-enamel junction at 6 sites per tooth: Mesiobuccal, center of buccal, distobuccal, mesiolingual, center of lingual and distolingual. The highest depth determined the presence or absence of periodontal pocket. Bleeding on probing (BOP) with a periodontal probe was determined by indicating sites as above that bleed within 30 s of probing. Each patient was required to have periapical radiograph of the affected tooth before treatment.
For the comparative analysis, we categorized the patients into two groups. Group A (control): Patients were allocated to each arm of the study group using computer generated numbers. Patients who underwent root planing only and B (experimental): Patients that underwent root planing in addition to arthocare forte treatment. The treatment procedures carried out in both groups on each tooth affected by chronic periodontitis were scaling and root planing. This procedure was done non-surgically by the combined use of hand instruments (Jacquette/hoe scalers, and curettes) and ultrasonic scaling devices by the dental therapist and the dental surgeon. The patients in both groups were given oral hygiene instructions and were also required to use warm saline mouth wash 6 times daily spaced out at intervals of 2 h from the following day after treatment for 1 week. The subjects in the two groups were placed on antibiotics (amoxicillin 500 mg × 8 h, metronidazole 400 mg × 8 h, for 10 days and panadol 1000 mg 8 h for 2 days). The Group B (experimental) patients in addition to the above treatment regimen received arthocare forte, one tablet × 12 h for 2 weeks as therapeutic dose, and then one tablet daily in the subsequent 4 weeks as maintenance dose. The subjects were recalled at 1, 3, and 6 weeks after commencement of treatment. The presence of tooth mobility and periodontal pockets, and bleeding on probing these pockets were re-assessed clinically in the two groups of patients at 6 weeks. Successful treatment was defined as the absence of teeth mobility, periodontal pockets, and bleeding on clinical examination. The diagnosis and treatments in this study were carried out by the same dental surgeon and dental therapist, and the study was double blinded.

The variables recorded were patient’s ages, gender, degrees of tooth mobility before and after treatment, and periodontal pocket/bleeding after treatment. The gain or loss of periodontal tissue attachment level was re-assessed clinically by comparing probing depth before and after treatment, and by re-evaluating bleeding on probing after treatment. Statistical analysis was performed using EPI INFO 7, version 0.2.0, 2012 software package (CDC, Atlanta, GA, USA). Chi-square (c²) and Student’s t-test were used to compare the degree of mobility. The level of significance was set at 0.05 where $P < 0.05$ is considered significant and $P > 0.05$ non-significant.

### Results

A total of 162 patients underwent routine root planing, out of which 81 (experimental group) were treated with arthocare forte, and the rest (control group) received nothing. Table 1 shows the distribution of age, gender, and degree of mobility of the teeth before treatment. Majority of the patients were recorded between 46 and 75 years in both Group A ($n = 59/81, 72.8\%$) and Group B ($n = 52/81, 64.2\%$). The ages of patients ranged from 24 to 81 years with a mean of 47.3 (6.5). In both groups, there were 86/162 (53.1\%) males and 76/162 (46.9\%) females, giving a male-to-female ratio of 1.1:1. The degree of teeth mobility is shown in Table 1. The severity of teeth mobility increased with patient’s age. Table 2 shows the distribution of age, gender, and degree of teeth mobility after treatment in the two groups. The study shows that the higher the degree of teeth mobility before treatment, the less likelihood of complete reattachment of the periodontal tissues to the teeth in both the control and the experimental groups. In the experimental and control groups, those who had successful treatment had their periodontal pockets completely obliterated, while those that were unsuccessfully treated in the experimental group had

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Gender (n)</th>
<th>Total (n (%))</th>
<th>Degree of mobility (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
<td>M1</td>
</tr>
<tr>
<td>Group A</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>16-25</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>26-35</td>
<td>4</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>36-45</td>
<td>3</td>
<td>6</td>
<td>9</td>
</tr>
<tr>
<td>46-55</td>
<td>15</td>
<td>10</td>
<td>25</td>
</tr>
<tr>
<td>56-65</td>
<td>9</td>
<td>12</td>
<td>21</td>
</tr>
<tr>
<td>66-75</td>
<td>7</td>
<td>6</td>
<td>13</td>
</tr>
<tr>
<td>76-85</td>
<td>2</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>42</td>
<td>39</td>
<td>81</td>
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</table>

