## Serratiopeptidase a Hope in a Rapid and Better Improvement of **Inflammatory Acne Vulgaris**<sup>#</sup>

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### **Abstract**

Acne vulgaris is a very common, chronic disorder, involving inflammation of the pilosebaceous units that can be varied in presentation and difficult to treat. Inflammatory acne may yield both scarring and pigmentary changes so early and adequate therapy will, in all cases, decrease its severity and may entirely suppress this disease. Serratiopeptidase has anti-inflammatory, anti-edemic and fibrinolytic activity and acts rapidly on localized inflammation. Serratiopeptidase was added in aim to hasten acne resolution. During March to July 2010, A comparative study for a 50 healthy patient suffering from acne was divided into 2 groups: 1st group treated by common acne modalities and the 2<sup>nd</sup> one with same modalities plus serratiopeptidase. All patients were followed up in out patient clinic by a dermatologist after 1st week of treatment and once weekly through the period of treatment. The results of this study showed that the effect of serratiopeptidase as adjuvant therapy for acne treatment result in a significant rapid improvement, this might be explained by serratiopeptidase ability in enhancing antibiotic efficacy and also increase the possibility of excellent improvement in acne appearance which may be due of it's anti-inflammatory, anti-edemic. Serratiopeptidase was found to create a good hope as additional therapy for complicated acne vulgaris and bring a rapid and better improvement in treating acne.

Key words: Acne ,Serratiopeptidase.

# إنزيم السيراتوببتايديز أمل جديد بتحسن أسرع وأفضل لحب الشباب الملتهب الملتهب الملتهب الملتهب الملتهب المهاب مضر ميخائيل\* و مهدي يحيى محمد \*\* فرع الصيدلة السريرية ، كلية الصيدلة ، جامعة بغداد ، بغداد ، العراق . \*\*قسم الجادية ، مستشفى ابو غريب العام ، بغداد ، العراق .

حب الشباب مرض منتشر و مزمن يتضمن التهاب خلايا الجلد، له أشكال مختلفة ومن الصعوبة علاجه حبوب الشباب الالتهابية تسبب أثارا في الوجه وتصبغات جلدية لذا فمن الضروري علاجها بسرعة وبشكل مثالي للتقايل من حدة المرض وإيقافه. إنزيم السيراتوببتايديز له خواص مضادة للالتهاب والوذمة كما ًانه يعمل موقعيا للتقليل من الالتهابات. تمت إضافة إنزيم السيراتوببتاًيديز بهدف الإسراع من علاج حب الشباب. خلال المدة من أذار وحتى تموز ٢٠١٠ ، دراسة مقارنة لخمسون مريضاً يعانون من درجات مختلفة من حب الشباب تم تقسيمهم إلى مجموعتان : المجموعة الأولى عولجت بالأدوية المعتادة لعلاج حب الشباب ، والمجموعة الثانية عولجت بذات العلاجاتُ مضافا أبها إنزيم السيراتوببتايديز ِ جميع المرضى تمت متابعتهم بعيادة خارجية من قبل طبيب جلَّدية مختص بُعد الأسبوع الأول من العلاج وثُم مرة أسبوعيا خلَّال فترة العلاج هذه الدراسة أظهرت بان تأثير إنزيم السيراتوببتايديز كعلاج مساعد لحب الشباب هام ومعنوي لاستجابة أسرع للعلاج وقد يفسر هذا بقابلية الإنزيم لزيادة فاعلية المضادات الحيوية وكذلك يزيد احتمالية الشفاء الأفضل لحبوب الشباب بسبب تأثيره المضاد للالتهاب والوذمة لقد وجد إن الإنزيم السيراتوببتايديز قد يُخلق املاً جيدا كعلاجا إضافيا لعلاج حب الشباب المستعصى ، كما انه يضمن علاجاً أفضل وأسرع لعلاج حب

الكلمات المفتاحية: حب الشباب، سيراتوببتايديز.

