

Chloasma – The Mask of Pregnancy

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ABSTRACT

Chloasma is a required hypermelanosis of sun-exposed areas occurred during pregnancy and it can affect 50–70% of pregnant women. It presents as symmetric hyperpigmented macules, which can confluent or punctuate. The most common locations are the cheeks, the upper lip, the chin and the forehead. The exact mechanism by which pregnancy affects the process of melanogenesis is unknown. Estrogen, progesterone, and melanocyte-stimulating hormone (MSH) levels are normally increased during the third trimester of pregnancy. However, nulliparous patients with chloasma have no increased levels of estrogen or MSH. In addition, the occurrence of melasma with estrogen- and progesterone-containing oral contraceptive pills has been reported. The observation that postmenopausal woman who are given progesterone develop melasma, while those who are given only estrogen do not, implicates progesterone as playing a critical role in the development of melasma. UV-B, UV-A, and visible light are all capable of stimulating melanogenesis. The condition is self-limited; however spontaneous resolution is time-consuming and may take months to resolve normal pigmentation. Therefore, it is worthwhile to prevent the onset of chloasma, by strict photoprotection. Prudent measures to avoid sun exposure include hats and other forms of shade combined with the application of a broad-spectrum sunscreen at least daily. Sunscreens containing physical blockers, such as titanium dioxide and zinc oxide, are preferred over chemical blockers because of their broader protection. Chloasma can be difficult to treat. Quick fixes with destructive modalities (eg, cryotherapy, medium-depth chemical peels, lasers) yield unpredictable results and are associated with a number of potential adverse effects. The mainstay of treatment remains topical depigmenting agents. Hydroquinone (HQ) is most commonly used.

Key words: *chloasma, melasma, chemical peelings, hydroquinone, tretinoin, sunscreens, prevention*

Chloasma is a required hypermelanosis of sun-exposed areas and it can affect 50–70% of pregnant women. It presents as symmetric hyperpigmented macules, which can confluent or punctuate. The most common locations are the cheeks, the upper lip, the chin and the forehead¹. Chloasma is a synonymous term sometimes used to describe the occurrence of melasma during pregnancy. Chloasma is derived from the Greek word *chloazein*, meaning »to be green.« *Melas*, also Greek, means »black.« Since the pigmentation is never green in appearance, melasma is the preferred term².

Chloasma is more common in women than in men, and women are affected in 90% of cases. It can affect 50–70% of pregnant women. Melasma is rare before puberty. Persons of any race can be affected. However, it is much more common in constitutionally darker skin ty-

pes than in lighter skin types. More than 30% of patients have a family history of melasma. Identical twins have been reported to develop melasma³ while other siblings under similar conditions did not.

The pathophysiology of melasma is uncertain. The most important factor in the development of melasma is exposure to sunlight. Ultraviolet radiation can cause peroxidation of lipids in cellular membranes, leading to generation of free radicals, which could stimulate melanocytes to produce excess melanin. Sunscreens that primarily block UV-B radiation (290–320 nm) are unsatisfactory because longer wavelengths (UV-A and visible radiation, 320–700 nm) also stimulate melanocytes to produce melanin. In many cases there is a direct relationship between melasma and female hormonal activity⁴ because melasma most often occurs in pregnancy and while

using contraceptive pills⁵. Hormonal influences play a role in some individuals. The mask of pregnancy is well known to obstetric patients. The exact mechanism by which pregnancy affects melasma is unknown. Estrogen, progesterone, and melanocyte-stimulating hormone (MSH) levels are normally increased during the third trimester of pregnancy. The other factors that also contribute are photosensitizing medications, mild ovarian or thyroid dysfunction, and certain cosmetics. The clinical picture of melasma is tan to brown macular hyperpigmentation. Sometimes blue or black pigmentation can develop in patients with dermal melasma. The depth of the pigment can be visualized by use of a Wood lamp (wavelength, 340–400 nm). Epidermal pigment is enhanced during examination with a Wood light, whereas, dermal pigment is not. In individuals with dark-brown skin, examination with a Wood light does not localize pigment, and these patients are thus classified as indeterminate. There are three types of distribution: centrofacial, malar, or mandibular¹.

Recent studies showed that melasma was related with significant reduction in quality of life. Results of the interviewed women showed that 65% of women were bothered all the time or most of the time, was frustrated (55%), embarrassed (57%). Furthermore, they reported significant influence of the disease on interpersonal relationships⁶. After the treatment, the number of women who still reported disturbances reduced significantly. The differential diagnosis includes Addison Disease, drug-Induced Photosensitivity, discoid Lupus Erythematosus, mastocytosis, poikiloderma of Civatte¹. The clinical picture of melasma is typical and usually the no laboratory tests are indicated. If thyroid dysfunction is the potential causative agent, one can check thyroid function test. Wood light examination usually helps to localize the pigment to the epidermis or the dermis. Note that in many cases, the pigment is found in both locations. Melanin is increased in the epidermis, in the dermis, or (most commonly) in both locations. Epidermal melanin is found in keratinocytes in the basal and suprabasal area. In most cases, the number of melanocytes is not increased, yet the melanocytes that are present are larger, more dendritic, and more active. Dermal melanin is found in the superficial and mid dermis within macrophages, which often congregate around small, dilated vessels. Inflammation is sparse or absent².

