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DRUG DELIVERY ANESTHETIC METHOD WITH LIDOCAINE FOR USING FRACTIONAL CO2 LASER ON THE FACE: PILOT STUDY

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ABSTRACT

Introduction*:* The CO_2 laser, widely used for rejuvenation and aesthetic treatments can cause intense discomfort, making it necessary to use anesthetics. Depending on its application, lidocaine is an effective resource for anesthesia before applicating fractional lasers. Microneedling has shown to be an extremely effective resource for the transdermal delivery of medications through the stratum corneum, including anesthetics. ***Objective****:* To collect preliminary results on the efficacy of microneedling associated with lidocaine drug delivery to the skin in order to enable appropriate anesthesia for the use of fractional CO_2 laser on the face. ***Materials and methods:*** Twenty-one adult patients with mild to moderate facial sagging were selected for treatment with a fractional CO_2 laser, excluding those with contraindications related to the technique. The split-face study compared the analgesia provided by lidocaine drug delivery before the application of fractional CO_2 laser. The procedure involved microneedling with simultaneous infusion of lidocaine on one side of the face, while saline solution was infused on the other, followed by application of the fractional CO_2 laser. Two brands of equipment were used (HYBRID® and YOULASER®). Thus, dosimetric parameters were standardized for both equipment utilized. After treatment, patients answered a questionnaire about their perception of pain and comfort during the procedure. ***Results:*** The analysis of comfort showed that most patients considered the procedure with fractional CO_2 laser uncomfortable, with no statistically significant difference between the brands of equipment tested. The most sensitive areas varied between the groups, with emphasis on the eye and forehead regions. The comparison between hemifaces showed that analgesia with microneedling and lidocaine significantly reduced pain during laser treatment, confirming the effectiveness of drug delivery with lidocaine in enhancing the anesthetic effect necessary for performing the procedure. ***Conclusion****:* Anesthesia with lidocaine drug delivery associated with microneedling was effective in reducing discomfort and enabling the application of fractional CO_2 laser. However, as this is a preliminary investigation, some factors may have influenced the results and should be considered for the continuation of this study.

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INTRODUCTION

Microneedling maybe considered as a new transdermal drug delivery system to deliver drugs through the stratum corneum, the outermost physical barrier of the skin, in a minimally invasive manner (Yang *et al*., 2020; Zhang *et al*., 2012; Ornelas *et al*., 2016; Luz *et al*., 2017).

Lidocaine is a local anesthetic agent commonly used in the form of injection and topical cream. However, these types of formulations have limitations of being painful or slow acting, thus hindering the effective and complete clinical performance of lidocaine (Yang *et al*., 2020). Dissolving microneedling ((Yang *et al.,* 2020; Zhang *et al.,* 2012; Henrique *et al.)* or traditional microneedling (Ornelas *et al.,* 2020; Luz *et al*., 2017) has been suggested to overcome these limitations due to its quick onset time of anesthesia and minimally

invasive delivery methods. In this way, microneedling can enhance the absorption of lidocaine, providing more effective pain relief and greater comfort to the patient during the application of high-power laser. The CO_2 laser was one of the first devices in which gaswas used as an active medium, having been designed by Kumar Patel in 1964. In the production process of CO_2 laser, after stimulating the gas contained in the tube through high-energy electrical discharges, the atoms composed in the gas reach higher energy levels, emitting photons with a wavelength of 10,600 nm when they return to their previous resting state (Artiaga and Borges, 2025). Since the fractional CO_2 laser has a wavelength of 10600 nm, its main chromophore of action is water (Ramsdell, 2012), it uses the process of fractional photothermolysis to produce its results by creating microscopic thermal wounds on the skin surface. Such woundsare divided into unaffected areas of the skin, necessary for local tissue recovery, thus avoiding side effects and prolonged recovery (Petrov, 2016). One of the main indications for using this type of laser on the face is resurfacing, which has been used since 2007, with its efficacy and safety confirmed by clinical practice described in the literature (Carniol *et al*., 2015). Therefore, it is considered an efficient resource for skin rejuvenation through laser resurfacing of the facial skin; however, a careful approach is necessary to adjust the appropriate treatment parameters to minimize complications and optimize results (Ramsdell, 2012). Fractional CO_2 laser is also indicated for the treatment of various dermatological conditions, as well as for various aesthetic dysfunctions (Omi and Numano, 2014). The use of this kind of fractional laser has been described by authors (Hoogstra, 2024; Ni Gao *et al*., 2024; Oram and Akkaya, 2014).

