

Manuscript ID ZUMJ-2110-2377 (R1)

DOI 10.21608/ZUMJ.2021.100983.2377

Original article

## Potential Therapeutic Effect of Platelet Rich Plasma in Acne Vulgaris

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Submit Date 17-10-2021

Revise Date 01-11-2021

Accept Date 2021-11-09



### 1-INTRODUCTION:

Acne vulgaris is a complex dermatological disease, affecting over 85% of adolescence all over the world. However, it commonly appears during puberty and becomes more severe during adolescence, studies reported that it can be manifested at any period [1]. It is a chronic inflammatory skin disorder that affects the pilosebaceous units and it is caused by various factors including genetics, increase sebum secretion under effect of androgens, abnormal follicular keratinization, bacterial colonization with *Cutibacterium acnes* (formerly called *Propionibacterium acnes*) and immunity induced inflammation [2]. According to acne type and severity, several medications are available to use based on each of the predisposing factors. Treatments include topical (e.g. antibiotics, retinoids or benzoyl peroxide) and/or systemic treatments (e.g. systemic antibiotics, antiandrogens or isotretinoin) [3]. Platelet rich

### ABSTRACT

**BACKGROUND:** Acne vulgaris is a worldwide chronic inflammatory dermatological disorder of pilosebaceous unit that adversely affects patients' quality of life, so safe and effective treatment options are needed. Platelet rich plasma is an autologous highly concentrated platelets in a little amount of plasma. Various growth factors are released after platelet activation that have significant role in angiogenesis, inflammation and wound healing.

**AIM:** to assess the efficacy and safety of platelet rich plasma injection in management of acne vulgaris.

### METHODS:

Thirty patients with acne vulgaris of different severity and duration received four sessions of platelet rich plasma that injected intradermal, one session every two weeks for 8 weeks.

### RESULTS:

The obtained results showed a statistically significant decrease in the total lesion count ( $P<0.05$ ) and high statistically significant decrease in acne severity index ( $P<0.01$ ) from baseline. Also, high statistically significant decrease was observed in pustules count ( $P<0.01$ ) after treatment. Mild side effects were detected in the form of mild to moderate pain, erythema and edema immediately after treatment with Intradermal platelet rich plasma injection.

**CONCLUSIONS:** Intradermal Platelet Rich Plasma injection is promising and effective treatment option for acne vulgaris with tolerable side effects.

**KEY WORDS:** Acne Vulgaris; Platelet Rich Plasma; Anti-inflammatory; Treatment

plasma (PRP) is concentrated platelets in small blood volume. It contains various growth factors, including platelet derived growth factor (PDGF), transforming growth factor (TGF), fibroblast growth factor (FGF), vascular endothelial growth factor (VEGF), and hepatocyte growth factor (HGF) [4]. These growth factors have important role in wound healing, cellular chemotaxis, angiogenesis and metabolism [5]. The anti-inflammatory role of PRP is mainly mediated by the interruption of transcription nuclear factor *kappa B* (NF- $\kappa$ B) signaling, that has vital role in regulation of inflammation. Moreover, the anti-inflammatory mechanism of HGF was apparently due to its effect on cyclo-oxygenase (COX-1, COX-2), and prostaglandin E2 (PGE2) production [6]. The aim of study was to assess the potential therapeutic role of platelet rich plasma in patients with acne vulgaris.

## 2-METHODS:

This study was conducted at outpatient clinic of Dermatology, Venereology and Andrology Department at Zagazig University Hospitals from January 2021 to August 2021. The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans. It is approved by the Zagazig University Hospitals Institutional Review Board. The experimental study included thirty male and female patients with acne vulgaris of different severity, distribution and durations. Patients had history of systemic diseases and women who are pregnant or lactating were excluded from participation. Other exclusion criteria included using topical or systemic anti-acne medications, hormonal treatment or isotretinoin in the last 3 months. All patients received four sessions of platelet rich plasma that injected intradermal, one session every two weeks for 8 weeks.

All participants underwent a complete history taking, full general examination, routine laboratory investigations were done including Complete Blood Count (CBC), random blood glucose level, bleeding time and coagulation time, the patient with abnormal findings were excluded. Dermatological examination was done and the severity of acne lesions were assessed in all patients before starting of treatment according to Global Acne Grading System [7]. At the onset of study, every two weeks of treatment and at the end of study photographs taken for all the patients. A written consent was got from each case before their involvement in the study. Side effects of the treatment were recorded at each visit.