#### Introduction

Acne vulgaris is a very common, chronic disorder, involving inflammation of the pilosebaceous units that can be varied in presentation and difficult to treat. (1) Four key factors have been identified in the etiology of acne: increased sebum production, follicular hyperkeratinization, colonization pilosebaceous unit with Propionibacterium acnes and the production of inflammation; (2) The inflammatory lesions vary from small

papules with a red border to pustules to large, tender, fluctuant nodules . Some of the large nodules were previously called cysts and the term nodulocystic has been used to describe cases of inflammatory severe (3)Inflammatory acne may yield both scarring and pigmentary changes (4) so early and effective treatment is essential to prevent and disfigurement minimize the cosmetic associated with acne scarring.

Received: 12/3/2011 Accepted: 1/4/2012

Based on oral presentation in the eighth scientific conference of the College of Pharmacy /University of Baghdad held in 23-24 February 2011.

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Adequate therapy will, in all cases, decrease its severity and may entirely suppress this disease. (1, 2) Moderate or severe acne treated by use of topical therapy, plus antibiotics<sup>(5)</sup> inflammatory lesions decrease and new lesions stop appearing within 2 to 6 weeks; (1) However, with the known therapy of acne patients should be counseled that an improvement may not be seen for at least a couple of months, (6) because antibiotic therapy can't be truly evaluated until 6 weeks after starting. (1). General treatment guideline of moderate - severe acne according to Global Alliance algorithm (7) include antibiotic such as Doxycycline which may play a therapeutic role in acne by reducing inflammation through anticollagenolytic, antimatrix-degrading metalloproteinase, and cytokine downregulating properties (8) plus topical retinoid with or without topical benzyl peroxide. Late-onset and persistent adult acne are now more widely recognized and may necessitate consideration of an alternative approach to therapy. (2) Serratiopeptidase (Serratia) is a proteolytic enzyme (protease) produced by enterobacterium Serratia sp. ( Some alternative medicine proponents claim that serratiopeptidase is beneficial for pain and inflammation (10) serratiopeptidase has antiinflammatory, anti-edemic and fibrinolytic activity and acts rapidly on localized inflammation. (11). In this study we added serratiopeptidase to the standard treatment to limit the duration of active disease (hasten acne resolution) by early and effective treatment; Therefore offers the possibility of minimizing both the physical and emotional scarring caused by acne. (2)

#### **Methods**

During the period from March to July 2010, A comparative study for a 50 patients suffering from acne with varying degree of severity ranging from papulopustular acne to nodulocystic acne was divided into 2 groups: 1st group 25 patients, (20 females and 5 males), age (18.36±2.464) years.

In this group patients were received standard therapy according to guideline of Global Alliance algorithm: doxycycline capsule 100mg twice daily + Retin A cream (isotretinoine 0.05%) twice daily plus Panoxyl

Gel 5% (benzyl peroxide) once daily, for 3 months. Where as the 2<sup>nd</sup> group include 25 patients, (20 females and 5 males), age (18.28±2.372) years. Patients were given same therapy as in the 1<sup>st</sup> group (for 3 month) plus Danzen® tablet (Serratiopeptidase) 5 mg orally 3 times per day during the 1st month of treatment only. All patients were followed up in out patient clinic by a dermatologist after 1<sup>s</sup> week of treatment and once weekly for the 1st month and then monthly in the next 2 months.Clinical improvement based on: Subside of inflammation, stop appearing of new lesions and finally acne subsides and starts remodeling with removal of residual hyperpigmentation. Improvement more than 85% considered excellent, (65 – 85%) moderate, (50 - 65%) mild, while less than 50% considered as bad improvement.

#### Results

A majority of patients showed significant (X2 = 4.0, P = 0.05) mild moderate improvement after 2 weeks in Danzen treated group compared to control group; however there is non significant difference in this period between the 2 groups in term of excellent improvement. Mean while. after 4 weeks, there is insignificant difference in the improvement of acne at different level between two groups, despite the significant difference ( X2 = 3.857 , P = 0.05 ) in excellent improvement between treated and control groups. After 4 weeks of treatment (Danzen was stopped), recurrence reported in two patients who developed only mild improvement during the 1<sup>st</sup> month.Only one patient didn't show any improvement ( resistant nodulocystic acne ) , another one patient suffer from GIT upset and erythematous papules in the body due to Danzen use which led to stop danzen treatment just after 2 weeks despite his moderate improvement in acne appearance ( see table1 and 2 and figure 1). After 3 months (at end of clinical trial ) despite non significant difference between treated and control group in number of acne patients that improved or showed excellent improvement, there is a reasonable percent of difference as shown in table 3 and 4.