Anesthesia methods in laser resurfacing are divided into non-invasive and invasive. Non-invasive methods of anesthesia include topical anesthesia, cryoanesthesia, or a combination of both. These methods provide the benefit of avoiding needles, intravenous (IV) access, or the need for intubation. However, if a stronger analgesic effect than that provided by non-invasive methods is desired for the laser resurfacing procedure once in the case of deep resurfacing, invasive methods that include injectable anesthesia and supervised anesthesia can be applied (Gaitan and Markus, 2012). Injectable forms of anesthesia include local infiltration anesthesia, specific nerve blocks, and tumescent anesthesia. One of the main disadvantages of this anesthesia method is that it requires needles, which can cause anxiety or fear in patients (Sokolowski *et al*., 2010). Another disadvantage is the use of a large amount of injectable anesthetic, and even so, the patient still feels discomfort. Using anesthesia to reduce the usual discomfort during the use of the fractional CO_2 laser in resurfacing procedures is consideredvery important and it is difficulty patients' acceptanceof using more invasive anesthesia applied by needles.Thus, this pilot study sought to gather preliminary results about the efficacy of microneedling associated with the drug delivery of lidocaine to the skin to enable appropriate anesthesia for the use of fractional CO_2 laser, and because it is considered an innovative method and a possible substitute for the use of traditional needles common in more aggressive anesthetic methods.

MATERIALS AND METHODS

Patient selection: Twenty-one male and female patients over 18 years of age with complaints of facial aging were selected for the study. The inclusion criteria were patients with mild to moderate sagging in the facial and neck region. The informed consent form was signed by each of the study participants. The following patients were excluded from the study: a) those who had a sensitivity to lidocaine; b) those who were pregnant or lactating; c) those with decompensated disease or undergoing medical treatment; d) those with heart or immunological problems; e) those who had diabetes; f) those who had a history of cancer or; g) those with abnormal health conditions such as: active herpetic lesions in the treatment area, sunburn or overexposure to the sun in the last few weeks prior to treatment, those who had used isotretinoin up to 6 months prior to treatment, and those who had eczematous skin conditions.

Study Design: Patients were treated with microneedling equipment (Tinexpen®, manufactured by YIWU CITY SOLONG IMP EXP CO - Zhejiang, China) with a disposable cartridge of 45 needles (Emalla) (Figure 1), and the needle length adjusted on the equipment was 0.5 mm; as dosimetric adjustments, the microneedling pen was set at speed 3 (medium), being applied to each hemiface with an average application time of 2 minutes. Tinexpen is a device that simultaneously performs microinfusion of active ingredients with microneedling. The product to be infused (in this study it was lidocaine with vasoconstrictor) is collected by simply contacting the needle cartridge with the product, and microinfusion occurs with the incoming and outgoing movements of the microneedles on the skin surface. With this system of microinfusion simultaneous to microneedling, we found that there is a great use of the product and/or medication to be infused since there is no need for dripping after microneedling.As well, there is no difficulty in substance'spenetration due to exudate resulting from the microneedling process itself or due to the closure of the microchannels.

(Source: authors)

Figure 1. Microneedling pen used in this study for drug delivery

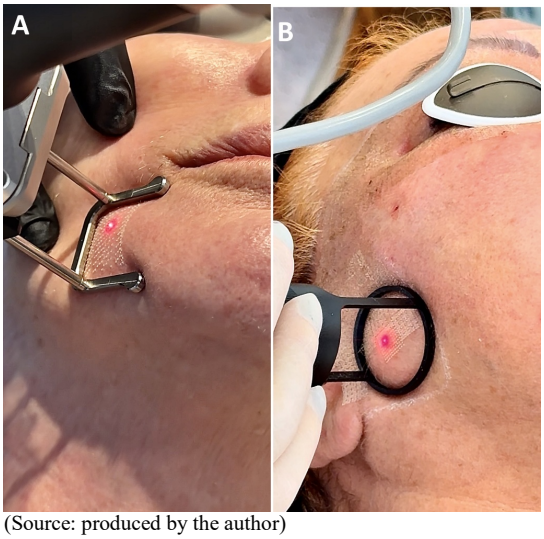
The following equipment was used for the fractional CO_2 laser procedure: HYBRID® (LMG® - Laser Medical Group) and YOULASER MT (Quanta System) (Figure 2). The dosimetric parameters chosen for the treatment were: power of 10W to 15W; pulse duration of 2 to 2.5 ms; application density of 125 to 160 DOT/cm^2. Since the machines have different setups, the parameters were adjusted for similar treatment protocols. All patients received only one microneedling and fractional CO^2 laser session. The topical anesthetic used pre-needlingwas handled in a teaching pharmacy and composed of tetracaine 7%, lidocaine 23% and epinephrine 0.025%, qsp gel. After the procedure, patients were instructed to apply Desonide 0.5 mg cream (non-fluorinated corticosteroid) and sunscreen during the day and Desonide 0.5 mg cream and solid petroleum jelly at night, until the surface barrier recovered (around 5 to 7 days).

