Therapeutic Effect of Superficial Cryotherapy versus Intralesional Corticosteroids injection in Alopecia Areata

Thesis

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Nour El-dissouki Ibrahim

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List of Abbreviations

Abb.	Full term
AA	Alopecia areata
AIRE	Auto-immune Regulator
AT	Alopecia Totalis
AU	Alopecia Universalis
BDs	Black dots
BH	Broken hair
CTLA-4	Cytotoxic T lymphocyte-associated antigen 4
EMHs	Exclamation mark hairs
GWAS	Genome-wide association studies
HF	Hair follicle
HLA-A	Human Leucocyte antigen- A
HLA-B	Human Leucocyte antigen- B
HLA-C	Human Leucocyte antigen- C
HLA-DQB1	Human Leucocyte antigen- DQ beta 1
HLA-DRB1	Human Leucocyte antigen- DR beta 1
IFNγR	Interferon gamma receptor;
IL15RA	IL15 receptor subunit alpha;
IL2RB	IL2 receptor subunit beta;
ILCS	Intra-lesional Cortico-Steroid
INFγ	Interferon gamma;
JAK	Janus kinase
JAK	Janus kinase;
LD	Linkage disequilibrium
MICA	MHC class I polypeptide-related sequence A
NOTCH4	Neurogenic locus notch homolog protein 4
OP	Ophiasis

List of Abbreviations Cont...

Abb.	Full term
P	Phosphorylated
PTPN22	Protien Tyrosine Phosphatase non- receptor type 22
SD	Standard Deviation
Sisaphio	Ophiasis inverus
SNP	Single nucleotide polymorphism
STAT1	Signal transducer and activator of transcription 1
SVH	Short vellus Hair
T/V ratio	Terminal Hair/Vellus hair ratio
TCR	T cell receptor
TGFB	Transforming growth factor beta
THs	Terminal Hairs
ULBP	Unique-long 16 binding proteins
V	Vellus Hair
YDs	Yellow dots

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INTRODUCTION

Alopecia areata (AA) is an autoimmune disease of the hair follicles leading to non-cicatricial hair loss. The estimated lifetime prevalence of AA is 1%~2%. It affects all age groups with no preference for gender or ethnicity. It is usually associated with other autoimmune diseases, as atopy and autoimmune thyroiditis ***(Gilhar et al., 2012; Seetharam, 2013; Mirzoyev et al., 2014)***.

Topical or intralesional corticosteroid is the accepted therapeutic option for mild AA patients. However, possible adverse effects of potent corticosteroids, such as skin atrophy or telangiectasia are sometimes difficult, if not impossible, to reverse, and intralesional corticosteroid injection might not be suitable when dealing with young AA patients due to its painful nature ***(Alkhalifah et al., 2010; Messenger et al., 2012).***

In some extreme cases, anaphylaxis in patients receiving intralesional corticosteroid for treatment of AA has been reported ***(Downs et al., 1998; Laing et al., 2007).***

The therapeutic efficacy of superficial cryotherapy in AA has been studied by various studies. Cryotherapy was introduced for the 1st time as a treatment of AA in 1986. When the exposure to liquefied nitrogen is limited to a few seconds "superficial" cryotherapy, reactive vasodilation and an associated increase in blood flow may improve

microcirculation and nutritional status around hair follicles ***(Huang et al., 1986; Lei et al., 1991)***.

There is currently no established theory of how superficial cryotherapy works in the treatment of AA. It can induce clinical improvement of AA by blocking a yet unrevealed pathophysiologic process associated with abnormal melanocytes with large and bizarre melanosomes, found around the hair follicles of AA patients. Cold-induced inflammation may alter the immunologic process and structural components of the hair follicle responsible for AA ***(Lee et al., 1994, Radmanesh et al., 2013).***

Superficial cryotherapy has a conflicting mechanism with the traditional AA treatments. It could be a meaningful adjuvant treatment option for AA patients especially when the disease status is limited to minimal to mild, or the conventional AA treatment is not applicable considering that it is less painful and easier to perform ***(Singh et al., 2016, Myungsoo et al., 2017).***

AIM OF THE WORK

The aim of the present work was to evaluate and compare the efficacy and safety of superficial Cryotherapy and intralesional corticosteroids in the treatment of patchy AA as well as reporting the side effects.

Review of Literature

Alopecia Areata

Definition:

Alopecia areata is a common disorder that causes non-scarring hair loss. The hair loss associated with AA is not painful or disabling. However, it causes changes in a person's appearance that can profoundly affect quality of life and self-esteem. In some people, the condition can lead to depression, anxiety, and other emotional or psychological issues ***(Peloquin and Castelo-Soccio, 2017; Korta et al., 2018).***

Terminology:

"Alopecia Areata" was a term used to refer to the appearance of the common coin-sized areas of hair loss. "Alopecia" is a Latin term that means baldness, and "areata" refers to the patchy nature of the hair loss that is typically seen with this condition ***(Korta et al., 2018).***

Epidemiology:

