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CLINICAL AND RADIOGRAPHIC EVALUATION OF THE EFFECT OF HYALURONIC ACID SURFACE TREATMENT VERSUS SANDBLASTED ACID ETCHED SURFACE TREATMENT ON STABILITY OF DELAYED DENTAL IMPLANT IN POSTERIOR MAXILLA (COMPARATIVE RANDOMIZED CLINICAL TRIAL)

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ABSTRACT

This randomized clinical trial evaluated the stability of delayed dental implants in the posterior maxilla, comparing hyaluronic acid surface treatment to sandblasted acid-etched surface treatment. Twenty patients, aged 18-60, were divided into two groups: Group A (hyaluronic acid) and Group B (acid-etched sandblast). Implant stability was measured at baseline and three months postoperatively using AnyCheck devise implant stability. Additionally, soft tissue healing and bone density were assessed through clinical examination and CBCT scans, respectively. Results indicated no significant difference in AnyCheck scores between the two groups at baseline and three months. However, within-group analysis showed a significant increase in AnyCheck scores for the acid-etched sandblast group after three months, while the hyaluronic acid group did not exhibit significant changes. Bone density measurements revealed no significant differences between the groups at any time point, though the acid-etched sandblast group showed significant improvement over time. Implant success rates were 70% for the hyaluronic acid group and 100% for the acid-etched sandblast group, with no statistically significant difference between the groups. In conclusion, while both treatments are effective, sandblasted acid-etched implants demonstrated superior stability and bone density improvement over time compared to hyaluronic acid-treated implants.

KEYWORDS: Hyaluronic acid; Sandblasted acid-etched; Dental implants; Implant stability; Osseointegration

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INTRODUCTION

A dental implant is a root-like biomaterial placed surgically in the jaw bone of partially or completely edentulous patients with subsequent crowns and\or bridges to replace missing teeth (Kowalski et al., 2021; Rao et al., 2019; Spatz & Pasciucco, 2023)[1,2,3].

It's more advantageous over conventional prostheses owing to their high success rate with the preservation of vertical and horizontal bone dimensions without compromising adjacent teeth. Besides, implants enable clinicians to perform more reliable, convenient, and life-changing treatment plans for completely edentulous patients compared to removable prostheses (Rao et al., 2019; Spatz & Pasciucco, 2023)[2,3].

For dental implants to succeed, intimate contact between the implant surface and surrounding bone should be achieved and maintained. This contact is paramount and leads to interaction and integration between both structures in a process called osseointegration which gives the implant the desired stability. To enhance implant osteointegration, several factors have been studied and developed. One of the most important factors is implant surface treatment (Cervino et al., 2021)[4].

Surface treatment is the method of modifying the implant surface to enhance the osseointegration. This could be achieved through increasing the surface roughness which in turn increases the surface area available for osseointegration and \ or altering the surface via adding biocompatible materials to encourage bone cells to migrate and populate implant surface leading to improved and amended osseointegration (J. Kim et al., 2021; Velasco-Ortega et al., 2020)[5,6].

Altering the topography of the implant surface via sandblasting and acid etching has been implemented for years and is considered a reliable method to obtain better outcomes regarding osteointegration.

Recently, biocompatible additives such as hyaluronic acid which plays an important role in the morphogenesis of healing tissue, have been reported to stimulate cell migration, adhesion, proliferation, and differentiation, leading to bone formation speeding up osseointegration (Yazan et al., 2019)[7].

AIM OF THE STUDY

The present study aimed to evaluate the effect of hyaluronic acid surface treatment versus sandblasted acid etched surface treatment on the stability of delayed dental implants in the posterior maxilla.

MATERIALS AND METHODS

Study design

This prospective, parallel, randomized, controlled trial was conducted on twenty adult patients included in this study five male and fifteen female, who needed to restore missing teeth in the posterior maxilla with delayed dental implants, twenty implants were performed, one implant for each patient. The study was approved by the Research Ethics Committee at the Faculty of Dentistry, Cairo University, Cairo, Egypt. Patients were selected from the outpatient clinic of the Faculty of Dentistry, Cairo University from May 2023 and December 2023.