Treatment: Patients were treated in a clinic located in São Paulo,SP, Brazil, that complies with health standards for that kind of procedure. Before treatment, patients were initially evaluated using the following

assessment methods: photographic images in frontal position, at 45 degrees (right and left) and right and left profile (Canon EOS Rebel T6 camera with EF 100mm f/2.8L Macro IS USM lens); and sensitivity analysis research using a questionnaire containing the questions described in Table 1.

Table 1. Research survey for sensibility evaluation during and after fractional CO_2 laser procedure

QUESTIONS	ANSWER OPTION
1.How would you rate your overall comfort experience during the fractional CO_2 procedure?	( ) Very comfortable; ( ) Comfortable; ( ) Neutral; ( ) Uncomfortable; ( ) Very uncomfortable.
2.During the laser application, did you notice any difference in sensitivity in different areas of the face?	( ) No; ( ) Yes, which ones? ( ) Forehead; ( ) Around the eyes; ( ) Cheeks; ( ) Around the mouth; ( ) Chin ( ) Other
3.Have you had fractional CO_2 laser procedures before? If you have had other fractional CO_2 laser procedures, how would you compare the pain/discomfort experience of this procedure compared to previous ones?	( ) No; ( ) Yes; ( ) It was more comfortable now; ( ) It was less comfortable now; () There was no difference between both treatments.
4.On a scale of 0 to 10, how would you rate the discomfort or pain felt on each side of your face? (With 0 = no pain/discomfort and 10 = unbearable pain/discomfort)	a) Left side: ____ b) Right side: ____



(Source: produced by the author)

Figure 2. Treatment using fractional CO_2 laser A) YOULASER e B) HYBRID

Before the procedure, patients received facial cleansing using 30% urea foam (prepared in a pharmacy of manipulation), gauze, and saline solution to remove residue. Then, they received topical anesthetic application on the entire hemiface (Lidocaine 23%, Tetracaine 7%, Epinephrine 0.025%, qsp gel (prepared in a pharmacy of manipulation). After 30 minutes, the topical anesthetic was removed, and the skin was cleaned with gauze and 70° GL alcohol only on the left hemiface. Then, the patients were treated with microneedling and drug delivery of 1.5 ml of 2% lidocaine hydrochloride with epinephrine hemitartrate (1:200,000) only on the left hemiface. Just after absorption of the anesthetic, the left hemiface was treated with the fractional CO_2 laser (Figure 2). Immediately after treatment of the left hemiface, the contralateral side had the topical anesthetic removed, as previously described and was microneedled with drug delivery with 0.5 ml of saline solution, followed by treatment with fractional CO_2 laser.Patients were unaware that they were receiving different products on each hemiface treated. Immediately after applicating fractional CO_2 laser to the entire face, patients answered a questionnaire about their feeling of comfort during treatment with fractional CO_2 laser.

Statistical Analysis

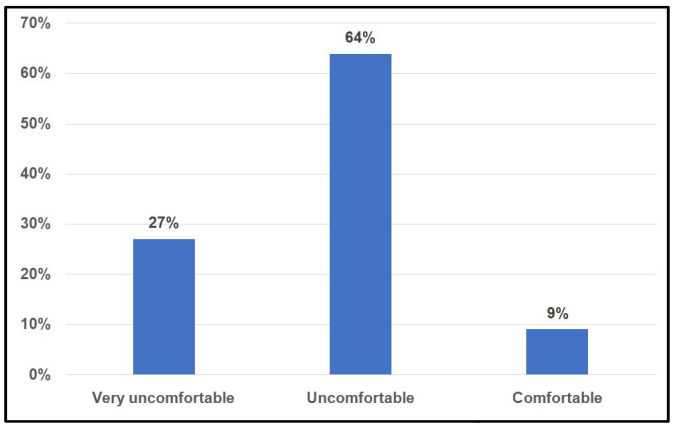
Statistical analysis was performed using the SPSS program and Excel to construct the graphs. Pearson's chi-square test was used to compare the perception of comfort between the laser brands (Youlaser® vs Hybrid®). The pain/discomfort scale was analyzed using the nonparametric Mann-Whitney test. In addition, the chi-square test was applied to evaluate the distribution of sensitivity by region of the face.