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<th>Age (years)</th>
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<th>Total (n)</th>
<th>Degree of mobility (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
<td>M1</td>
</tr>
<tr>
<td>Group B</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16-25</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>26-35</td>
<td>5</td>
<td>3</td>
<td>8</td>
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<td>36-45</td>
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<td>56-65</td>
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<td>66-75</td>
<td>7</td>
<td>7</td>
<td>14</td>
</tr>
<tr>
<td>76-85</td>
<td>3</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>Total</td>
<td>44</td>
<td>37</td>
<td>81</td>
</tr>
</tbody>
</table>
residual pocket depths ranging from 1 to 3 mm and those in the control group were between 2 and 5 mm. However, the number of patients who had successful treatment outcome were greater in Group B \( (n = 77/81, 95.1\%) \) than in A \( (n = 32/81, 39.5\%) \) which was statistically significant \( (P < 0.001) \) in favor of the experimental group as shown in Table 3. The test of significance on the degree of mobility between the experimental and control groups was statistically significant at all levels of tooth mobility \( (M1: P < 0.001; M2: P < 0.001; M3: P < 0.001) \) in favor of the experimental group [Table 4]. In those patients who did not have successful treatment outcome in the two groups (Group A, \( n = 49/81, 60.5\% \); Group B, \( n = 4/81, 4.9\% \)), there was decreased teeth mobility relative to that at presentation. Furthermore, in this category of patients with unsuccessful treatment, periodontal pocketing/bleeding persisted in those with M2 and M3 mobility (Group A, \( n = 27/81, 33.3\% \); Group B, \( n = 0/81 \)) but not in those with M1 mobility. In general, in both groups of patients, those that were unsuccessfully treated improved on their periodontal attachment level.

In those with unsuccessful treatment outcome in Group A, there were 27/49 (33.3%) males and 22/49 (27.2%) females with male-to-female ratio of 1.2:1. The age of patients ranged from 33 to 81 years with a mean of 58.4 (3.3) years. In the experimental group, there were 2/4 (50.0%) males and 2/4 (50.0%) females with male-to-female ratio of 1:1. The age of patients ranged from 63 to 79 years with mean at 69.3 years. There was no record of allergic reaction or side effects to the drugs used during treatment.

### Discussion

From available literature, certain risk factors have been associated with the development and progression of chronic periodontitis\,[24-26] The clinical consequences of some of these factors and the side effects of the experimental drug guided the exclusion criteria in this study. This study shows that age is related to the incidence of periodontal tissue destruction. This incidence increases with age, the highest rate occurs between 50 and 60 years, and gingival recession is the predominant lesion before 40 years, while periodontal pocketing is the principal mode of destruction between 50 and 60 years of age\,[26] Unlike previous reports where males were more predisposed to this condition, the present study showed almost equal gender disposition. This may be due to other confounding variables apart from genetics that influence the development of this condition\,[27,28]

Chronic periodontitis induced by bacterial plaque is associated with a variable microbial pattern, but it is initiated by Gram-negative tooth-associated bio-film that elicits host response resulting in the destruction of the periodontal tissues\,[29] These anaerobic bacteria microbial films include porphyromonas gingivalis, bacteroides forsythus, treponema denticola, prevotella intermedia, fusobacterium nucleatum, and eubacterium specie\.[30] In response to endotoxins derived from these periodontal pathogens, several osteoclast-related mediators target the destruction of alveolar bone and other supporting connective tissue structures like periodontal ligament\.[29,31] The major drivers of this aggressive periodontal tissue destruction are matrix metalloproteinases, cathepsins, and other osteoclast-derived enzymes\.[31-33] The extent of the disease progression is influenced adversely by the presence of risk factors and the duration of disease before patient presents for treatment. These factors directly determine the degree of teeth mobility and depth of the periodontal pockets formed.

As reported earlier, the scaling and root planing carried out in the two groups of patients as treatment modality to remove supragingival plaque/calculus and subgingival debridement including oral hygiene instructions and use of warm saline mouth wash after treatment enhanced healing and bacterial plaque control by reducing clinical inflammation, periodontal pocket depth, microbial shift to a less pathogenic subgingival flora, gain in the clinical attachment level of the periodontal tissues and less disease progression\.[1,6-8] However, the periodontal pocketing/bleeding persisted in 33.3% of Group A patients and none was recorded in the experimental group. BOP is a very important clinical measurement to assess clinical response since its absence can be used as a criterion for periodontal tissue stability\.[32] Furthermore, from the existing literature, the use of antibiotics in the management of chronic periodontitis is controversial. However, adjunctive systemic antibiotics uses have been shown to offer some advantages to the treatment outcome in severe and refractory periodontitis\.[1,13] Consequently, these groups of patients benefitted from the two treatment approaches used in this study. However, the beneficial effect was more in the experimental (95.1%) than the control (39.5%) group \( (P < 0.01) \) which is likely due to the effect of arthocare forte medication speeding up the regenerative capacity and stability of the periodontium. This better treatment outcome in this group may also be due to genetic predisposition, lesser age of the patients, and better post operative compliance including maintenance of good oral