Alopecia areata is one of many recognized forms of alopecia; AA is the second most common form after androgenetic alopecia (male-pattern baldness in men and female-pattern baldness in women) with approximately 2% a life-time incidence to develop AA before age of 30 ***(Peloquin and Castelo-Soccio, 2017; Renert-Yuval and Guttman-Yassky, 2017).***

Alopecia areata affects men and women equally, while some studies have suggested that men tend to be diagnosed earlier than women. It can occur in people of any ethnic background. While other studies suggested that pediatric population are with the greatest incidence of AA and risk decreases with each subsequent decades ***(Mirzoyev et al., 2014; Strazulla et al., 2018).***

Etiology and Pathogenesis:

The biological cycle of hair follicle (HF) is divided into three phases: anagen (growth phase), catagen (regression) and telogen (resting phase). At the end of the telogen phase, the original hair falls out (exogenous phase) and is replaced by a new hair at early growth stage. The duration of anagen is 2-8 years, catagen 2-3 weeks and telogen about 3 months. Normally, anagen comprises 80-90% of scalp hair, catagen 1-2% while telogen 10-20% ***(Paus et al., 1999).***

The pathogenesis of AA is not fully understood, recent studies have supported an autoimmune mechanism involving cytotoxic T-cell infiltration that disrupts hair growth ***(Peloquin and Castelo-Soccio, 2017).***

However, in patients with AA, hair loss could be due to an alteration of one of these follicle growth phases, in other words, a premature transition from the anagen to the catagen or the anagen to telogen phase could happen. Since this event cannot occur alone, several reports have suggested that genetic,

immunologic, and environmental factors may be responsible for its development **(Fig.1)** ***(Juárez-Rendón et al., 2017).***

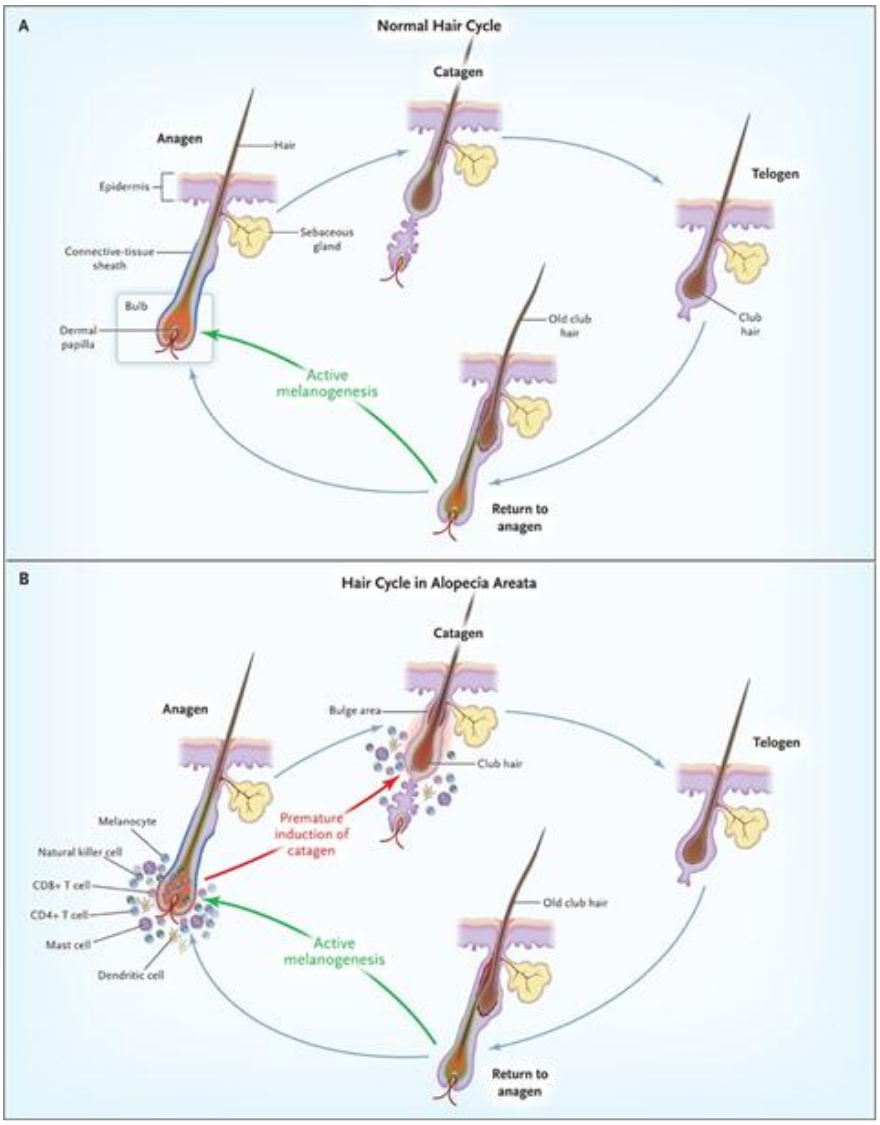

Figure (1): a) Normal Hair cycle **b)** Hair cycle in Alopecia Areata ***(Gilhar et al., 2012).***