RESULTS AND DISCUSSION

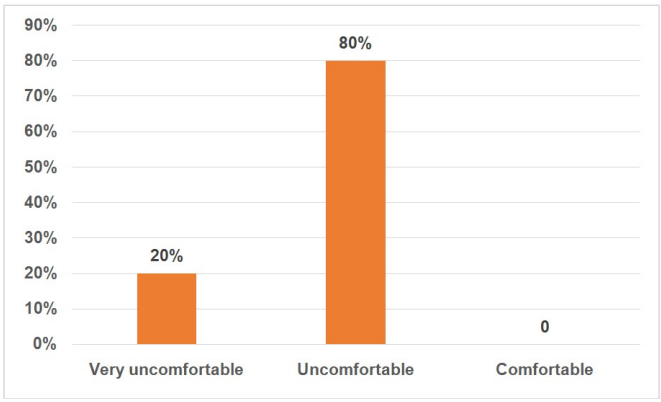
The CO_2 laser has several physiological effects that contribute to skin rejuvenation. The fundamental principle behind its use is controlled destruction followed by skin reconstruction (Guo *et al*., 2013). This kind of laser emits light radiation with a wavelength that is highly absorbed by the water present in skin tissues (Omi and Numano, 2014). This energy absorption causes a rapid increase in temperature, leading to vaporization of intracellular water and tissue ablation. Therefore, one of the main physiological effects is the denaturation of collagen by the action of heat, which can reach temperatures close to 70 degrees Celsius. This denaturation leads to an immediate contraction of collagen, which is one of the main mechanisms of skin retraction (Hoogstra, 2024). This retraction effect mightbe seen in Figure 3, as well as the tissue rejuvenation effect. Despite the positive aesthetic effect, the procedure causes moderate to severe pain during the procedure, and pain is controlled with anesthesia (Triana *et al*., 2015). In this study, we first sought to understand the general perception of comfort of patients during the fractional CO_2 laser procedure. When using the Youlaser® brand device, most patients (64%) considered the procedure uncomfortable (Graph 1). We then observed whether the level of comfort was correlated with the brand of laser used and repeated the test with the Hybrid® brand. We observed that most patients (80%) also considered the laser uncomfortable (graph 2). We then compared the brands (graph 3) to assess whether there was a difference in comfort between them and applied the Mann-Whitney test to analyze whether the difference was statistically significant, using the SPSS statistical program. Regarding the overall comfort experience during the fractional CO_2 procedure, comparing the two brands used in this study (Pearson's Chi-square statistical test), we did not identify a significant difference between the frequencies of classification of the degree of comfort ($\chi 2 = 1.22$; $p = 0.54$). Despite this, it is known that pain is a subjective experience and influenced by multiple factors in addition to the laser brand.

(Source: produced by the author).

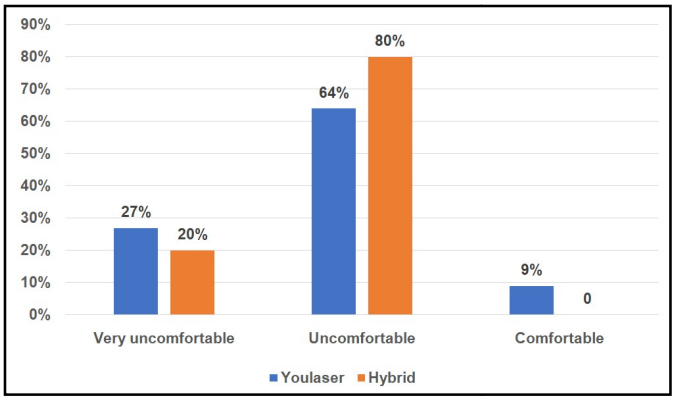
Figure 3. Skin rejuvenation effect produced by fractional CO_2 laser



Graph 1. Analysis of patient comfort during the Youlaser® fractional CO_2 laser procedure



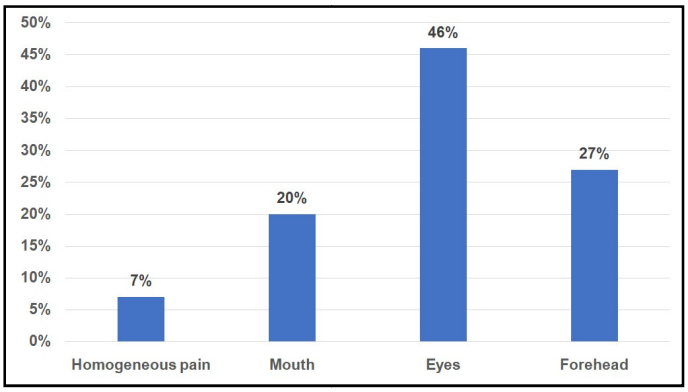
Graph 2. Analysis of patient comfort during the Hybrid® brand fractional CO_2 laser procedure