Eligibility criteria

Healthy adult participants with missing teeth in the posterior maxilla, both genders males and females were included. Patients were excluded from the study if they had subjected to irradiation in the head and neck area less than 1 year before implantation, untreated periodontitis, Poor oral hygiene and motivation, Uncontrolled diabetes and Pregnant .

Patients who met the inclusion criteria were informed about the treatment procedure and its possible risks and signed a written informed consent before enrollment. Patients were informed that they could stop participating in the study at any time.

Patient recruitment and randomization

Online randomizer (www.random.org) was used for random patient allocation. A minimum sample of twenty patients (10 per group) was necessary to detect the differences. Chi-square- test was used with 95% confidence level and 80% power (PASS program, version 23).

Patients were classified into two group of placement was group (A) study group was hyalurnic acid, group (B) control group was acid etched sandy blasted. Outcomes were measured implant stability, soft tissue healing and bone density.

Treatment protocol

Clinical evaluation

- All patients involved in this study were divided into two groups, Group A (hyaluronic acid) and Group B (acid-etched sandblast). Each group received the same technique of delayed dental implant placement (Titanium dental implants).

Preoperative procedures (For both groups):

- A thorough medical and dental history followed by a clinical examination was carried out for all patients. Clinical measurements were taken to ensure patient adherence to the initial inclusion criteria before further investigations.
- A pre-operative CBCT X-ray was done to evaluate the quality and quantity of the bone available and the proximity of vital structures to create a treatment plan..

Surgical procedures (For both groups)

- Participants who fulfilled the inclusion criteria were consecutively recruited and eventually treated to performed surgical and prosthetic interventions.
- All patients were instructed to use chlorhexidine mouthwash 0.2% for 1 minute, twice a day, starting three days before the intervention and thereafter for one week.
- A powerful anti-microbial prophylaxis was obtained such as 1 gm of Augmentin* every 12 hours from the day before surgery to the sixth postsurgical day or Klacid** 500 mg 1 hour before the intervention and 250 mg twice a day for one week.
- Patients were treated under appropriate local anesthesia with adrenaline of 1:100,000.

For study group (Hyaluronic acid surface-treated)

- A pre-operative CBCT X-ray was done to evaluate the quality and quantity of the bone available and the proximity of vital structures to create a treatment plan.(Figure 1)

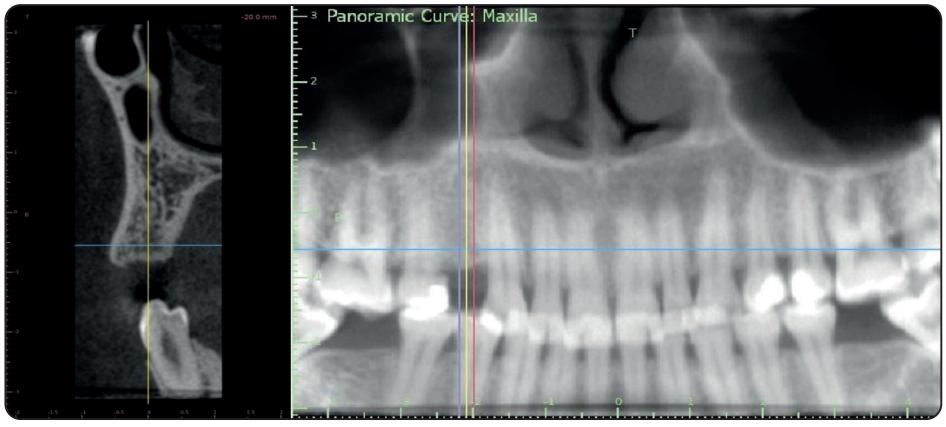

Fig. (1) Preoperative CBCT image showing the missing tooth

* amoxicillin and clavulanic acid 1g, Glaxo Smith Kline, Egypt
** clarithromycin 500 mg, Viatris Ltd., New Zealand

