

Effect of Caesalpinia Sappan Extract on the Preventive of Relapse After Orthodontic Treatment

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Abstract

Caesalpinia Sappan is a common used by public in Asian especially Indonesia as a traditional medicine to treat various diseases, one for osteoporosis. In previous studies, Caesalpinia Sappan was shown to increase osteoblasts invitro and invivo.

The purpose of this study was to investigate the effects of caesalpinia sappan extract on bone remodeling process by looking at their effect on the amount of osteoblasts and TGF levels in post orthodontics treatment.

39 White New Zealand male rabbits divided into 4 treatment groups (without CSE, CSE with dose of 325 gr /kgBW, 650 gr/kgBW, and 1300 gr/kgBW). Histopathological preparations with Hematoxilin Eosin staining were performed to observe the amount of osteoblasts and examination of TGF β levels performed with Elisa. Analysis of varian (ANOVA) and Tukey HSD was utilized the data.

Showed significant difference in TGF- β level, on day 35 it was found that the increase of TGF β concentration, especially at 1300 gr/kgBW (620,692), the increase of osteoblast group 650 gr/kgBW on day- 35 which is 51.57 although not significant and the distance between incisive is greater in the group 1300 gr/kgBW (1.18).

The result of this research can be concluded that the CSE has effectivity to TGF- β , and inter incisive distanceso that can reduce relapse after orthodontic treatment.

Experimental article (J Int Dent Med Res 2018; 11(3): 884-887)

Keywords: Incisive Distance, Osteoblast, Relapse, Remodeling, TGF- β .

Received date: 22 May 2018

Accept date: 12 August 2018

Introduction

Relapse often occurs after orthodontic treatment although ideal occlusion has been achieved and retainer tools have been used to maintain new tooth positions. Al Yami (1999) showed that 33% of patients relapsed after 10 years of orthodontic treatment retention. 50% of the relapse patients were experienced by patients taking a 2-year retention tool, 28% in retention 2 to 5 years and 12% in patients with retention for 5 to 10 years.¹ Data on baseline the biology of tooth relapse after the success of

orthodontic treatment is not yet known, the existing study is largely descriptive in that it shows that relapse is caused by fibrous structures in the tooth supporting tissues. This, therefore, is the basis for determining the length of retention until this structure is reorganized during the period after orthodontic treatment.² However, other data suggest remodeling of periodontal ligament collagen, gingival fibers especially transeptal fibers occur rapidly so that collagen remodeling in the periodontal ligament is not the most important factor in the etiology of relapse, there are other matrix components of extracellular which have an important influence on the relapse process.

In the relapse process, the benefits of various growth factors, cytokines, colony stimulating factors will affect the biological activity of periodontal tissue during relapse.²⁻⁶ Therefore, another way to prevent relapse is to prescribe medications locally or systemically. It has been scientifically proven both invitro and in vivo that

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the CSE has been tested for its ability as an antiosteoporosis by evaluating the sample's ability against osteoblast cell proliferation. Osteoblast cells are responsible for bone remodeling (bone resorption and resorption). In previous studies it is proven that CS contains flavonoid compounds that have activity as antiosteoporosis.⁷

Caesalpinia Sappan (Secang Wood) is known to contain flavonoids and function in the formation of osteoblasts are expected to play a role in bone remodeling and prevent relapse. Many factors play a role in alveolar bone remodeling and relapse one of them is Transforming Growth Factor β (TGF β).⁸ The Role of Secang Wood on orthodontic driven orthodontic bone remodeling process and its effect on relapse to date has not been proven. The purpose of this study was to analyze the difference of TGF β , the number of osteoblasts, and the inter-incisive distance in giving CSE to prevent relapse after orthodontic treatment.

Materials and methods

Extracting procedure of Caesalpinia Sappan

The simplicia used is Caesalpinia Sappan obtained from Congeang Sumedang Forestry Hall, Indonesia. The making CSE is done by maceration method, dry secang weighing 600 gr in 5 L methanol for 1*24 hours while occasionally stirring. Then filtered and given a solution, evaporated with an evaporator until extracting the gels. Furthermore, the preparation of CSE suspension, in 1 mL of suspension contains 325 mg of CSE.

Animals. A total 39 male New Zealand White rabbits (6-8 months), weighed 2.5-3Kg were purchase from *Unit Balai Penelitian Ternak Fakultas Kedokteran Hewan Institut Pertanian Bogor*. The Animals were adapted for two weeks before treatment.