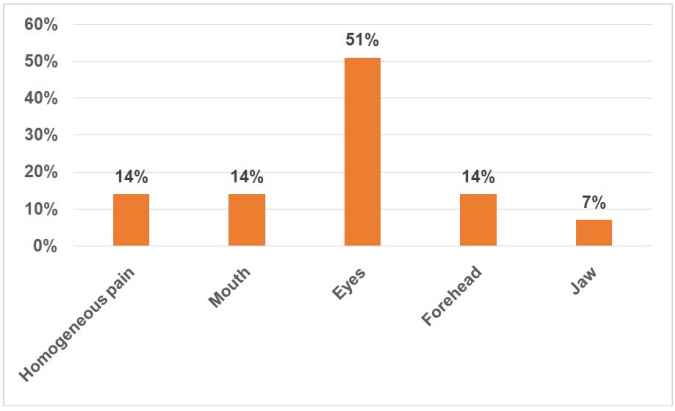
Graph 3. Comparison of comfort between the Youlaser® and Hybrid® brands when applying the fractional CO_2 laser

These data validate the reports of Yumeen and Khan (2023) who reported that an appropriate means of pain control should be selected prior to fractional CO_2 laser resurfacing treatment. Authors (Hoogstra, 2024; Edkins *et al*., 2025) stated that although effective, the use of fractional CO_2 laser is painful, and efficient pain control measures are essential to allow patients tolerate all treatment. However, in a study with 53 patients with postmenopausal vaginal atrophy treated with fractional CO_2 laser (Di Donato *et al*., 2020), treatment-related discomfort was lower than expected for 60.4% of patients and as expected for 34%. Still on the aspect involving pain during the procedure, the fact that it was used two different equipment, a point that could generate a bias of doubt about a greater or lesser degree of discomfort generated by the procedure, Campos *et al*. (2010) recommended that the adjustment parameters should already be defined before the start of the session and can be changed according to the patient's pain sensation. Therefore, in this study, we sought adjustments to the equipment that would most closely match a standard of effectiveness and control of discomfort commonly seen in our clinical practice. The patients were then asked about the most sensitive area of the face during the application of the CO_2 laser. Patients who used the Youlaser® equipment reported greater pain in the eye region (46%) (Graph 4).The same question regarding sensitivity by region was asked to patients treated with the Hybrid® brand equipment (Graph 5). It was observed that the majority (51%) also felt more discomfort in the eye region.

Then, we compared whether the brands presented significant differences between the regions of greatest sensitivity (Graph 6).

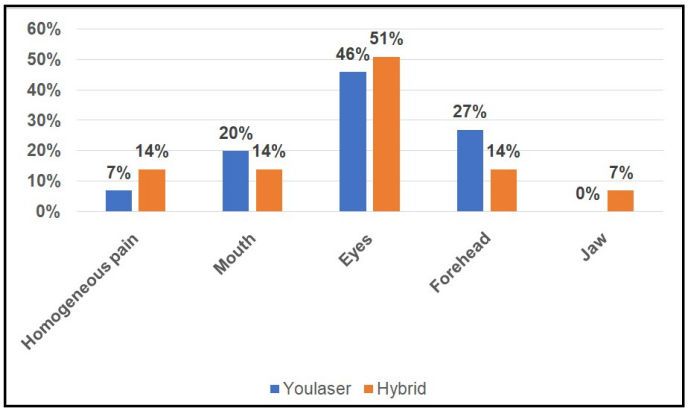


Graph 4. Comparison of sensitivity by face area of the Youlaser® brand



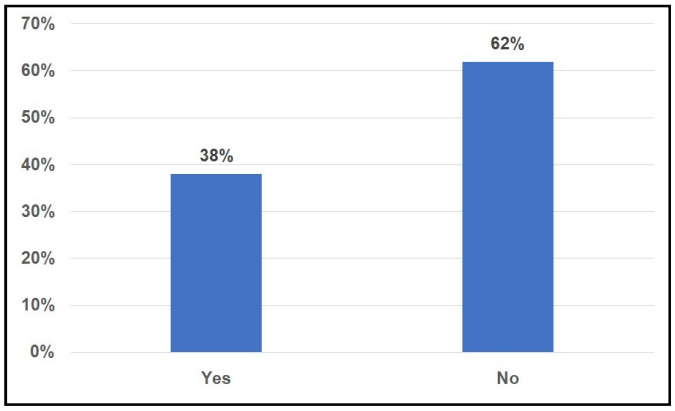
Graph 5. Comparison of sensitivity by face area of the Youlaser® brand

It was noticed that in both brands, the eye area was the most painful and the difference between the brands was not statistically significant. Despite this, we did not find specifications in the scientific literature about whether any facial region is more painful than another during the procedure.However, according to Toyos (2017), patients report great discomfort in the eye area when using the fractional CO_2 laser, but the technological evolution of the equipment has sought to maximize the thermal effect without a large accumulation of heat, thus reducing pain, side effects and downtime.