- The intervention group utilized Hyaluronic acid* surface-treated dental implants (Figure 2).
- Full-thickness pyramidal flaps were elevated with a minimal extension to reduce patient discomfort after that reflection of the soft tissue flap and implant placement (Figure 3).
- Implant-motors** with contra-angle handpiece6 with normal saline irrigation was used.
- After implant placement, a healing collar was inserted into the implant, and primary stability was measured by using the Anycheck*** device****, it is requires initial calibration using the manufacturer-supplied calibration block prior to each measurement session. For implant stability assessment, firmly screw the sterilized healing abutment into the implant platform, ensuring hand-tightened seating without excessive force. Position the handpiece probe perpendicular to the implant long axis, maintaining a physical contact between device and healing abutment. Activate the device to capture Percussion based tapping to measurements; record the highest stable Implant Stability Test (IST) value displayed after three consistent readings (Figure 3), then the healing collar was removed, and an implant cover screw was inserted and suturing (Figure 3).

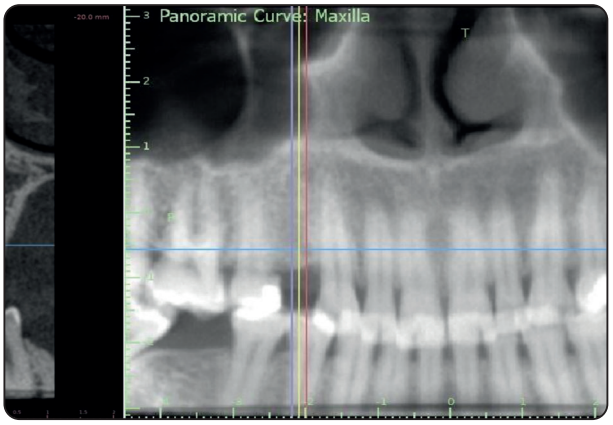

Fig. (2) Hyaluronic acid surface-treated dental implant

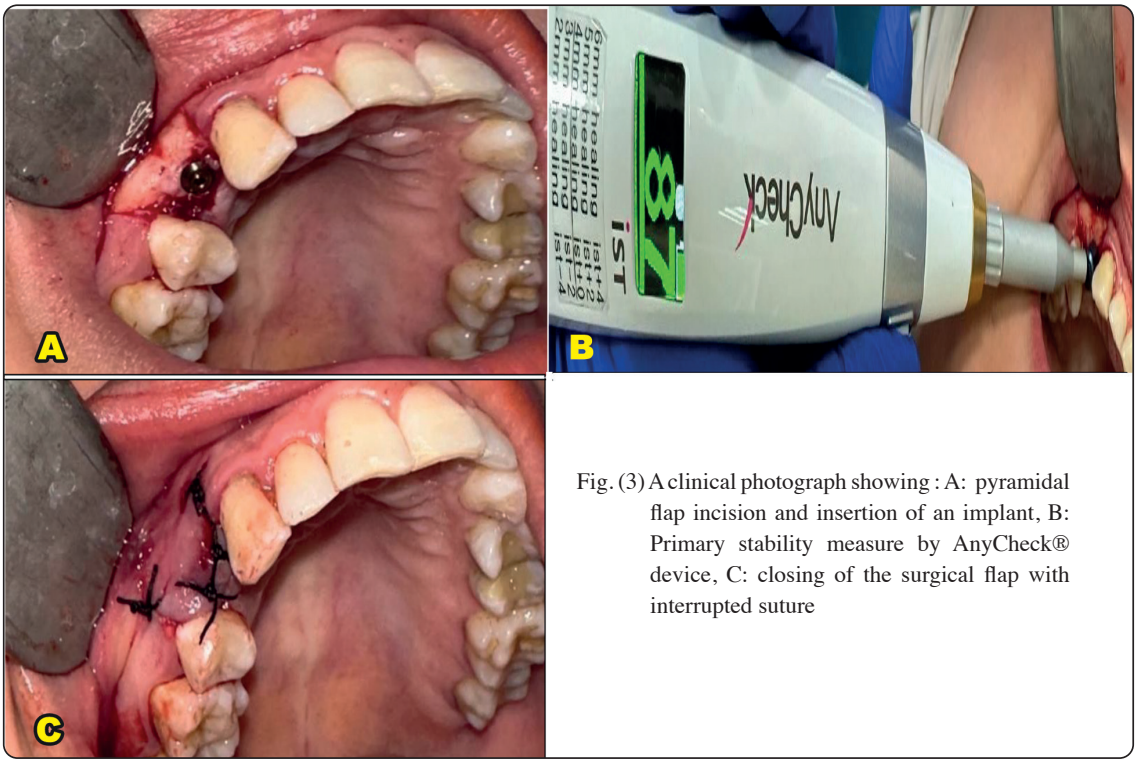

Fig. (3) A clinical photograph showing : A: pyramidal flap incision and insertion of an implant, B: Primary stability measure by AnyCheck® device, C: closing of the surgical flap with interrupted suture

* Hyalgan, Italy ** Woodpecker, China *** Woodpecker, Chin
**** AnyCheck - Implant Stability Tester, Neobiotech, US

- After 10 days, the sutures were removed, and after three months CBCT was done (Figure 4).
- A crestal incision flap was used to put a healing collar and second stability was done using Anycheck followed by flap repositioning and suturing (Figure 5).
- After healing was confirmed, a prosthetic protocol was accomplished (Figure 6) .

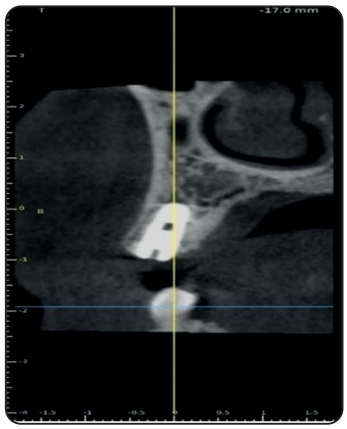

Fig. (4) A photo-radiograph showing a postoperative CBCT image

Fig. (5) Secondary stability measure by AnyCheck® device

Fig. (6) A photograph showing the placement of the crown

For control group (Sandblasted acid-etched):

- The comparator group utilized Sandblasted acid-etched* surface-treated dental implants.
