Supplementary File 2 – PRISMA P review protocol

Title: Weight loss and dietary modifications as therapies for hidradenitis suppurativa: protocol for a systematic review

Authors: Arunima Sivanand[1] (arunima.sivanand@mail.utoronto.ca); Patrick J Fleming[2] (flemingp@mun.ca)

1. MD Program, University of Toronto, Toronto, ON, Canada
2. Division of Dermatology, University of Toronto, Toronto, ON, Canada

Corresponding Author:

Dr. Patrick Fleming

Division of Dermatology

University of Toronto

Sunnybrook Health Sciences Centre (M1-722)

2075 Bayview Avenue

Toronto, ON, Canada M4N 3M5

Contributions: AS and PJF designed the study and prepared the review protocol.

Amendments: In the event that amendments to the protocol need to be made, the date of the amendment, a description of the change and the rationale for it will be recorded.

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Introduction

Rationale: Hidradenitis suppurativa (HS) is a chronic inflammatory condition that commonly presents in intertriginous skin areas. HS symptoms, including malodorous discharge, painful eruptions, and lesions in sensitive areas, have a significant associated burden and stigma, with studies demonstrating that patients with HS experience a poorer quality of life compared to other dermatologic conditions such as psoriasis and alopecia[1,2].

The association between HS and obesity has been established, with numerous studies demonstrating increased disease severity with increasing Body Mass Index (BMI) [3-8]. Various mechanisms have been proposed to explain the role of obesity, including larger skin folds contributing to increased mechanical friction, humid microenvironments encouraging bacterial proliferation and obesity contributing a systemic inflammatory state [9,10,11]. Despite this, one study showed that obesity was not associated with treatment escalation in HS, whereas smoking

was, suggesting that a greater focus needs to be placed on the possible role of weight loss in disease management[20].

In targeting obesity, surgical therapies, such as bariatric surgery, and medical therapies, such as the use of liraglutide, have shown promise when used to promote weight loss in HS patients [12,13,14]. With regards to lifestyle behaviour changes, diet modifications to promote weight loss have demonstrated symptom reduction [15]. Additionally, diets excluding potential HS triggers such as dairy products, high glycemic index foods, brewer's yeast and high fat foods have also been reported to reduce HS symptoms [16-19].

To date no review has been conducted to our knowledge that synthesizes the literature on dietary modifications and weight reduction to ameliorate symptoms of HS. Considering the prevalence of HS, its significant morbidity and the potential impact of safe, low-cost interventions such as weight loss and dietary changes, a study to synthesize the effectiveness of these strategies is warranted.

Objectives: The primary objective of this systematic review is to determine the effect of lifestyle interventions (dietary modifications, weight loss, and/or exercise), compared to placebo or no intervention, on symptom severity in adult patients with hidradenitis suppurativa.

Methods

Eligibility criteria: Studies will be selected based on the following guidelines:

Study design – Randomized Controlled Trials (RCTs), cohort studies and case-control studies will be included. Case-series that involve more than 5 subjects will also be included. Case series that involve fewer than 5 subjects, cross-sectional studies or individual case reports will be excluded.

Participants – Studies conducted on humans, that include adult (age >18) subjects will be included. Studies conducted solely on children (age <18) will be excluded.

Interventions – Lifestyle interventions will be defined in our review as:

- Dietary modifications that include, but are not limited to, changes to promote weight loss and the elimination of potential triggering foods
- Weight reduction interventions that include, but are not limited to, lifestyle changes (diet or exercise), medical therapies and bariatric surgery

Comparison – All comparators will be considered including placebo interventions and usual-care

Outcomes – Outcomes assessed include

- Hurley stage
- Sartorius score
- Hidradenitis Suppurativa Clinical Response (HiSCR)

- Total abscess and inflammatory-nodule count
- Number of locations of lesions
- Patient quality of life (as assessed by various tools such as DLQI or SF-36)
- Depression score (e.g. Beck Depression Inventory, HADS, HAM-D)
- Anxiety Score
- Pain (as assessed by various tools)
- Body Mass Index (BMI)
- Percent Body Fat
- Waist Circumference
- Hip-to-Waist Ratio

Where outcomes are reported as a composite measure, attempts will be made to extract both the composite and individual outcomes as included in the study.