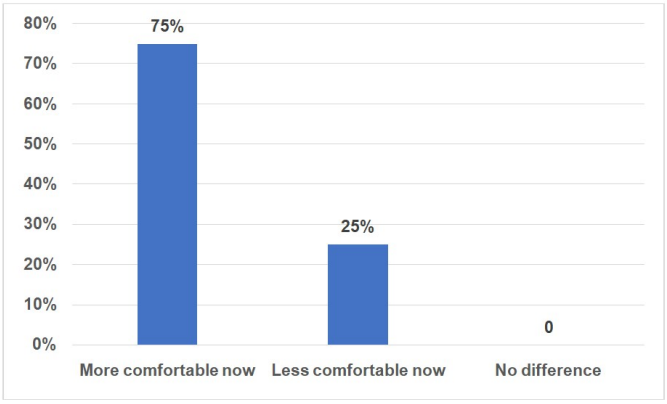
Graph 6. Comparison of sensitivity by face area between the two brands of lasers

Patients were also asked whether they had previously undergone treatment with the CO_2 laser (graph 7). The majority (62%) had not undergone the procedure. The overall experience of comfort during the fractional CO_2 procedure was compared between patients who had previously undergone the procedure and those with no previous experience. It was used the Pearson's Chi-square test for that comparison andthere was no significant difference in the frequencies of comfort ratings between the two groups (χ^2= 3.47; p= 0.18). Despite this, Tierney *et al*., (2011) observed that a single session of fractional ablative treatment has an appreciable but limited effect on periorbital wrinkles, and that multiple sessions are probably necessary for a more significant improvement. The study by Alcolea *et al*., (2024) indicates that fractional procedures performed with single passes have rapid recovery and few side effects, allowing 2 or 3 treatments to be performed in an interval of at least 3 months between them. This same article also mentions the possibility of performing up to 3 overlapping passes in a single session, depending on the tissue reaction. Therefore, the decision to perform the procedure in a single session or with reapplications varies between studies is related to the treatment objective, the severity of the condition and the expectations of results. Therefore, some protocols seek to optimize results with a single intense session, while others prefer multiple sessions with lower intensity to minimize side effects and allow for safer recovery.



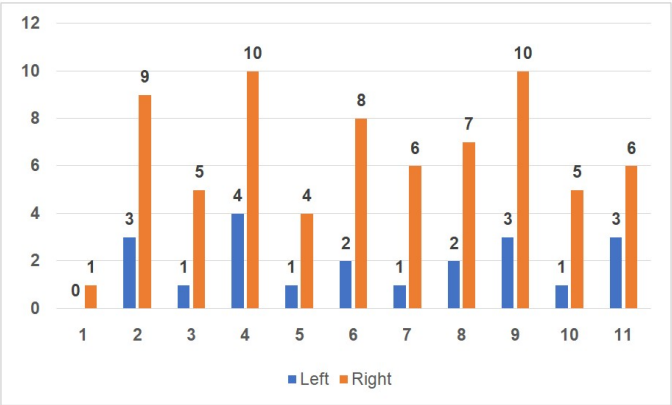
Graph 7. Analysis of recurring use of CO_2 laser

Next, among those who responded that they had already undergone the laser procedure more than once, the comfort of the current procedure was compared with previous experiences (graph 8). The majority (75%) reported that they felt more comfortable with the new procedure. Considering that microneedling can be used to administer analgesic medications such as lidocaine through microneedles (Henriquez *et al*., 2023), we concluded that the greater comfort reported in the second procedure was due to the effectiveness of the lidocaine drug delivery technique used in this study. It is also worth to mention that the recommendation of minimum intervals between fractional laser sessions suggests the importance of allowing skin's recovery before a new treatment (Alcolea *et al*., 2024), since it may be more sensitive, resulting in a greater perception of pain. In the present study, the previous fractional CO_2 laser sessions occurred a few months after the previous session, allowing the recovery of the skin's natural sensitivity. It is also important to highlight that the application of the anesthetic associated with microneedling was performed on only one side of the face. Furthermore, when applying for the statistical test, since the sample was very small (cells with expected values less than 5), Fisher's exact test was more appropriate than the chi-square test and resulted in a statistically non-significant difference (p=1), indicating the reassessment of this comfort level with a larger sample.