### 2.1. Preparation of Platelet rich plasma (PRP):

Ten milliliter of venous blood sample was collected from every patient with thorough aseptic circumstances and then divided into 2 sterile sample tubes equipped with anticoagulant sodium citrate solution. Then the tubes were placed in a centrifuge machine to spin at 3000 rpm, for 7 minutes at room temperature, resulting in the following three layers: the lower layer included red blood cells, the middle layer composed of white blood cells (the buffy coat) and the upper layer contained plasma. The upper two layers (plasma and buffy coat) were collected using sterile 5ml syringe then centrifuged again for another 5 minutes at 4000 rpm. After the second spin, a soft erythrocyte pellet was formed at the bottom of the tube. The PRP was gently aspirated in sterile 3 ml syringes and activated with calcium chloride ( $\text{CaCl}_2$ ) 1% with proportion of 0.1 ml  $\text{CaCl}_2$  per 1 ml of plasma immediately before the

injection. The site of injection was disinfected using ethyl alcohol 70% then anaesthetized using topical Lidocaine anesthetic cream half an hour before starting the session. The patients were injected in the recombinant position. 0.1 ml of PRP was injected intradermal in each inflammatory lesion (papules and pustules) or subcutaneously in deep lesions (nodules and cysts) using insulin syringe. The patient was instructed to use topical antibiotic cream twice daily for 3 days after session and to continue the normal skin care regimen (including sunscreen lotion).

### 2.3. Assessment of clinical response:

The final assessment to detect the efficacy of the treatment was evaluated by the following two formulations:

- "Total lesion count (TLC) = comedones + papules + pustules"
- "Acne severity index (ASI) = papules + (2 x pustules) + (comedones/4)" [8].

### 2.4. Statistical analysis

Data were tested and evaluated using SPSS (Microsoft Excel software. Inc., Chicago, Illinois, USA), version 23 for data processing. Qualitative variables were stated as number and percentage, whereas quantitative data were stated as mean  $\pm$ SD. The comparison was done using Wilcoxon signed-rank test to check paired data before and after a time and  $\chi^2$  test to explain the association between row and column variables. P value of  $< 0.05$  indicates significant results.

## 3-RESULTS

### 3.1. Characteristics of the patients:

This study included 30 acne vulgaris patients, 10 males (33.3%) and 20 females (66.7%), their ages ranged from 16 to 28 years old with mean  $\pm$  SD 23.77  $\pm$  3.6 and duration of acne ranged from 1 to 6 years with mean  $\pm$  SD 4.98  $\pm$  1.50 (Table 1).

### 3.2. Response to treatment with intradermal platelet rich plasma injection:

After 8 weeks of intradermal injection of platelet rich plasma, one session every two weeks for 4 sessions, a high significant reduction in papules number ( $P < 0.01$ ) was observed from base line while, no significant reduction was detected in comedones and pustules number from base line ( $p > 0.05$ ). TLC showed significant reduction ( $p < 0.05$ ) and ASI showed high significant reduction ( $p < 0.01$ ) after platelet rich plasma treatment (Table 2).

**3.3. Side effects:** Mild tolerable side effects were observed in the form of mild to moderate pain during injection in (100%) of patients, erythema in (90%) and edema in (86.7%) of patients immediately after session (Table 3)

**Table (1):** Demographic data of participants

Variables		Patients (N=30)
Age (years) Mean ± SD (Range)		23.77±3.6 (16-28)
Sex	Male	10 (33.3%)
	Female	20 (66.7%)
Acne duration (years) Mean ± SD		4.98 ± 1.50 (1-6y)
Disease severity	Mild	18 (60%)
	Moderate	12 (40%)

**Table (2):** Comparison between number of lesions before and after treatment with platelet rich plasma injection in acne vulgaris patients

Variable	platelet rich plasma		P-value <sup>†</sup>
	Before treatment	After treatment	
	mean ± SD	mean ± SD	
Comedone	13.69 ± 9.41	11.35 ± 7.22	0.28
Papule	15.73 ± 11.12	8.29 ± 2.98	≤ 0.01**
Pustule	3.78 ± 2.98	2.87 ± 1.65	0.15
TLC	29.67 ± 13.12	22.61 ± 10.43	≤ 0.05*
ASI	22.94 ± 15.54	11.84 ± 7.36	≤ 0.01**

\* Significant difference (P ≤ 0.05)

\*\* Highly significant difference (P ≤ 0.01)

†: Mann-Whitney test

TLC (total lesion count)

ASI (acne severity index)

**Table (3):** Side effects of platelet rich plasma injection in acne vulgaris treated patients

Platelet rich plasma

Symptoms	(n=30)	%
Side effects	30	100%
Pain	30	100%
Edema	26	86.7%
Erythema	27	90%