### Table 3: Test of significance on the success rate between the experimental and control group

<table>
<thead>
<tr>
<th>Degree of mobility</th>
<th>Control ( (n=81) )</th>
<th>Experimental ( (n=81) )</th>
<th>( \chi^2 )</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remission</td>
<td>32 (39.5)</td>
<td>77 (95.1)</td>
<td>41.38</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Nonremission</td>
<td>49 (60.5)</td>
<td>4 (4.9)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 4: Test of significance on the degree of mobility between the experimental and control group

<table>
<thead>
<tr>
<th>Degree of mobility</th>
<th>Control ( (n=81) )</th>
<th>Experimental ( (n=81) )</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>M1</td>
<td>4.6 (2.9)</td>
<td>0.6 (0.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>M2</td>
<td>4.4 (4.8)</td>
<td>0.0 (0.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>M3</td>
<td>2.6 (2.3)</td>
<td>0.0 (0.0)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
hygiene; clinician’s ability to remove sub-gingival deposits, and treatment of teeth with less advanced chronic periodontitis.

A capsule of arthocare forte contains glucosamine sulfate potassium chloride 500 mg, MSM 250 mg, chondroitin sulphate sodium 400 mg, Vitamin E 12.5 mg, manganese sulfate 20 mg, bora 0.5 mg, and selenium dioxide 0.06 mg. According to the manufacturer, glucosamine is an amino sugar that stimulates chondrocytes to synthesize the cartilage building blocks and inhibits lysosomal enzymes which degrade cartilage. It stabilizes the cell membrane and is an effective inhibitor of cyclooxygenase and inflammatory mediators including bradykinin, serotonin, and histamine. It was suggested that activation of protein kinase C could be one of the mechanisms through which glucosamine restores fibrillated cartilage chondrocyte adhesion to fibronectin, hence improving the repair process in osteoarthritic cartilage. Chondroitin sulfate stimulates the synthesis of proteoglycans, hyaluronic acid, and inhibits the synthesis of proteolytic enzymes, nitric oxide, and other substances that contribute to damage cartilage matrix and cause death of chondrocytes. It is used for its flexibility in joints and strengthening of muscle. Bassleer et al. noted that chondroitin sulfate causes reduction in collagenolytic activity and increases matrix component production as it has a protective effect on the damaged cartilage, allowing it to continue to re-synthesize proteoglycans. Both glucosamine and chondroitin are naturally occurring in the human body, but can also be extracted from shell-fish which explains the reason for their availability in commercial quantities. MSM is helpful in improving joint flexibility, reducing stiffness and swelling, improving circulation and cell vitality, reducing pain and scar tissue, and in breaking up calcium deposits. MSM is thought to work due to sulfur which is believed to strengthen collagen and some researchers suggested that it also has anti-inflammatory effects. Vitamin E is an antioxidant, while boron is used as a proton donor and manganese acting as a cofactor of enzymes, enhances the synthesis of proteoglycans that is needed for the formation of cartilage and bone.

It should be noted that inflammatory diseases can occur simultaneously at different anatomical sites in the same patient, and this sometimes may complicate treatment because a medication effective for one disorder may exacerbate the other. The anti-arthritic medication dexamethasone, alleviates joint disease but can worsen periodontal bone disease, while on the other hand, calcitonin had little effect on arthritis but did protect against alveolar bone loss in chronic periodontitis. On the contrary, the anti-arthritic drug DTRp8-β-MSH (DTrp), which acts through the melanocortin (MC) system to reduce both arthritic joint inflammation and chronic periodontitis is a peptide that simultaneously selectively activates MC3 receptors which prevents both arthritis and alveolar bone loss. This is the gold standard, and thus arthocare forte has the same therapeutic spectrum as DTrp, as it has both beneficial effects in the treatment of arthritis as well as chronic periodontitis.

This study was limited by the inability to estimate the depth of the periodontal pockets before treatment, and the follow-up period was short. Furthermore, chronic periodontitis involving multiple teeth and furcation areas in posterior teeth were excluded from the study. It should be noted that the limitations of consecutive recruitment of patients include overestimation of the pool of available patients who meet the inclusion criteria; along with insufficient or untimely patient recruitment.

This study has shown that generalized chronic periodontitis is more prevalent in the older age group with males more slightly affected than females. The arthocare forte administered to patients in the experimental group was of significant benefit as it speeds up the regenerative capacity and stability of the periodontium more than the control. As this medication can be administered safely, multicentre clinical trials are recommended to validate its use in the treatment of chronic periodontitis.

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