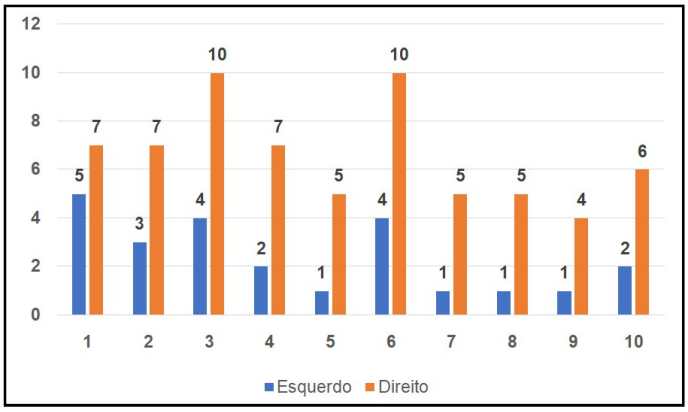
Graph 8. Comparison of patient comfort during the procedure compared to previous experiences

Immediately after, the discomfort or pain on both sides of the face was compared: topical anesthetic, microneedling and drug delivery with lidocaine were applied to the left side of the face.And topical anesthetic followed by microneedling with saline solution was applied to the right side. Patients who used the Youlaser® equipment evaluated the pain, with a score from 0 to 10 per side of the face, as shown in graph 9. It was observed that all patients (100%) reported greater pain on the right side, where microneedling with saline solution was used.



Graph 9. Assessment of pain levels in patients undergoing Youlaser® CO_2 laser therapy

To determine the statistical relationship between the reported discomfort, the results between the right and left sides of the face were compared using the Mann-Whitney test for the two laser brands evaluated. There was a significant difference between the sides of the face for both the Youlaser® [Z(U)= 3.25; p<0.01] and the Hybrid® laser [Z(U)= 3.51; p<0.01], as well as a difference in the pain/discomfort scale for the face sides regardless of the laser used [Z(U)= 4.80; p<0.01]. The right side of the face, on which microneedling was performed followed by saline solution, showed the most pain/discomfort in all comparisons of both brands (Table 2). This shows that the anesthetic used after microneedling improved comfort during the application of lasers of both brands on the left hemiface of the patients.



Graph 10. Assessment of the pain level of patients undergoing the Hybrid® brand CO_2 laser

Table 2. Descriptive measures of the pain/discomfort scale of the laser brands evaluated (Youlaser® vs Hybrid®)

Descriptive measures	Pain/discomfort scale Youlaser®	Pain/discomfort scale Hybrid®
Sample	22	20
Minimum	0	1
Maximum	10	10
TotalAmplitude	10	9
Median	3	4.5
Interquartile deviation	4,5	4,3
Arithmetic mean	3,8	4,5
Standard Deviation	2,89	2,78
Standard Error	0,62	0,62
Coefficient of Variation	75,7%	61,8%

Source: Research data.

The results of the pain/discomfort scale were also compared between the 21 patients treated with the two brands of CO_2 laser, using the nonparametric Mann-Whitney test. No significant difference was found between the two devices used when both sides of the face were analyzed together [Z(U)= 0.87; p=0.38]. Furthermore, the comparison between the lasers was made separately for the right and left sides of the face. There was also no significant difference between the lasers on the left side [Z(U)= 0.67; p=0.50], nor on the right side [Z(U)= 0.63; p=0.53] (Table 3). It means that the brand of laser device (Youlaser® or Hybrid®) did not significantly influence the pain/discomfort reported by the patients, regardless of the face side analyzed. This suggests that both devices caused a similar level of pain during the procedure.

Table 3. Descriptive measures of the pain/discomfort scale of the sides of the face

Descriptive measures	Pain/discomfort scale of left side	Pain/discomfort scale of right side
Sample	21	21
Minimum	0	1
Maximum	5	10
Total Amplitude	5	9
Median	2	6
Interquartile deviation	2	2
Arithmetic mean	2,1	6,2
Standard Deviation	1,4	2,4
Standard Error	0,3	0,5
Coefficient of Variation	63,1%	38,1%

Source: Research data.