Melasma can be difficult to treat. The pigment of melasma develops gradually, and resolution is also gradual. Resistant cases or recurrences occur often and are certain if strict avoidance of sunlight is not rigidly heeded. All wavelengths of sunlight, including the visible spectrum, are capable of inducing melasma. Quick fixes with destructive modalities (eg. cryotherapy, medium-depth chemical peels, lasers) yield unpredictable results and are associated with a number of potential adverse effects, including epidermal necrosis, post inflammatory hyperpigmentation, and hypertrophic scars^{7,8}. The precise manner in which these modalities can be used has not been fully delineated. However, in some experienced hands,

they have been anecdotally reported to be safe, effective, and produce results much quicker than topical medications⁹. More careful study is needed before they can be recommended as a standard treatment. In an attempt to hasten resolution, many practitioners attempt mild exfoliation with superficial chemical peels¹⁰. The rationale is that if melanogenesis is inhibited with bleaching agents and keratinocyte turnover is increased, the time to resolution can be reduced. A number of studies have shown that treating melasma with superficial chemical peels and a bleaching agent is safe and effective. Whether superficial chemical peels versus bleaching agents alone actually hasten the resolution of pigment is debated. Studies comparing bleaching agents alone to the combination of bleaching agents and superficial chemical peels are ongoing and may help to resolve the debate. The mainstay of treatment remains topical depigmenting agents. Hydroquinone¹¹ (HQ) is most commonly used¹². The mechanism of action is inhibition of tyrosinase, leading to the decreased production of melanin. HQ can be applied in cream form or as an alcohol-based solution. Concentrations vary from a 2% to 4% concentration and even higher when compounded. All concentrations can lead to skin irritation, phototoxic reactions with secondary post inflammatory hyperpigmentation, and irreversible exogenous ochronosis. Another treatment option is use of tretinoin^{13,14} (*trans*-retinoic acid) but is less effective than HQ. However, the response to treatment is less than with HQ and can be slow, with improvement taking 6 months or longer. As such, combinations of tretinoin with HQ, with or without a topical corticosteroid¹⁵, have been promoted. The retinoid is believed to work by increasing keratinocyte turnover and thus limiting the transfer of melanosomes to keratinocytes. The major adverse effect is skin irritation, especially when the more effective, higher concentrations are used. Temporary photosensitivity and paradoxical hyperpigmentation can also occur. The mechanism of action by which azelaic acid¹⁶ act is not certain, but it seems that azelaic acid targets only hyperactive melanocytes and thus will not lighten skin with normally functioning melanocytes. The primary adverse effect is skin irritation.

Regardless of the treatments used, all will fail if sunlight is not strictly avoided. Prudent measures to avoid sun exposure include hats and other forms of shade combined with the application of a broad-spectrum sunscreen at least daily. Sunscreens containing physical blockers, such as titanium dioxide and zinc oxide, are preferred over chemical blockers because of their broader protection^{17,18}.

All of this therapy reduces epidermal pigment. Dermal pigment may take longer to resolve than epidermal pigment because no effective therapy is capable of removing dermal pigment. However, treatment should not be withheld simply because of a preponderance of dermal pigment. The source of the dermal pigment is the epidermis, and, if epidermal melanogenesis can be inhibited for long periods, the dermal pigment will not replenish and will slowly resolve.

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KLOAZMA – MASKA TRUDNOĆE

SAŽETAK

Kloazma je stečena hipermelanoza koja nastaje na fotoekspoziranim područjima tijekom trudnoće, a može se javiti i kod 50–70% trudnica. Prikazuje se u vidu simetričnih hiperpigmentiranih makula koje mogu biti pojedinačne ili konfluirajuće. Predilekcijska mjesta su obrazi, gornja usnica, brada i čelo. Točan mehanizam nastaka ovog stanja nije potpuno jasan. Razine estrogena, progesterona i MSH su normalno povišene tijekom posljednjeg trimestra trudnoće. Ipak, prvorotkinje s ovim poremećajem nemaju povišene vrijednosti estrogena i MSH. Pored toga, dokumentirani su i slučajevi pojave kloazme kod žena koje su uzimale peroralne kontraceptive bazirane na estrogenima i gestagenima. Podatak da postmenopauzalne žene koje uzimaju samo gestagene mogu razviti kloazmu, za razliku od onih koje uzimaju samo estrogene, govore u prilog važnosti progesterona u patogenezi ovih promjena. UV-B, UV-A zrake, kao i sunčevo svjetlo mogu stimulirati melanogenezu. Kožne promjene kod kloazme se povlače same, ali je spontana rezolucija vrlo spora i može trajati mjesecima. Stoga je vrijedno striktnom fotoprotekcijom pokušati spriječiti nastanak. Mjere fotoprotekcije uključuju široke šešire i druge oblike fizičke zaštite uz dodatnu primjenu fotozaštitnih krema. Kreme koje sadrže fizičke zapreke kao titanov dioksid ili cinkov oksid su preporučljivije od kemijskih tipova zaštite. Jednom kada nastane, liječenje kloazme može predstavljati terapijski izazov. Brzo liječenje destruktivnim postupcima (krioterapija, kemijska abrazija, laser) može biti nepredvidivog ishoda i uz to povezano s mogućim nuspojavama. Zlatni standard u terapiji su lokalna depigmentirajuća sredstva, od kojih je najčešće korišten hidrokinon.