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| Journal Name: | [**Journal of Advances in Medicine and Medical Research**](https://journaljammr.com/index.php/JAMMR) |
| Manuscript Number: | **Ms\_JAMMR\_131637** |
| Title of the Manuscript: | **Association of Trichloroacetic Acid Peeling with Photobiomodulation in the Treatment of Photoaging of the Hands: A Randomized, Controlled, Double-Blind Clinical Trial** |
| Type of the Article | **Original Research Article** |

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| **PART 1: Comments** | | |
|  | **Reviewer’s comment**  **Artificial Intelligence (AI) generated or assisted review comments are strictly prohibited during peer review.** | **Author’s Feedback** *(Please correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)* |
| **Please write a few sentences regarding the importance of this manuscript for the scientific community. A minimum of 3-4 sentences may be required for this part.** | Aging of the skin of the hands is not only a dermatological problem, but also a psychosocial one. This explains the scientific search for procedures to improve skin regeneration. Those that do not cause discomfort and are accessible to more people, regardless of their social status, are preferable. |  |
| **Is the title of the article suitable?**  **(If not please suggest an alternative title)** | Yes, the title of the article is suitable. |  |
| **Is the abstract of the article comprehensive? Do you suggest the addition (or deletion) of some points in this section? Please write your suggestions here.** | Yes, the abstract of the article is comprehensive. |  |
| **Is the manuscript scientifically, correct? Please write here.** | Yes |  |
| **Are the references sufficient and recent? If you have suggestions of additional references, please mention them in the review form.** | **The paper needs to be updated** ….currently, one 2020 citation, one 2019 citation and seven 2018 citations.  **Some are irrelevant to the topic under consideration**:  44. Popa-Wagner A, Mitran S, Sivanesan S, Chang E, Buga A. ROS and Brain Diseases: The Good, the Bad, and the Ugly. OXIDATIVE MEDICINE AND CELLULAR LONGEVITY. 2013;**2013**. doi: 10.1155/2013/963520. PubMed PMID: WOS:000328378800001.  49. Chow R, Johnson M, Lopes-Martins R, Bjordal J. Efficacy of low-level laser therapy in the management of neck pain: a systematic review and meta-analysis of randomised placebo or active-treatment controlled trials. LANCET. **2009**;374(9705):1897-908. doi: 10.1016/S0140-6736(09)61522-1. PubMed PMID: WOS:000272646900023.  51. Stergioulas A, Stergioula M, Aarskog R, Lopes-Martins R, Bjordal J. Effects of low-level laser therapy and eccentric exercises in the treatment of recreational athletes with chronic achilles tendinopathy. AMERICAN JOURNAL OF SPORTS MEDICINE. **2008**;36(5):881-7. doi: 10.1177/0363546507312165. PubMed PMID: WOS:000255752900007.  52. Smoot B, Chiavola-Larson L, Lee J, Manibusan H, Allen D. Effect of low-level laser therapy on pain and swelling in women with breast cancer-related lymphedema: a systematic review and meta-analysis. JOURNAL OF CANCER SURVIVORSHIP**. 2015**;9(2):287-304. doi: 10.1007/s11764-014-0411-1. PubMed PMID: WOS:000354988400016.  57. Prabhu K, Cleghorn M, Elnahas A, Tse A, Maeda A, Quereshy F, et al. Is quality important to our patients? The relationship between surgical outcomes and patient satisfaction. BMJ QUALITY & SAFETY. **2018;**27(1):48-52. doi: 10.1136/bmjqs-2017-007071. PubMed PMID: WOS:000418324600008.  62. Hamblin MR. Shining light on the head: Photobiomodulation for brain disorders. BBA Clinical. **2016**;6:113-24. doi: 10.1016/j.bbacli.2016.09.002. | The references have been updated to ensure greater relevance and alignment with the topic under consideration. |
| **Is the language/English quality of the article suitable for scholarly communications?** | The language (English) quality of the article suitable for scholarly communications. |  |
| **Optional/General** comments | INTRODUCTION  „However, controlled studies on PBM and chemical peeling’s combined effects are scarce. Investigating these complementary, low-cost therapies may optimize photoaging treatments, advancing minimally invasive skin rejuvenation approaches.“  „However, there is a lack of controlled studies in the literature regarding the combined effects of photobiomodulation and chemical peeling—two complementary, low-cost therapies that may optimize the benefits in treating photoaging.“   1. These two paragraphs of the introduction have the same meaning and could be merged.   material and methods   1. Eligibility criteria for participants: What about the inclusion and exclusion criteria? 2. What about the skin preparation? How it was done? 3. How was randomization done? 4. In Fig.1 for group 1 it is written: ATA 20% +**PBM,** and for group 2: ATA 20% +**Simulated PBM,** after that for group 1: Monthly Treatment Sessions: Application of Peeling and **PBM** (3x), and for group 2: Monthly Treatment Sessions: Application of Simulated Peeling and **PBM** (3x). What was group 2 done: Peeling or Simulated Peeling? 5. What kind of red LED was used for photobiomodulation and what about the methodology? 6. What superficial and deep wrinkles and abnormal pigmentations assessment method was used? 7. What statistical methods were used? 8. On Fig. 8, it would be good to write exactly when (month, week or day) it is „after treatment“.   DISCUSSION  1) Only in the „discussion“, the gender and the education of the participants are discussed. It would be good to present the main demographic characteristics of the participants in the „material and methods“.  2) What about the age of the participants? Is it related to skin aging and what is the age range in which it most often starts?  