- A Titanium Implant with dimensions was used in the posterior maxilla**.
- A pre-operative CBCT X-ray was done to evaluate the quality and quantity of the bone available and the proximity of vital structures to create a treatment plan.
- Full-thickness pyramidal flaps were elevated with a minimal extension to reduce patient discomfort after that reflection of the soft tissue flap and implant placement .
- Implant-motors*** with contra-angle handpiece**** with normal saline irrigation was used.
- After implant placement, a healing collar was inserted into the implant, and primary stability was measured by using the Anycheck® device*****, it is requires initial calibration using the manufacturer-supplied calibration block prior to each measurement session. For implant stability assessment, firmly screw the sterilized healing abutment into the implant platform, ensuring hand-tightened seating without excessive force. Position the handpiece probe perpendicular to the implant long axis, maintaining a physical contact between device and healing abutment. Activate the device to capture Percussion based uses tapping to measurements; record the highest stable Implant Stability Test (IST) value displayed after three consistent readings, then the healing collar was removed, and an implant cover screw was inserted and suturing.

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* Sandblasted acid etched, Titan Industries, Industrial Zone, 3rd settlement, Egypt

** Dual implant, Titan Industries, Industrial Zone, 3rd settlement, Egypt

*** Woodpecker, China

**** Woodpecker, China

***** AnyCheck - Implant Stability Tester, Neobiotech, US

- After 10 days, the sutures were removed, and after three months CBCT was done .
- A crestal incision flap was used to put a healing collar and second stability was done using Anycheck followed by flap repositioning and suturing .
- After healing was confirmed, a prosthetic protocol was accomplished.

Outcomes

Primary outcome (Implant stability)

- Implant stability was measured using the Anycheck® device* .
- It was measured in a time frame of 0 and 3 months.

Secondary outcome (Soft tissue healing)

- Soft tissue healing was determined through clinical examination in a time frame of 10 days.

Tertiary outcome (Bone density)

- Bone density in Hounsfield was measured using a CBCT image.

