



Intradermal Injection of Botulinum

Toxin A in Oily Skin

Thesis

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By

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LIST OF ABBREVIATION

5- α DHT	5-Dihydrotestosterone
PPARs	Peroxisome proliferator-activated receptors
GH	Growth hormone
IGF-I	Insulin like growth factor-I
MC-1R	Melanocortin-1 receptor
MC-5R	Melanocortin-5 receptor
α -MSH	α -melanocyte stimulating hormone
CRH	Corticotropin-releasing hormone
HPA	Hypothalamus– pituitary–adrenal
CRH-BP	Corticotropin-releasing hormone binding protein
CRH-Rs	Corticotropin receptors
DHEA	Dehydroepiandrosterone
POMC	Proopiomelanocortin
RAR	Retinoic acid receptors
RXR	retinoid X receptors
atRA	Tretinoin
13cRA	13-cis retinoic acid
ECS	Endocannabinoid system
ACTH	Adrenocorticotrophic hormone
EGF	Epidermal growth factor
EGFR	Epidermal growth factor receptor
GHR	Growth hormone receptor
IGFR	Insulin growth factor receptor
InsR	Insulin receptor
FGF7	Fibroblast growth factor-7
FGFR2b	Fibrosblast growth factor receptor-2b
SP	Substance P
Pi3K	Phosphoinositol-3-kinase

GR	Glucocorticoid receptor
AR	Androgen receptor
ERs	Estrogen receptors
VDR	Vitamin D receptor
LXR	Liver-X receptor
PKC	Protein kinase C
MAPK	Mitogen-activated protein kinase
[Ca ²⁺] ic	Intracellular Ca ²⁺ concentration
TRPV1	Transient receptor potential vanilloid 1
CB2	Cannabinoid receptor subtype 2
AA	Arachidonic acid
2-APB	2-aminoethoxydiphenyl bora
BoNT	Botulinum toxin
BoNTA	Botulinum toxin type A
BoNTA-Ona	Onabotulinum toxin A
BoNTA-inco	Incobotulinum toxin A
BoNTA-abo	Abobotulinum toxin A
BoNTB-rima	Rimabotulinum toxin B
SV-2	Synaptic vesicle protein 2
Ach	Acetylcholine
FDA	Food and Drug Administration
HHD	Hailey-Hailey disease
HIV	Human immune deficiency virus
PCO	Polycystic ovary

Introduction

Oily skin (seborrhea) is a common cosmetic problem, affecting men as well as women and typically starting just before puberty. Oily skin looks shiny and greasy, and is frequently accompanied by large pores. It contributes to the development of acne. It can negatively affect the patients' self-image and have detrimental psychosocial effects (*Arbuckle et al., 2009*).

The sebaceous glands are microscopic glands in the skin. They are located in the reticular dermis, where they are usually found in association with hair follicle, forming the pilosebaceous unit (*Tóth et al., 2011*).

The sebaceous gland excretes a complex mixture of lipids called sebum onto the skin surface. The average composition of human sebum in adults consists of 57.5%

triglycerides and their hydrolysis products, 26.0% wax esters, 12.0% squalene, 3.0% cholesterol esters and 1.5% cholesterol (*Greene et al, 1970*).

The fully developed adult sebaceous gland contains sebocytes. The terminally differentiated sebocytes disintegrate and release their content to the skin surface via holocrine secretion (*Picardo et al., 2009*).

The sebaceous gland is an androgen target organ. Thyroid stimulating hormone, hydrocortisone and, especially, insulin significantly stimulate proliferation of human sebocytes indicating that other hormones may modulate sebocyte activity (*Zouboulis et al, 1998*).

A variety of skin resurfacing modalities have been described to reduce sebum and facial pores including isotretinoin, chemical peeling, laser resurfacing and other topical therapies but results have been mixed and

inconsistent. One potential reason for this limitation is that the location of the sebaceous gland is in the deeper portion of the dermis, a difficult area to reach by resurfacing modalities (*Shash, 2008*).

Botulinum toxin A is produced by *Clostridium botulinum*. Botulinum neurotoxin type A blocks neuromuscular conduction by inhibiting the release of acetylcholine from motor or autonomic nerve terminals. When injected intramuscularly, it produces a localised chemical denervation of the muscle, resulting in localised muscle weakness or paralysis. When injected intradermally, the toxin produces chemical denervation of glands. The denervation is reversible. Nerve endings recover over three or more months during which muscle tone increases and glandular secretion recommences (*Scheinberg, 2009*).

Aim of the Work

The aim of study is to evaluate the efficacy and safety of intradermal injection of botulinum toxin A in reducing sebum production in oily skin.

Oily skin

Oily skin or seborrhea is a common problem, affecting men as well as women and typically starting just before puberty. Oily skin looks shiny and greasy, and is frequently accompanied by large pores and it may be a cosmetic problem. It can negatively affect the patients' self-image and has psychosocial effects. Many individuals feel embarrassed and annoyed with the appearance of their oily skin, and the unpleasant feeling of uncleanness is also a source of complaint. Sebum overproduction is an important causative factor in a variety of dermatologic diseases and may be related to seborrheic dermatitis and acne, thus oil control is an important part of the therapeutic regimen for these conditions (*Arbuckle et al., 2009*).

Types of Sebaceous Glands

Sebaceous glands can be grouped based on their location, on whether or not they are associated with the hair follicles, or on their function.

Sebaceous glands are scattered all over the body except for hands, soles and the dorsum of the feet. The greatest number of the glands is on the face, back, chest and it may range between 400 and 900/ cm² (**Wójcik et al., 2011**).

They are located in the reticular dermis, where they are usually found in association with hair follicles, forming the pilosebaceous unit (**Schneider et al., 2009**).

There are four classes of pilosebaceous unit: terminal on the scalp and beard, apopilosebaceous in axilla and groin, vellus on the majority of skin, and sebaceous

(lanugo) on the chest, back and face (**McGrath and Uitto, 2010**).

The lanugo pilosebaceous units of the face can be of two types: the most common type is superficial, tiny and its ostia and minute hairs are invisible to the naked eye. Its sebaceous glands are disproportionately large, as are all lanugo follicles. The less numerous type has multilobular sebaceous glands of extravagant size and depth, greater in volume than the much smaller glands of the superficial, tiny follicles. It empties to the skin surface through a wide duct, which is in fact the follicle, and is joined by a tiny hair of insignificant proportions. Their ostia are easily visible as the pores of adult facial skin and the gaping orifices are highly prominent in many oily patients, especially on the cheeks. This type of sebaceous follicles is

practically limited to the face, scalp and upper trunk (*Sakuma and Maibach, 2012*).

Those glands that are not associated with hairs are called free sebaceous glands. These glands are particularly prevalent in transitional zones between the skin and mucous membranes, e.g., anogenital region, periareolar skin, vermillion border of the lips, and eyelids where they are known as meibomian glands. Sebaceous glands are also found in the oral mucosa and atypically in other regions of the digestive tract, the respiratory tract, the uterus, and vagina (*Thody and Shuster, 1989*).

Development and Differentiation

Differentiation of the pilosebaceous unit occurs in the embryonic stage between 2nd and 4th month of gestation. During this process, a complex, in many aspects still