3) It is good to indicate the Fitzpatrick skin type of the participants. | **INTRODUCTION**  1) The paragraphs have been rewritten to combine the information and avoid repetition.  **MATERIAL AND METHODS**  1) The eligibility criteria for participants are in the "Inclusion Criteria" and "Exclusion Criteria" sections of the supplementary material as described below. The clinical trial included male and female participants aged 40 to 70 years, either without comorbidities or with controlled comorbidities (ASA Physical Status Classification I and II . Participants were also required to have a skin phototype of I, II, III, or IV according to the Fitzpatrick classification. Participants were excluded from the study if they had any of the following conditions: history of photosensitivity, suspected malignant skin lesions on the hands, use of corticosteroids, anticoagulants, immunosuppressants, drugs that increase dermal photosensitivity, systemic retinoids, or topical retinoic acid within the past 12 months, uncontrolled diabetes or hypertension, malnutrition, anemia, immunosuppression, oncological diseases, predisposition to hypertrophic scarring and keloids, history of dermatological diseases, hand surgeries, uncontrolled psychiatric disorders, active smoking, pregnancy, previous procedures on the dorsal hands, collagen diseases (even if adequately controlled), or use of medications affecting skin pigmentation, such as amiodarone, tetracyclines, and tricyclic antidepressants like phenothiazines  2) All participants underwent appropriate skin preparation on the dorsal hands before treatment to enhance exfoliation effects, ensure uniform chemical penetration, accelerate healing, and reduce risks of post-inflammatory hyperpigmentation. Preparation involved daily application of 0.05% retinoic acid, 4% hydroquinone, and 0.01% fluocinolone acetonide for three weeks. **(supplementary material)**.  3) The randomization was conducted by the principal investigator using the random sequence generator available on randomizer.org. Sequentially numbered opaque envelopes contained group allocation information based on the generated randomization. These envelopes were sealed and opened by the principal investigator in order of participant attendance at the clinic, immediately before the first treatment session **(supplementary material)**.  4) Group 2 received the treatment with peeling and simulated PBM, not simulated peeling. The correct description was provided in the flow chart.  5) The irradiation device used was the BlackBox® LED (BioLambda), modified to accommodate both hands. It had a power output of 100 mW, delivering an energy density of 5 J/cm² after 150 seconds of irradiation. The wavelength was 660 nm **(supplementary material)**.  6) Photoaging was evaluated using a photographic scale developed and validated by McKenzie. Photographs were independently assessed by two board-certified plastic surgeons for four distinct clinical features indicative of photoaging: Superficial wrinkles, Deep wrinkles, Abnormal pigmentation, and Global assessment.The global evaluation provided an overall impression of photodamage. Each feature was scored separately on a scale from 0 to 9, where 0 indicates the absence of changes and 9 represents the maximum extent of alterations.  It is noteworthy that all photographs were anonymized and assigned coded identifiers before being presented to the specialists, preventing recognition of participants and ensuring blinding to both the treatment stage and group allocation.  For the concordance analysis, the mean scores assigned by the specialists were used. Contingency tables and kappa coefficients were not applied, as the study variables were continuous rather than categorical **(supplementary material)**.  7) The statistical analyses employed in this study utilized the general linear model for repeated measures with Type III sum of squares, also referred to as repeated measures ANOVA. The normality of the variables was assessed using the Shapiro-Wilk and Kolmogorov-Smirnov tests. Post-hoc differences between means were evaluated using the Waller-Duncan test, with patterns represented through inference graphs based on confidence intervals  8) The evaluation shown in Fig. 8 was conducted at time point 7, which corresponds to 30 days after the last treatment session.  **DISCUSSION**  1) These details are provided in the "Inclusion Criteria" section of the supplementary material.  2) The clinical trial included male and female participants aged 40 to 70 years. The age of the participants is directly associated with skin aging. The clinical manifestations of photoaging become more pronounced after the age of 30, with an accelerated progression in intensity from that point onward [1]. In individuals with lighter skin tones (Fitzpatrick skin types I, II, and III), clinical features such as wrinkles, pigmentary alterations, and loss of elasticity are detectable in 80–90% of adults [2].  **Reference**   1. Green A, Hughes M, McBride P, Fourtanier A. Factors associated with premature skin aging (photoaging) before the age of 55: a population-based study. Dermatology. 2011;222(1):74–80. 2. Maddin S, Lauharanta J, Agache P, Burrows L, Zultak M, Bulger L. Isotretinoin improves the appearance of photodamaged skin: results of a 36-week, multicenter, double-blind, placebo-controlled trial. J Am Acad Dermatol. 2000;42:56.   3) The participants were required to have a skin phototype of I, II, III, or IV according to the Fitzpatrick classification. |

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| **PART 2:** | | |
|  | **Reviewer’s comment** | **Author’s comment** *(if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)* |
| **Are there ethical issues in this manuscript?** | *(If yes, Kindly please write down the ethical issues here in details)* |  |