Statistical analysis

- Numerical data were explored for normality by checking the distribution of data and using tests of normality (Kolmogorov-Smirnov and Shapiro-Wilk tests). All data showed normal (parametric) distribution. Data were presented as mean and standard deviation (SD) values.
- For parametric data, repeated measures Analysis of Variance (ANOVA) was used to compare between the groups as well as to study the changes by time within each group. Bonferroni's post-hoc test was used for pair-wise comparisons when the ANOVA test was significant. Implant success data were presented as frequencies and percentages. Fisher's Exact test was used to compare implant success in the two groups. The significance level was set at $P \leq 0.05$. Statistical analysis was performed with IBM SPSS[12].

Sample size

Recorded data were analyzed using the statistical package for social sciences, version 23.0 (SPSS Inc., Chicago, Illinois, USA). The quantitative data were presented as mean± standard deviation and ranges when their distribution was parametric (normal) while non normally distributed variables (non-parametric data) were presented as median with inter quartile range (IQR). Also, qualitative variables were presented as numbers and percentages. Data were explored for normality using the Kolmogorov-Smirnov and Shapiro-Wilk Test.

RESULTS

This study was designed as a randomized controlled clinical trial to evaluate the effect of hyaluronic acid surface treatment versus sandblasted acid etched surface treatment on the stability of delayed dental implants in the posterior maxilla. The patients who met the inclusion criteria were divided into two groups; Group A (Hyaluronic acid) and Group B (Acid-etched sandblast). The dental implants were tested for their stability at baseline and after three months. They were also clinically examined for soft tissue healing ten days postoperative. The bone density was also measured through a CBCT scan.

Baseline characteristics

Descriptive statistics of participants' characteristics at the baseline in both tested groups are shown in Table 1. In Group A, three males (30%) and seven females were included (70%). Group B included two males (20%) and eight females (80%).

* AnyCheck - Implant Stability Tester, Neobiotech, USA
** SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp

The participants' age ranged from 18 to 60 years with a mean age of 46.6±7.4 years in Group A and 45.4±8.9 years in Group B.

TABLE (1) Distribution of participants in Groups A and B and their age at baseline

Tested group	Gender [n (%)]		Age (Mean ± SD)
	Male	Female	
Hyaluronic acid	3 (30%)	7 (70%)	46.6±7.4
Acid-etched sandblast	2 (20%)	8 (80%)	45.4±8.9

Implant stability test

Comparison between hyaluronic acid and acid-etched sandblast groups

The Implant Stability Test was measured for all participants in both groups at baseline and after 3 months (T2) (Table 2 and Figure 7). There was no statistically significant difference between hyaluronic acid and acid-etched sandblast concerning Implant Stability Test IST percentage (*P*- value= 0.697, Effect size= 0.01) at the baseline and after 3 months (*P*-value = 0.158, Effect size = 0.128).

TABLE (2) Comparison between Group A (hyaluronic acid) and Group B (acid-etched sandblast) regarding Implant Stability Test (IST) mean scores at baseline and 3 months (T2) and changes within both groups

Time	**Implant Stability Test (IST) (%) (Mean ± SD)**		**P-value**	**Effect size (Partial eta²)**
	Hyaluronic acid	**Acid-etched sandblast**		
Baseline	78.3±6.8	79.6±6.7	0.697	0.01
T2	83.0±5.6	85.9±2.3	0.158	0.128
P-value	0.061	0.006*		
Effect size (Partial eta²)	0.215	0.411		

: Significant at P£0.05

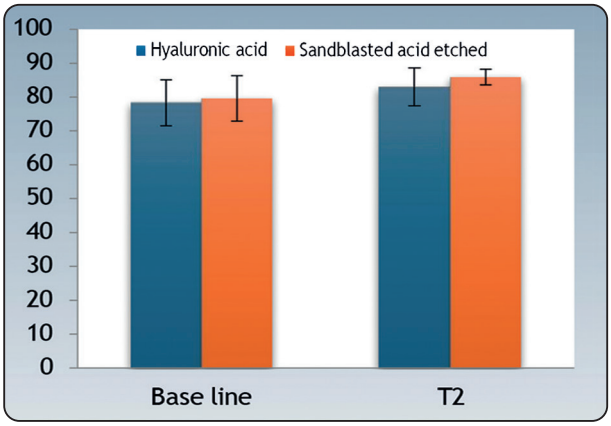

Fig. (7) Bar chart showing Implant Stability Test (IST) means scores at baseline and 3 months (T2) in hyaluronic acid and acid-etched sandblast groups

Changes within each group

Changes in the mean IST scores in the hyaluronic acid group showed no statistically significant differences after 3 months (*P*-value = 0.061, Effect size = 0.215). On the other hand, changes in the mean IST scores in the acid-etched sandblast group showed statistically significant increases in the mean IST scores after 3 months (*P*-value = 0.006, Effect size = 0.411).