Experimental procedure. All animals were divided into 4 treatment groups. Group 1 orthodontic treatment without CSE, Group 2 orthodontic treatment + CSE 325 mg/kg BW, Group 3 orthodontic treatment + CSE 650 mg/kg BW, Group 4 orthodontic treatment + CSE 1300 mg/kg BW. On the first day, all animals were measured the lower incisive distance and blood sampling for TGF β examination. All animals were orthodontic treatment using open coil with

force of 20 grams to move the incisive tooth distally for 14 days.⁹ CSE in the form of suspension was administered orally using *sonde* and syringe, administered from day 14 to day 35 (Figure 1). On the 14th day until day 28, the orthodontic style is retained (open coil is not removed). On day 28 open coil is released. On the 14th, 21th, 28th and 35th day, sampel were measured the lower incisive distance with digital caliper, blood sampling for TGF β examination by Elisa method and sample were sacrificed then alveolar bone were collected. Alveolar bone was fixed in 10% formalin and stained with Hematoxilin Eosin to determine the amount of osteoblast. Data analysis was then analyzed using statistical analysis of varian (ANOVA) test with Tukey HSD.

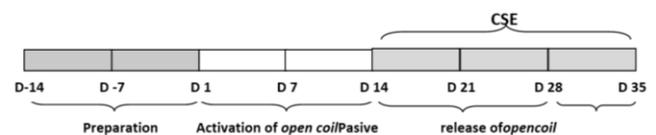


Figure 1. Experimental Design.

Results

In this study, CSE with flavanoid compound had an effect on TGF β , it can be seen on graph 1 shows that based on the dosage of CSE giving effect on the increase of TGF β level. At day 21, CSE groups, either 325 mg/kg BW dose (720.440 pg/ml), 650 mg/kg BW (677.317 pg/ml) and 1300 mg/kg BW (715.451 pg/ml) showed greater TGF β levels compared with the group without CSE (657.14 pm/ml). On day 35 it showed that TGF levels of β relative decreased due to relapse, but statistically proved significant differences P value <0.005 , TGF levels β KS 1300 mm/kg BW (620.692 pg/ml) greater than *kel* without CSE (481.421 pg/ml). This proves that on the 35th day CSE 1300 mm/kg BW effect on TGF β level. This condition corresponds to the function of TGF β in maintaining the balance between resorption and bone formation (Figure 2).^{10,11}

Giving of CSE extract had an effect on the number of osteoblasts seen on the 28th day of CSE group 1300 mg/kg BW (46.47) more than CSE0 (44.87) (Figure 3). Similarly, on day 35 the total osteoblasts of CSE group were higher than those of No CSE, especially in KS 650 mg/kg BW group (51.57) although there was no statistically significant difference. This shows that CSE has

an effect on osteoblast formation especially at CSE dose 650 mg/kg BW.

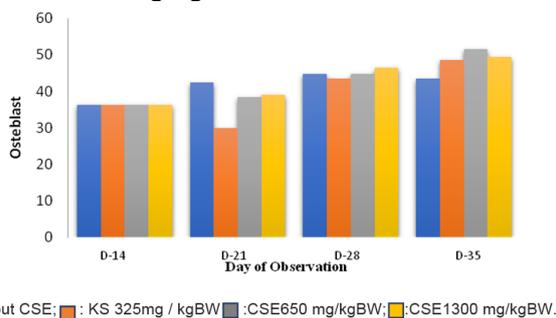


Figure 2. Effect of CSE on TGF β. Show the Relationship between Observation Day (days 1, 14, 21, 28, and 35) with TGF β Level.

The effect of CSE on incisive distance was observed on day 35, the group without CSE (1.59+0.02) was significantly different (*P* value <0.05) with the 650 mg/kgBW group (1.72+0.02) and 1300 mg/kgBW (1.81+0.06).

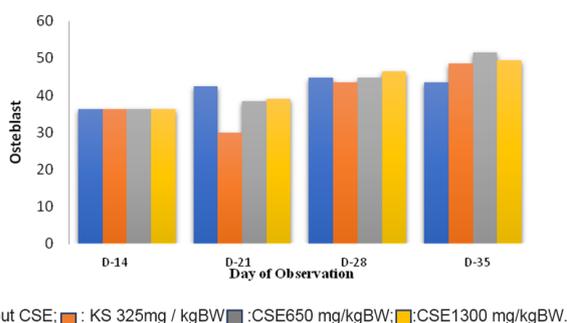
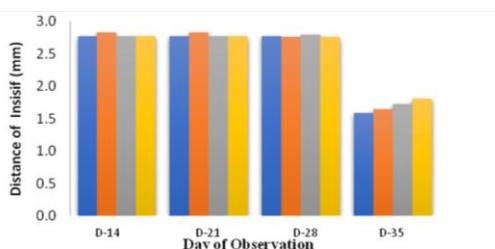


Figure 3. Effect of CSE on Osteoblast. Shows the Relationship Between Observation Days (days 14, 21, 28, and 35) with the Number of Osteoblasts.