Table 1: Improvement in danzen treated group.

| Number<br>of weeks | Bad<br>improvement | No. of cases that show mild improvement | No. of cases that show moderate improvement | No. of cases that show excellent improvement |
|--------------------|--------------------|---|---|--|
| 1                  | 20                 | 4                                       | 1   | nill   |
| 2                  | 9                  | 12                                      | 3   | 1  |
| 3                  | 5                  | 4                                       | 8   | 8  |
| 4                  | 2                  | 3                                       | 5   | 15   |
| 8                  | 3                  | 1                                       | 3   | 18   |
| 12                 | 2                  | 1                                       | 1   | 20   |

Table 2: Improvement in control group.

| Number<br>of weeks | Bad<br>improvement | No. of cases that show mild improvement | No. of cases that show moderate improvement | No. of cases that show excellent improvement |
|--------------------|--------------------|---|---|--|
| 1                  | 23                 | 2                                       | 0   | 0  |
| 2                  | 18                 | 5                                       | 2   | 0  |
| 3                  | 11                 | 8                                       | 4   | 2  |
| 4                  | 6                  | 8                                       | 5   | 6  |
| 8                  | 5                  | 5                                       | 2   | 13   |
| 12                 | 4                  | 3                                       | 2   | 16   |

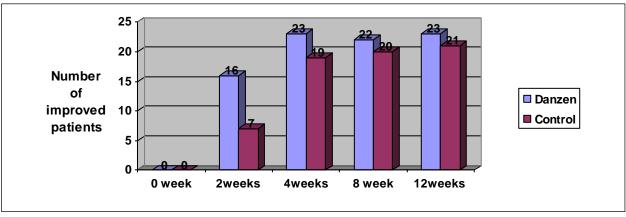
Table 3: Percent of improvement in danzen treated group

| Number<br>of weeks | % of patients that showed<br>Bad improvement | % of patients that show mild improvement | % of patients that show moderate improvement | % of patients that show excellent improvement |
|--------------------|--|--|--|---|
| 1                  | 80   | 16                                       | 4  | 0   |
| 2                  | 36   | 4  | 12   | 4   |
| 3                  | 20   | 16                                       | 32   | 32  |
| 4                  | 8  | 12                                       | 20   | 60  |
| 8                  | 12   | 4  | 18   | 72  |
| 12                 | 8  | 4  | 4  | 80  |

**Table 4: Percent of improvement in control group** 

| Number<br>of weeks | % of patients that showed<br>Bad improvement | % of patients that show mild improvement | % of patients that show moderate improvement | % of patients that show excellent improvement |
|--------------------|--|--|--|---|
| 1                  | 92   | 8  | 0  | 0   |
| 2                  | 72   | 20                                       | 8  | 0   |
| 3                  | 44   | 32                                       | 16   | 8   |
| 4                  | 24   | 32                                       | 20   | 24  |
| 8                  | 20   | 20                                       | 8  | 42  |
| 12                 | 16   | 12                                       | 8  | 64  |

Figure 1: Comparison between the numbers of improved patients of the 2 groups that treated with or without Danzen



#### Discussion

The results of this study showed that the effect of serratiopeptidase as adjuvant therapy for acne treatment result in a significant rapid improvement, this might be explained by serratiopeptidase ability in enhancing antibiotic efficacy as was shown in other related studies to Staphylococcus infections. (12) The addition of Serratiopeptidase not only result in rapid improvement but also increase the possibility of excellent improvement in acne appearance which may be due of it's anti-inflammatory, anti-edemic and fibrinolytic activities and it's ability to act rapidly on localized inflammation. (11) in addition to that serratiopeptidase have synergistic effect with antibiotics. (13) After 12 months (at end of clinical trial) there is no significant difference between the 2 groups, this simply can be explained by the short period ( only one month ) usage of serratiopeptidase, however additional studies on large scale and for longer period of time are needed to confirm the benefit of addition of serratiopeptidase to acne treatment.

#### Conclusion

Serratiopeptidase was found to create a good hope as additional therapy for complicated acne vulgaris and bring a rapid and better improvement in treating acne; however, more studies on large scale and for longer period are needed to confirm this result.

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