Bone density measurements

Comparison between hyaluronic acid and acid-etched sandblast groups

Comparison between hyaluronic acid and acid-etched sandblast groups concerning bone density is shown in Table 3 and represented in Figure 8. Results showed that there was no statistically significant difference in bone density between both groups at baseline and 3 months (T2) (*P*-value = 0.424, Effect size = 0.036) and (*P*-value = 0.909, Effect size = 0.001), respectively.

Changes within each group

Changes in the bone density values in the hyaluronic acid group showed no statistically significant differences after 3 months (*P*-value = 0.6, Effect size = 0.016). On the other hand, changes in the mean bone density value in the acid-etched

sandblast group showed statistically significant increases in the mean IST scores after 3 months (*P*-value = 0.004, Effect size = 0.374).

TABLE (3) Comparison between Group A (hyaluronic acid) and Group B (acid-etched sandblast) regarding bone density value (HU) at baseline and 3 months (T2) and changes within both groups

Time	Bone density (HU) (Mean ± SD)		P-value	Effect size (Partial eta²)
	Hyaluronic acid	Acid-etched sandblast		
Baseline	505.2±153.2	454.2±124.3	0.424	0.036
T2	516.7±184.6	524±123.4	0.909	0.001
P-value	0.6	0.004*		
Effect size (Partial eta²)	0.016	0.374		

: Significant at P£0.05

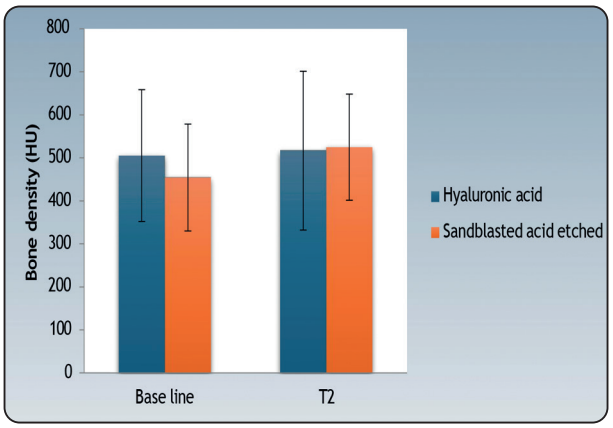

Fig. (8) Bar chart showing bone density value (HU) at baseline and 3 months (T2) in hyaluronic acid and acid-etched sandblast groups.

Implant success assessment

The implant success was measured for all participants in hyaluronic acid and acid- etched sandblast groups and statistically analyzed (Table 4 and Figure 9). In the hyaluronic acid group, 70% of participants showed implant success (30 % failure). However, in the acid- etched sandblast, 100% of participants showed implant success. There was no statistically significant difference between implant success in the two groups (*P*-value = 0.211, Effect size = 0.412).

TABLE (4) The implant success rate measured in hyaluronic acid regarding the success and failure rates after 6 months

Implant success rate	Distribution [n (%)]		P-value	Effect size (Partial eta²)
	Hyaluronic acid	Acid-etched sandblast		
Success	7 (70)	10 (100)	0.211	0.412
Failure	3 (30)	0 (0)		

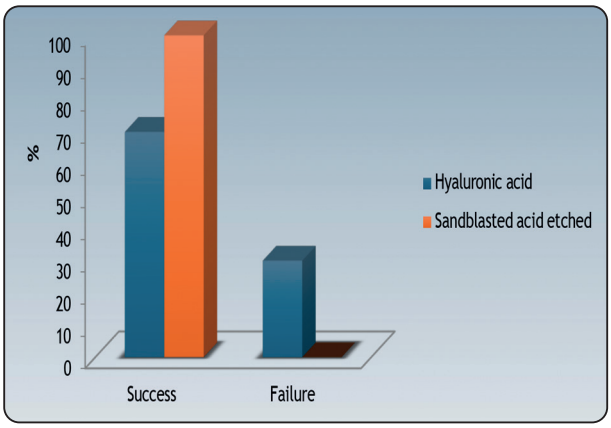

Fig. (9) Bar chart showing the implant success and failure rates in hyaluronic acid and acid-etched sandblast groups.