These results agree with the literature, since microneedling acts in two ways: one, by stimulating the natural production of collagen in response to the inflammatory process, and another, by facilitating the Transdermal Ingredient Access System (TIAS), also known as *drug delivery*, which promotes increased permeability of active ingredients (Kalil *et al*., 2017; Ferreira *et al*., 2020). In the case of anesthetics, drug delivery facilitates their deeper penetration, enhancing their effect and reducing the sensation of pain (El-Fakahany *et al*., 2016). It is known that among the multiple functions attributed to the integumentary system, its ability to act as a route of administration for therapeutic substances stands out. However, the efficiency in the release, retention and permeation of these substances through the layers of the skin can be a limiting factor in the effective delivery of active ingredients to the target tissue. To overcome these barriers, several strategies have been developed, such as iontophoresis, phonophoresis, electroporation, and microneedling (Banga, 2011). Among these methods, microneedling stands out for its simplicity, accessibility, and effectiveness. By creating microchannels that directly break the stratum corneum, it facilitates the absorption of anesthetics (Luz and Pereira, 2017) without the need for additional devices. Furthermore, unlike iontophoresis and phonophoresis, microneedling does not depend on the electrical or physicochemical properties of the substance applied, making it anadaptablealternative for different anesthetic formulations. The creation of microchannels in the skin through the microneedles of the microneedling equipment breaks the stratum corneum barrier, significantly facilitating the transdermal delivery of topical substances (Luz and Pereira, 2017). Thus, during preparation for CO_2 laser treatment, we found in this study that this technique can be used to administer anesthetics and thus ensure important comfort for applicating this type of laser.

It is important to emphasize that microneedling devices vary in size, quantity, diameter and material of the needles. The Dermaroller®, considered standard, has 192 2 mm needles and generates approximately 250 perforations per cm² without causing damage to the epidermis; The Derma-stamp, applied by pressure and indicated for localized scars; the Dermapen®, which resembles a pen and allows adjustment of the length of the needles for mechanical resurfacing; and the DermaFrac®, which combines microneedling with microdermabrasion, LED and infusion of active ingredients. In addition to these, there are microneedling systems for painless administration of substances and fractional radiofrequency, that uses needles which release electric current to stimulate collagen production (Braghiroli, and Conrado, 2018). Randomized controlled clinical trials would be interesting to evaluate the best method for drug delivery of anesthetics. From this study, we can confirm that the equipment used (Tinexpen®) proved to be extremely efficient for the delivery of the anesthetic. It is also worth highlighting that several types of anesthesia mightbe usedalong with the CO_2 laser. Using anesthetic creams containing lidocaine and prilocaine is often recommended, and these are applied to the skin thirty minutes before the procedure to reduce sensitivity (Mazzaro *et al*., 2014). This approach is common for treatments in smaller areas or procedures with less ablation depth, such as some facial rejuvenation protocols with fractional CO_2 laser (Hoogstra, 2024). The effectiveness of topical anesthesia can be increased by using occlusive dressings over the cream (Salimi *et al*., 2024). For more extensive or painful procedures such as the treatment of perioral wrinkles with high-energy and high-density fractional CO_2 laser, truncal anesthesia of the infraorbital and mental nerves with 2% lidocaine associated with epinephrine mightbe used. Injectable local anesthesia provides effective pain blockades in specific areas. Furthermore, cooling the skin with cold air during the laser procedure can help minimize discomfort, especially when combined with topical anesthesia in the facial region (Yumeen and Khan, 2023). After completing this work, it was possible to understand that we can add to all these forms of anesthetic therapy the use of microneedling for drug delivery given the efficacy proven in this study.

CONCLUSION

This study demonstrated that fractional CO_2 laser is a safe procedure for skin rejuvenation, but it is associated with significant discomfort during its application. The comparison between the fractional CO_2 laser brands, Youlaser® and Hybrid®, did not reveal statistically significant differences in the level of pain reported by patients.It indicates that discomfort is intrinsic to the technique, regardless of the equipment used. In addition, sensitivity varied between facial regions,

with greater pain reported in the eye and forehead areas. The preliminary evaluation of the anesthesia protocol studied here showed that the combination of microneedling with lidocaine drug delivery provided significant pain relief when compared to the isolated use of topical anesthetic. This finding emphasizes the importance of the drug delivery technique as a complementary strategy to minimize discomfort in more aggressive dermatological procedures. Therefore, we understood that the choice of the appropriate anesthetic method can directly impact on the patient's experience and treatment adherence. We concluded that anesthesia with lidocaine drug delivery associated with microneedling is effective in reducing discomfort and enabling the application of fractional CO_2 laser. However, since this is a preliminary investigation, some factors may have influenced the results and should be considered for the continuation of this study. First, the relatively small sample size may limit the generalization of the findings, making a study with a larger number of participants necessary to increase statistical strength. In addition, the lack of complete randomization may have introduced bias, and it is recommended to use a randomized double-blind model to ensure greater control over confounding variables. Another relevant point is the individual variability in pain perception, which may be influenced by psychological factors, pain threshold, and previous experiences of the patients. Thus, the findings of this study work as a basis for future investigations that may ensure the dissemination of the best analgesia protocol using lidocaine drug delivery for fractional CO_2 laser procedures.

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