Cairo University

KASR ALAINY
CAIRO UNIVERSITY - FACULTY OF MEDICINE

Faculty of Medicine, Cairo University Postgraduate Research Protocol Template

(Please read carefully provided guidance documents for a comprehensive understanding and proper formulation of your thesis protocol and required forms)

1. Study

a- Proposed Study Title: Safety and efficacy of intralesional 0.5% triamcinolone acetonide in 0.2% fluconazole solution vs 0.1% topical mometasone furoate with 2% miconazole nitrate cream in the treatment of chronic paronychia: An intraindividual randomized controlled trial

2. Investigators Contact Information

a. Principal Investigator: Name: Professor Mohamed Hussein Medhat El-Komy

Department: Dermatology

Phone number: 01223415852.

E-mail addresses: mkomy@hotmail.com

b.Other Investigators: 1- Name: Yousra Abdul-Salam Muhammad Hasan Azzazi

Department: Dermatology

Phone: 01098709984

Email: yosrazzazi@cu.edu.eg

2- Name: Habiba Khaled Mostafa Edrees

Department: Dermatology

Phone: 01004545118

Email: Habibaedrees@gmail.com

3- Name: Basant Ahmed Mohamed Abdelaal Helal

Department: Dermatology

Phone: 011 44166922

Email: basant_helal@hotmail.com

4- Name: Khadija Abdullah Hussein Affify

Department: Dermatology

Phone: 01018198885

Email: Khadijaabdullah9392@gmail.com

1. Background and Rationale

Chronic paronychia (CP) is defined as inflammation of the nail fold(s) of more than 6 weeks duration (Shafritz and Coppage, 2014). It is now considered as a form of hand eczema, caused primarily by irritation of the nail folds by environmental allergens. This leads to recurrent inflammation of nail folds, followed by fibrosis and inability to generate the cuticle, ending in loss of the waterproof seal, moisture retention, and compromise of blood supply due to fibrosis. These can explain why CP is commonly resistant to topical and even systemic treatments. Candida infection is thought to be a secondary event in a subset of cases (Relhan and Bansal, 2022), with positive fungal culture in about 56.1% of cases (Bahunuthula *et al.,* 2015)

Important risk factors for the development of CP include occupations with excessive exposure to moisture and irritants (e.g. housewives, cooks, and health care providers), immunosuppression (e.g. diabetes mellitus and HIV); due to increased risk of secondary colonization, and some medications (e.g. retinoids) (Relhan and Bansal, 2022). A higher incidence of contact sensitization and Candida hypersensitivity in these patients has been reported, (Bahunuthula *et al.,* 2015) thus candidal control may be of help to ameliorate the disease.

Clinically, CP presents with erythema, pain and swelling of one or more of the nail folds for >6 weeks. It generally affects multiple fingernails, more commonly, of the dominant hand. Nail matrix may be secondarily affected leading to transverse ridging, discoloration, Beau's lines, or onychomadesis (Shafritz and Coppage, 2014, Atiş *et al.,*2018). The last updated severity scale for CP has been proposed in 2018, taking into account the number of affected nail folds, erythema, edema, nail plate and cuticle changes (Atiş *et al.,*2018).

Management of CP relies mainly on avoidance of the irritants and topical corticosteroids which are now considered the mainstay of treatment (Shafritz and Coppage, 2014). Systemic antifungals are used in cases with associated candida infection (Tosti *et al.,* 2002).

Intralesional steroid injection, in the form of monthly injections of triamcinolone acetonide (2.5- 10 mg/mL), is used for the treatment of nail psoriasis, nail lichen planus and twenty-nail dystrophy. It is, however, scarcely mentioned in literature in the management of CP (Baran, 2001). In addition, the optimal treatment regimen and injection technique have not yet been established, and no recent relevant studies exist.

Surgical treatment is reserved for cases of CP of more than 6-month duration, that has been resistant to medical treatment (Relhan et al., 2014)

3. **Objectives:** (describe specific objectives or hypotheses behind the study)

   Our objective is to compare the efficacy and safety of intralesional corticosteroids + fluconazole solution to corticosteroid with an antifungal topical preparation, in the management of chronic paronychia.