### 3-DISCUSSION

Acne vulgaris is a chronic inflammatory disease affecting pilosebaceous unit but it has a self-limiting course. It is the most common dermatological disease that can be manifested with inflammatory (papules, pustules and nodulocystic) and non-inflammatory (comedones) lesions and it appears mainly on the face but can also occur on other sites as the upper arms, chest, and back [9]. Management of acne vulgaris either by topical or oral treatments aim mainly to disrupt one or more factors that involved in pathogenesis

of acne. Topical formulations used for mild to moderate cases while systemic treatments are used for more severe or resistant types of acne. Each of these treatment modalities has its disadvantages [10]. Therefore, new treatment options for acne vulgaris are required to decrease adverse effects and overcome era of antibiotic resistance [11].

Platelet rich plasma (PRP) is an autologous blood product containing high concentration of platelets suspended in a tiny amount of plasma, above the baseline [12]. The antibacterial mechanism of

PRP is mainly enhanced after platelet activation and degranulation releasing multiple growth factors, antimicrobial peptides, and other active substances. It is also achieved by the leukocytes preparation, including neutrophils and lymphocytes; neutrophils can destroy bacteria directly and protect against pathogens to prevent infections and microbes' invasion, moreover lymphocytes inhibit bacterial growth by an antigen-specific immune response. It has shown that the leukocytes had chief role in antimicrobial mechanism and tissue remodeling [13]. Additionally, PRP established an anti-inflammatory effect due to hepatocyte growth factor (HGF) and tumor necrosis factor alpha (TNF- $\alpha$ ). These anti-inflammatory cytokines inhibit inflammation by disrupting the nuclear factor kappa B (NF- $\kappa$ B) signaling pathway and pro-inflammatory cytokine expression. Also, there is prevention of monocyte chemotaxis by expression of transforming growth factor (TGF- $\beta$ 1), which interrupts the effect on chemokine transactivation by TNF- $\alpha$  [14]. So, the present study was performed to evaluate the potential role of PRP in the treatment of patients of acne vulgaris.

In the current study, after 8 weeks of intradermal injection of PRP, one session every two weeks for 4 sessions, a high significant reduction in papules number was observed from base line while, no significant reduction was detected in comedones and pustules number from base line. TLC showed significant reduction and ASI showed high significant reduction after platelet rich plasma treatment. Regarding the side effects that observed during the course of PRP treatment, 100% of patients showed mild to moderate pain during injection time, 86.7% showed edema and 90% showed erythema immediately after session. These results are nearly comparable with those reported by Ibrahim et al. [15] who explored the outcome of PRP injection versus topical erythromycin 2% on treatment of acne vulgaris and showed statistically significant difference in PRP group before and after treatment in the number of papulopustular lesions and nodulocystic lesions, with no significant difference in number of comedonal lesions. Moreover, Zhu et al. [16] elucidated the efficacy of autologous PRP combined with erbium fractional laser therapy for facial acne scars and acne lesions and reported that most of inflammatory acne was cured, and after ablative erbium fractional resurfacing, there was no infected lesions. They indicated that PRP had a synergistic effect to laser as it controls inflammation and enhance healing by breaking P.

acnes colonization and increasing re-epithelialization and tissue remodeling. The obtained findings could be explained by the anti-inflammatory and antibacterial role of PRP, since inflammation is one of the earliest processes that occur in the acne pathogenesis due to the effect of multiple inflammatory cytokines and free radical release [17]. The anti-inflammatory and antibacterial effect of PRP are confirmed with several previous studies done in treatment of other diseases. Also, **Tohidnezhad et al.** [18] confirmed by immunohistochemistry and Western blot that antimicrobial peptide human beta-defensin 2 (hBD-2) has found in platelets, suggesting hBD-2 as the agent that promotes anti-infective capabilities against *E. coli* and *P. mirabilis*. Intravia et al. [19] showed in vitro studies that PRP can hinder the colonization of *Propionobacterium acnes*.

#### 4-CONCLUSIONS

The present study supports the efficacy and safety of platelet rich plasma (PRP) injection in the management of acne vulgaris. It is promising treatment option that can be used alone or in combination with other medications to overcome era of antibiotic resistance. We recommend that further controlled studies should be carried out on a higher number of patients and for longer treatment durations to evaluate the potential therapeutic role of platelet rich plasma (PRP) injection in treatment of acne vulgaris.

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### To Cite:

ali, A., Youssef, A., Nassar, A. Potential Therapeutic Effect of Platelet Rich Plasma In Acne Vulgaris. *Zagazig University Medical Journal*, 2024; (336-341): -. doi: 10.21608/zumj.2021.100983.2377