Setting – No restrictions will be made with regards to the setting of studies for the purposes of study selection.

Timing – Studies will be included where the outcome follows the intervention after any given follow up time.

Years considered – Studies from all years will be considered, only being limited by the date of inception of databases.

Language – Only English-language studies will be included

Publication status – No restrictions will be made with regards to the publication status of studies for the purposes of study selection.

Information sources: The databases that will be searched are Medline (OVID interface, 1946 onwards), EMBASE (OVID interface, 1947 onwards) and the Cochrane Central Register of Controlled Trials (Wiley interface, current issue). To ensure comprehensiveness, reference lists of included studies will be examined for additional articles.

Search strategy: PubMEd, EMBASE and Cochrane will be searched with no limits imposed on study design, date or language. The search strategies will be created by one reviewer (AS) in consultation with an academic librarian.

Study records

Data management: Literature search results will be exported to Covidence, a software program by the Cochrane Collaboration for the management of articles in the creation of systematic reviews.

Selection process: Two reviewers will independently screen articles by title and abstract using the inclusion and exclusion criteria. Full texts of included articles will be retrieved and then assessed for selection independently by the two reviewers using the same eligibility criteria. Duplicate articles will be identified and removed. If there is uncertainty regarding the inclusion of a study, a discussion will be held between the two reviewers. A third reviewer will be consulted in case the two reviewers cannot come to an agreement. Reasons for excluding studies will be recorded. The reviewers will not be blinded to the journals, study authors or institutions.

Data collection process: A standard form will be used to extract data by two reviewers independently. Uncertainties in data extraction will be resolved by discussion first, and then consultation with a third reviewer if there is no agreement. Study authors will be contacted if the reviewers require additional clarification.

Data items: Data will be extracted on the year of publication, study type, funding sources, setting of the intervention, sample size, subject characteristics (age, sex, duration of symptoms), intervention type, control, follow-up period and outcomes.

Outcomes and prioritization: The primary outcome will be HS severity as defined by:

- Hurley stage
- Hidradenitis Suppurativa Clinical Response (HiSCR)
- Total abscess and inflammatory-nodule count
- Number of locations of lesions
- Sartorius score

Secondary outcomes include:

- Patient quality of life (as assessed by various scales such as the Dermatology Quality of Life Index)
- Depression score (e.g. Beck Depression Inventory, HADS, HAM-D)
- Anxiety Score
- Pain (as assessed by various scales)
- Body Mass Index (BMI)
- Percent Body Fat
- Waist Circumference
- Hip-to-Waist Ratio

Risk of bias in individual studies: Since it is expected that the major of studies will be observational in nature, the risk of bias will be assessed by two reviewers independently using the Newcastle-Ottawa scale (NOS) for case-control and cohort studies. Adaptations of the scale

will be made for case-series studies. Any uncertainty will be resolved by discussion or consultation with a third reviewer. Randomized trials will use the Cochrane Risk of Bias tool.

Data synthesis: Given the expected heterogeneity of the studies, qualitative synthesis is planned. Narrative synthesis with text and tables will be presented. The focus will be on the target of the intervention (e.g. weight loss), the type of intervention (e.g. exercise), and the effect on the outcome. Results will be grouped in tables based on the intervention target. All included studies will be reported on regardless of risk of bias assessment.

Meta biases: Since a quantitative analysis is not planned, and it is expected that the majority of studies included will be observational, an assessment of bias due to non-study processes i.e. publication bias or outcome reporting bias across studies, will not be conducted.

Confidence in cumulative evidence: The Grading of Recommendations Assessment, Development and Evaluation (GRADE) criteria will be used by two reviewers independently to assess the quality of evidence for outcomes. Any uncertainty will be resolved by discussion or consultation with a third reviewer. The quality will be reported as high, moderate, low or very low.

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