DISCUSSION

The dental implant is a reliable technique used to substitute a lost or damaged tooth. Implant stability may be clinically defined as the ability to withstand rotational and axial-lateral forces without exhibiting movement. In implant dentistry, stability is a crucial need for treatment success (Guglielmotti et al., 2019)[8].

A successful dental implant technique entails osseointegration, a multi-phase process including blood clot formation, mesenchymal

tissue development, bone synthesis, and lamellar bone formation after implant placement. The commencement of osseointegration requires the adsorption of plasma proteins onto a hydrophilic surface (Zhang et al., 2022)[9].

It is essential to maintain enough stability to ensure effective osseointegration from the moment of implant insertion to the completion of osseointegration. The reduction in stability will cause micro-movement, transitioning the healing process from osseointegration to fibrointegration, ultimately resulting in implant failure (Cooper & Shirazi, 2022)[10].

Therefore, this study compared the stability and Osseointegration of dental implant placement by using hyaluronic acid versus sandblasted acid etched. This could be important for patients who have limited bone density in the posterior maxilla, as it could help to improve the success rate of implant placement in these challenging cases.

Sandblasting and acid etching are the main techniques used for altering the surface of dental implants. Facilitates osteoblast adhesion, hence enhancing osseointegration. The sandblasting process textures the implant's exterior layer, facilitating enhanced bone adhesion throughout the healing phase (El-Banna et al., 2020; Kligman et al., 2021)[11,12].

Hyaluronic acid is a natural substance found in the body that has beneficial properties for wound healing and tissue regeneration. Moreover, enhancing the bioactivity of implant surfaces with hyaluronic acid might enable the accurate placement of dental prostheses during the first loading period, hence meeting patient demands (Cervino et al., 2021; Thaidi et al., 2023)[4,13].

Hyaluronic acid (HA) enhances dental implant osseointegration through multiple biological mechanisms, though the literature presents both supporting and conflicting evidence. Supportively, HA-coated implants demonstrate accelerated bone formation by promoting osteoblast proliferation, migration, and differentiation, as evidenced by increased expression of osteogenic markers (e.g., RUNX-2, ALP, OCN) and higher bone-to-implant contact (BIC) ratios in animal models (yazan et al.,2019)[7]. HA's anti-inflammatory properties modulate the peri-implant microenvironment by suppressing pro-inflammatory cytokines (e.g., IL-1β, TNF-α) and enhancing angiogenesis, which facilitates early-stage healing. Additionally, HA improves implant surface hydrophilicity and protein adsorption, leading to faster fibrin clot formation and collagen matrix organization (Cervino et al.,2021)[14]. However, conflicting data exist regarding HA's biomechanical efficacy: while some studies report significantly greater BIC with HA-coated implants (Yazan et al.,2018b)[15], others found no significant differences in new bone volume or removal torque values between HA-coated and uncoated implants at longer timepoints (yazan et al.,2019)[7]. These discrepancies may arise from variables such as HA molecular weight (high MW >500 kDa favors anti-inflammatory effects, while low MW fragments may provoke inflammation), concentration, and application methods (Al-Khateeb et al.,2020)[16].

In this study, the baseline ISQ values and ISQ values after 3 months (T2) showed no statistically significant difference between the hyaluronic acid and the acid-etched sandblast groups. This suggests that both treatments were equally effective at maintaining implant stability initially (H et al., 2020)**17**. However, the changes in mean ISQ scores over the 3 months showed different results. The hyaluronic acid group did not show a statistically significant change in ISQ scores, indicating that implant stability remained relatively constant. On the other hand, the acid-etched sandblast group showed a statistically significant increase in ISQ scores, suggesting improved implant stability over time (Hamdy et al., 2024; H. G. Kim et al., 2021)[18,5].