4. **Study Design:** (Please fill in the appropriate study design, see attached PDF guide)

- Descriptive: - Survey (cross sectional)
  - Qualitative

- Analytic: - Observational: - Case-control study
  - Cross sectional analytic study
  - Cohort (Longitudinal) study

  - Experimental: - Randomized Clinical Trial ■
  - Non-randomized clinical trial
  - Animal study
  - Cellular study

- Others: Please describe:

5. **Study Methods**

- **Population of study:** (Please provide all details regarding participants including gender, age range and disease conditions. Also indicate if this protocol involves children, prisoners, pregnant women or cognitively impaired or mentally disabled subjects):

  1-Age above 18 years
  2-Both sexes

- **Study location:** (Please provide where the study will be conducted and from where study participants will be recruited)

Dermatology outpatient clinic, Kasr AlAiny, Faculty of medicine, Cairo University

- **Inclusion criteria:**

1-Patients with chronic paronychia affecting ≥ 2 fingernails in the dominant hand.
2- Patients not receiving any relevant systemic treatment for at least 4 weeks before initiation of our study
3- Patients not receiving any relevant topical treatment for at least 2 weeks before initiation of our study

- **Exclusion criteria:**

1- Patient with peripheral vascular disease or Raynaud's phenomenon
2-Pregnant and lactating females
3-Patients with autoimmune diseases e.g., connective tissue diseases, psoriasis, reactive arthritis, and pemphigus.
4-Patients with solid or hematological malignancies.
5- Patients on systemic drugs that are known to cause chronic paronychia e.g. retinoids.
6- Patients with any visible focus of infection at the injection site or in the vicinity, including patients with superimposed attack of acute paronychia.
7-Onychomycosis or any associated nail disease

- **Methodology in details:**

Each participant will be subjected to:

1- Written informed consent.
2- Detailed history taking and clinical evaluation.
3- Clinical photographing
4- CP severity index scale (Atiş *et al,* 2018*)*: On the scale, a dermatologist evaluates:
   - The proximal and lateral nail folds (involvement of 1 nail fold = 1; involvement of 2 nail folds [proximal or/and lateral] = 2; bilateral lateral nail fold involvement and proximal nail fold involvement = 3).
   - Edema (absent = 0; mild = 1; moderate = 2; severe = 3).
   - Erythema (absent = 0; mild = 1; moderate = 2; severe = 3).
   - Nail plate changes (absent = 0; mild = 1; moderate = 2; severe = 3).
   - Cuticle involvement (normal = 0; damaged = 1; absent = 2).

   A combined total score of (between 0 [min.] and 14 [max.]) is finally calculated.
5- Assessment of disease impact: Dermatology Life Quality Index (DLQI).
6- Assessment of pain severity by visual analogue scale (VAS)

7- All patients are advised to strictly avoid moist environments and irritants.

The affected fingernails in each patient are randomized, by simple randomization technique, to either receive intralesional or topical treatment.

- Topical treatment in the form of twice daily application of combined steroid and antifungal (mometasone furoate and miconazole nitrate, Elica-M®) till the end of treatment response or for a maximum of 3 months.
- Procedure: The proximal nail fold is cleansed with alcohol. Triamcinolone acetonide and fluconazole in the ratio of 1:7, yielding a triamcinolone acetonide concentration of 5mg/ml, is injected through the affected nail fold with a 30-gauge, 1-mL insulin syringe needle. The nail fold is divided into 2 halves and a maximum of 0.5 cc is injected in both halves or till there is swelling /edema of the nailfold. Injections are administered every 4 weeks until the end of treatment response, or for a maximum of 3 months.
- The CP severity index scale, DLQI and VAS will be documented monthly till the end of treatment period and 1 month after stoppage of treatment.
- Moreover, the pain associated with the intervention procedure will be evaluated using the VAS score immediately after the first session.
- Percentage of Participants with treatment- related Adverse Events (AEs) and Serious Adverse Events (SAEs) will be documented.

- **Intervention:**

☐ Diagnostic intervention (please describe):

■ Therapeutic intervention (please describe):

☐ No intervention

- **Does the research involve?**

■ Human participants

☐ Biological samples/Tissues

☐ Identifiable private data/Information

- **Type of consent of study participants:**

  ■ Written consent

  ☐ Oral consent

  ☐ No consent needed (Please justify)

- **Potential risks:**
  (Please mention all risks involved even mild ones as pain, discomfort, chance of infection)
  Pain at site of injection (measured by VAS), subungual hematoma, proximal nail fold hypopigmentation and atrophy (all these complications are largely preventable and fortunately reversible).
  Nicolau syndrome (Embolia cutis medicamentosa) is a very rare complication.

- **Confidentiality of data:** (Please explain how privacy and confidentiality of data and records will be maintained)

All participants' data will be confidential.

9- Study outcomes:

- **Primary outcomes** (Most important measurable outcomes)

- Comparison between the mean CP severity index scale before and after treatment in each group
- Comparison of absolute change in CP severity index scale between both groups
- Comparison of percentage of patients who achieved complete response (CP severity index scale =0) between both groups.

- **Secondary outcome parameters** (other outcomes to be assessed):

- Comparison of DLQI before and after treatment in each group
- Comparison of VAS before and after treatment in each group
- Comparison of absolute change in DLQI between both groups
- Comparison of absolute change in VAS between both groups
- Comparison of percentage of patients who developed treatment related side effects in each group.