Note: ■ Without CSE; ■ KS 325mg / kgBW; ■ CSE650mg /kgBW; ■ CSE1300mg / kgBW.

Figure 4. Effect of CSE on Inter Incisive Distance. Show the Relationship between Observation Day (Day 14, 21, 28, And 35) with Incisive Distance.

At 35 days observed the inter incisive distance is known that in the CSE group of 325 mg/kg BW the incisive distance of 2.83 mm or relapse of 1.19 mm, the CSE group 650 mg/kg

BW relapse of 1.05 mm, CSE 1300 mg/kg BW relapse of 0.96 mm. While the group without CSE, inter incisive distance of 1.59mm or experiencing a large relapse of 1.18 mm. This suggests that administration of CSE reduces orthodontically driven tooth relapse (Figure 4).

Discussion

CS is one of the plants that empirically believed the Indonesian people have efficacy as a traditional medicine, among others, used to treat diarrhea, anti allergic, anticoagulant, cough with phlegm, antioxidants, anti-inflammatory, and osteoporosis.^{7,9,12} CS contain tannin compounds, brazillin, fitoesterol, saponin, gallic acid, astiri oil, and flavonoids. Flavonoids contained in CSE are known to prevent osteoporosis and in some studies have been shown to increase osteoblast formation.¹²

Flavonoids are the largest phenol compounds consisting of 15 carbon atoms most of which are found in plant compounds, containing isoflavone compounds that have been shown to have an effect on bone metabolism. Based on the study, CS contains flavonoids that can increase osteoblast levels.¹⁴

In the relapse process after orthodontic treatment various growth factors, cytokines, colony stimulating factor will affect the biological activity of periodontal tissue during relapse such as TGF β.¹⁰ TGF β plays a role in the proliferation and differentiation of mesenchymal stem cells (MSCs) into osteoblasts. TGF β is one of the many cytokines in bone matrix and contributes to osteoblastic bone formation.¹⁵ TGF β has been known to increase osteoblast protein synthesis, including from hematopetically stimulated cells with RANKL and M-CSF.¹⁶

Because of the importance of extra cellular factors in remodeling and relapse of orthodontic treatment, it is necessary to find other ways to prevent relapse by local or systemic drug delivery. Currently the drugs to speed up the process of bone remodeling on orthodontic tooth movement have been found. However, treatment with chemical drugs often cause side effects. In vitro CS is reported to increase osteoblasts.⁷ Osteoblasts play a role in the process of bone remodeling.¹⁷ Utilizing the use of herbal remedies on orthodontic treatment is expected to facilitate remodeling and prevent relapse after orthodontic treatment, thus reducing dependence on the retainer.

The presence of flavonoids in the extract of Secang Wood serves to limit the release of inflammatory mediators. Isoflavone has the effect of stimulating bone formation and mineralization in the in vitro culture system and stimulating protein synthesis in osteoblast cells. Genistein increases the DNA content in osteoblastic cells indicating isoflavones stimulate cell proliferation. Isoflavones also increase the activity of alkaline phosphatase which is a marker enzyme in the differentiation of osteoblastic cells.¹⁵

Flavonoid flavonoids can reduce the occurrence of relapse due to its effect in increasing TGF β levels by inhibition of cyclooxygenase and lipooxygenase so as to limit the amount and timing of inflammation to be short and proliferation is not inhibited.⁸ With increasing levels of TGF β this will affect the synthesis of osteoblasts responsible for bone formation. In addition, the entangled Isoflavones in CSE increase the activity of alkaline phosphatase which is a marker enzyme in the differentiation of osteoblastic cells.¹⁵ Genestein also increases the DNA content in osteoblastic cells that indicate isoflavones stimulate osteoblastic cell proliferation. The effect of CSE in increasing levels of TGF β and the number of osteoblasts results in good bone remodeling so that relapse that occurs in incisive orthodontic tooth movement is less than that of a group without CSE.

Conclusions

The result of this research can be concluded that Ethanolic extract of Caesalpinia Sappan has effectivity to increase TGF- β , and the distance between incisive so that can reduce relapse after orthodontic treatment.

Declaration of Interest

The authors report no conflict of interest and the article is not funded or supported by any grand.

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