The significant increase in ISQ scores in the acid-etched sandblast group supports this, as the rougher surface likely provides more mechanical interlocking with the bone, leading to improved stability over time (Hamdy et al., 2024)[18].

The lack of significant change in ISQ scores in the hyaluronic acid group might indicate that while it supports soft tissue healing, it may not significantly enhance bone integration or implant stability (Alzoubi et al., 2024; Hamdy et al., 2024)**1**[9,18].

These results agreed with Elhadidi et al.,[20] who found no significant differences in bone density after the topical application of hyaluronic acid to dental implants in the posterior maxilla. However, there was a considerable difference in ISQ value at different time intervals (after 1, 3, and 6 months).

Results also coincided with Abhinga et al.,[21] who injected hyaluronic acid into the implant site and found a significant increase in implant stability and a reduction in crestal bone loss. The findings were similar to those of Hamdy et al.,[18] who compared the implant stability of hyaluronic acid-coated implant with sandblasted large thread acid-etched surface implant and they found at different intervals (baseline, 6, and 12 weeks) postoperatively, no statistically significant difference between both groups at the baseline. However, there were statistically significantly greater ISQ values in the HA-coated implant group than SAE implant group after 6 and 12 weeks of surgery.

These findings also coincided with Eldeeb et al.,[22] who observed a statistically significant increase in the ISQ and soft tissue thickness after the implant insertion at the baseline and 6-month follow-up.

In this study, results indicate that both treatments (hyaluronic acid and acid-etched sandblast) initially produced similar bone densities and maintained these levels similarly over 3 months. This lack of significant difference at baseline and after 3 months may suggest that both treatments are equally effective in maintaining bone density in the short-term (He et al., 2009)[23]. These findings were consistent with Velasco-Ortega et al.,[24] who found application of sandblast acid-etched dental implants increased bone-implant contact and osseointegration showing the development of new bones along the implant surface in a rabbit model. Results also agreed with Kim et al.,**6** when using the sandblast acid-etched surface implants in the posterior maxilla.

Regarding success rate, results revealed that there was a 70% success rate suggesting that most implants were successful with hyaluronic acid, but there was a notable failure rate of 30%. This could be due to the nature of hyaluronic acid, which is primarily beneficial for soft tissue healing and may not significantly enhance bone integration. Hydrogels and microparticles derived from hyaluronic acid that bind covalently to the surfaces of metal implants enhance osseointegration and osteogenesis by releasing bioactive components (Zhai et al., 2020)**25**. These results agreed with Genovesi et al.,**26** who demonstrated the benefits of hyaluronic acid in enhancing soft tissue healing. They found that patients who were treated with 0.12% chlorhexidine in addition to hyaluronic acid mouthwash showed better soft tissue healing than chlorhexidine alone.

The results aligned with those of Sánchez-Fernández et al.,**27** who demonstrated that the topical application of hyaluronic acid gel significantly mitigated the inflammatory response linked to peri-implant mucositis in the early healing phase. Besides, new data from several clinical studies suggested that hyaluronic acid supported postoperative symptom control and speeded up the healing process of soft tissues (Eldeeb et al., 2023; Hamdy et al., 2024; Shukla & Kiran Pebilli, 2023)[22,18,28].

The 100% success rate is highly favorable, indicating that all implants in this group were successful. Acid-etched sandblast surfaces create a rough texture on the implants, increasing the surface area for bone attachment and enhancing osseointegration (Velasco- Ortega et al., 2019)[6]. These findings were consistent with previous studies that used sandblasted acid-etched with dental implants (Hamdy et al., 2024; H. G. Kim et al., 2021; Ozel et al., 2021; Velasco-Ortega et al., 2019)[18,6,29,6].

There was no statistically significant difference between both groups concerning success rate. The lack of statistical significance suggests that the

observed difference in success rates might be due to chance rather than a real effect of the treatments. These results agreed with Elhadidi et al.,[20] and Hamdy et al.,[18] who also reported similar results.

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