10- Sample size (number of study subjects included and justification including the clinical and statistical assumptions supporting sample size calculation)

As considered the primary outcome, sample size calculation was done using the comparison of absolute change in CP severity index scale between both groups. Since this is the first study to be conducted on these parameters, a moderate to large effect size corresponding to Cohen's d=0.7 was assumed to be clinically significant. A statistical power analysis was performed for sample size calculation; with a two tailed alpha error probability set at 0.05, the projected sample size needed for the aforementioned effect size (d=0.7) is 19 patients to be able to reject the null hypothesis that this difference is zero with probability (power) 0.80. To account for expected 10% dropouts and to allow for sub-group analysis, a sample of 21 patients will be recruited. Sample size calculation was done using G*Power 3.1.9.2.

11- Statistical analysis (Please describe your data analysis plan)

Data will be collected anonymously and stored in a secure spreadsheet with unidentifiable keys. Normally distributed numerical data will be statistically described in terms of mean and standard deviation (SD), while not-normal data will be represented as median and range or inter-quartile range (IQR). Qualitative (categorical) data will be described in frequencies (number of cases) and percentage. Numerical data will be tested for the normal assumption using Kolmogorov Smirnov test.
Statistical analysis will be performed using the appropriate tests; on qualitative variables by Fisher's exact test and on quantitative variables by non-normal Wilcoxon rank-sum test and Wilcoxon signed-rank test. A probability value (p value) of less than 0.05 is considered statistically significant.
All statistical calculations will be done using computer programs Microsoft Excel 2019 (Microsoft Corporation, NY, USA) and IBM SPSS (Statistical Package for the Social Science; IBM Corp, Armonk, NY, USA) release 22 for Microsoft Windows.

12- Source of funding: (Please include source of funding even if self-funding)

- Faculty of Medicine, Cairo University ☐
- Other sources:

  Please specify: Self funding ■

References:

- Atış, G., Göktay, F., Altan Ferhatoğlu, Z., Kaynak, E., Sevim Keçici, A., Yaşar, Ş., & Aytekin, S. (2018). A proposal for a new severity index for the evaluation of chronic paronychia. *Skin Appendage Disorders*, *5*(1), 32-37.
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- Relhan, V., & Bansal, A. (2022). Acute and chronic paronychia revisited: A narrative review. *Journal of Cutaneous and Aesthetic Surgery*, *15*(1), 1-16.
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- Shafritz, A. B., & Coppage, J. M. (2014). Acute and chronic paronychia of the hand. *JAAOS-Journal of the American Academy of Orthopaedic Surgeons*, *22*(3), 165-174.
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1- Please fill in all the included sections and don't delete any part of the template
2- For choice brackets, please just use the fill in function in word

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KASR ALAINY
CAIRO UNIVERSITY - FACULTY OF MEDICINE

N-255-2024

Cairo University
Faculty of Medicine
Research Ethics Committee

NOTICE OF APPROVAL

Date: **17-8-2024**

Protocol title: **Safety and efficacy of intralesional 0.5% triamcinolone acetonide in 0.2% fluconazole solution vs 0.1% topical mometasone furoate with 2% miconazole nitrate cream in the treatment of chronic paronychia: An intraindividual randomized controlled trial**

Principal investigator: **Dr. Mohamed Hussein Medhat El-Komy**
Institution or organization: **Cairo University**

Decision: APPROVAL

Dear Dr. **Mohamed,**

The Research Ethics Committee **(REC)** has reviewed and **approved** the above-mentioned **protocol. You may begin your investigation**. Approval is granted for one year from the date of initial approval. At the end of this period as the principal investigator you will be asked to submit required documents for continuing review.

As principal investigator you will need to:

- Notify the REC Chair immediately after any **serious adverse events** experienced by participants of the investigational study or as reported to you by the sponsor/manufacturer/co- investigators.
- Submit End of trial notification at the end of trial.
- Submit Clinical study report at the end of trial.
- You may not initiate **changes** in approved research protocol without REC review and approval except where necessary to eliminate apparent immediate hazards to the human subjects.

FACULTY OF MEDICINE * CAIRO UNIVERSITY * RESEARCH ETHICS COMMITTEE

t 2024

Cairo University

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N-255-2024

- يحظر سفر أى عينات بشريه من المبحوثين خارج جمهوريه مصر العربية الا بعد موافقة الجهات الامنية .

- The below documents were included in the review:
  1. Study protocol
  2. Protocol Summary
  3. Application form
  4. ICF template
  5. CVs of the investigators
  6. Study tools

- If you have any questions, please contact REC Coordinator Dr. Eman Elsebaie e-mail: **kasralainyrec@kasralainy.edu.eg**

Sincerely

REC Chairman

Prof. Maher Fawzy, MD

Professor of Anesthesia

Cairo University

FACULTY of MEDICINE * CAIRO UNIVERSITY * RESEARCH ETHICS COMMITTEE

on: August 2024