The Benefits of Using the Iodine Solution in the Treatment of Acne at Pregnant Women

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Acne treatment during pregnancy is challenging and should be adapted to the clinical form, the lesions severity and their impact on the patient's quality of life. The therapeutic decision in such cases need to be based on the risk / benefit ratio and to take into account the FDA categories of drugs used during pregnancy and breastfeeding. Iodine solution is a valuable formula useful for the treatment of different dermatological diseases due to its immunomodulatory features. Even actually, it is less frequent used in dermatologic prescriptions, the purpose of this article is to highlight the benefits of topical treatment with iodine solution at pregnant women with severe acne.We present the management issues raised by a severe, conglobated acne in a 29-year-old woman in 22 weeks of pregnancy with a history of vulgar acne predominantly inflammatory since 16 years of age. Systemic treatment consisted in oral clindamycin for 7 days associated with oral dexamethasone (8 mg/day). Topical treatment was represented by metronidazole B and iodine solutions and was continued after the withdraw of antibiotic and corticosteroid therapy At 30 weeks of pregnancy the acne was significantly improved and fetal biological status was normal.

Keywords: iodine solution, pregnancy, anti-acne therapy, antibiotic treatment, severe acne

Recent studies show that 40% of pregnant patients consulted in a dermatology clinic suffered from acne [1]. The disease pathophysiological background involves complex hormonal, immunological, metabolic changes with partially understood mechanisms. The treatment of severe acne during pregnancy is challenging, given the safety concerns for the fetus and the absence of data regarding the level of evidence that prioritises the clinical efficacy of anti-acne agents in pregnant women. [2]

Oral antibiotic therapy for acne at pregnant woman is strictly controlled and involves risks both for fetus and mother. Retinoids should be considered the most teratogenic medication. Also, some studies in animals and in humans shows that a long time exposure during pregnancy to glucocorticoids that are not metabolized by placental 11β-HSD-2 dehydrogenase, such as dexamethasone or betamethasone, might reduce birth weight and predispose children to cardiovascular, metabolic or neuroendocrine disorders later in life [3].

Taking into account these issues, our therapeutical option included low doses of antibiotic and glucocortiocoids for a short period of time in association with topical treatment consisting in iodine solution and metronidazole solution. Iodine solution was used for a few weeks, without side effects on the mother or fetus. We observed that the major benefit in using topical iodine solution was maintaining clinical remission of the lesions.

Experimental part

Case report

Over time in our clinical activity we used topical iodine solution as a therapeutic option for treating different pathologies like inflammatory dermatoses, fungal infections or acne lesions. The efficiency of local therapy with iodine solution has been demonstrated in most cases, being an optimal choice especially in those where systemic therapy is contraindicated. We present such a case of acne at pregnant woman and the benefits of using local treatment with iodine solution.

A 29-year-old woman at 22-week of gestation without a history of notable pathology except for a vulgar inflammatory acne since 16 years old, without ovarian polycystic disease, treated with doxyciclin, topical drugs containing erythromycin, isotretinoin, azelaic acid, benzoyl peroxide, superficial peeling and laser for resurfacing with satisfactory results up to 23 years, reports the explosive recurrence of acne lesions 2 weeks ago.

The clinical examination releaved the presence of intense congestive papulonodular acne plaques on the chin, cheeks, forehead, accompanied by anxiety correlated to the burning sensation and major aesthetic discomfort (fig.1). Although the clinical aspect suggested a *Pyoderma faciale*, the history of vulgar acne, the presence of papulo-pustular lesions on the back and the absence of facial flushing episodes led to the diagnosis of severe, conglobated acne.

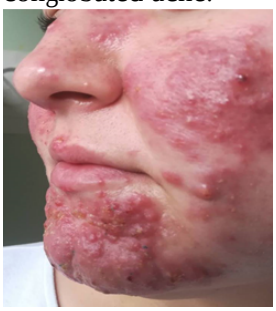

Fig.1. Papulopustular and nodular lesions prior to corticotherapy

The initial treatment recommended preceeding her consultation in our clinic consisted of clindamycin 1200 mg/day per os in combination with dermatocosmetics for cleansing. Non-beneficial clinical result after 7 days imposed oral treatment with dexamethasone (8 mg/day) in combination with metronidazole B dressings, alternatively with iodine solution dressings applied strictly on lesional areas. There was a significant improvement in the inflammation and papulonodular appearance after one week, which allowed the dose of dexamethasone to be

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reduced to 6 mg/day followed by an adjustment of the corticosteroid dose till 2 mg twice a week (fig. 2). The improved aspect persisted after systemic treatment was discontinued. The metronidazole B and iodine dressings were the maintenance tratment in combination with a dermatocosmetic cleansing gel.

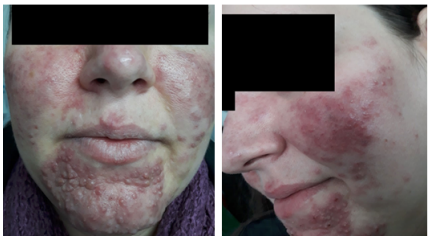

Fig.2. Clinical evolution favourable after a week of oral corticotherapy

However, when the corticosteroid dose was reduced to 2 mg/day at 25 week of gestation, a recurrence of inflammatory lesions occurred and a azithromycin 500 mg/day treatment was initiated in combination with a probiotic and zinc 10mg/day, as well as local dressings with metronidazole B solution alternatively with iodine solution.

This therapeutic regimen led to a significant improvement after 10 days. Corticotherapy was slowly reduced at 2 mg twice a week till 28 weeks of gestation and the topical treatment consisting in benzoyl peroxide cream 4%, ichthyol pale and zinc oxide, also dermatocosmetic cleansers was continued as a maintenance treatment. By the time of 30 weeks of gestation, the patient showed a significant decrease of inflammatory lesions (fig. 3).

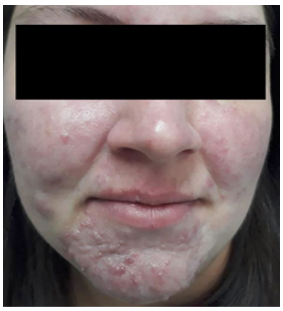

Fig. 3. Clinical improvement at 30 week of gestation

Results and discussions

Hormonal, immunological, metabolic changes can induce or exacerbate acne lesions with significant psychosocial impact during pregnancy. Placental and ovarian estrogen levels increase from the second month of pregnancy to the end, which explains acne improvement in the first trimester of pregnancy [4]. The progesterone secreted by placenta reaches a peak in the fifth month, explaining in our case the onset of exacerbated acne in the 20th week of pregnancy [5].

Acne treatment during pregnancy should be adapted to pregnancy age, its clinical form and severity, its impact on psychosocial status and takes into account, in the absence of data on the level of evidence for medication used in pregnancy, the 2014 FDA approved Pregnancy and Lactation Labelling Rule System [2,6]. The therapeutic regimens applied in vulgar acne in non-pregnant woman cannot be applied during the gestation period. Thus, from systemic therapy, isotretinoin per os, is contraindicated like antiandrogens (cyproterone acetate and spironolactone) due to serious fetal adverse effects [7]. Systemic antibiotics with a safety profile during pregnancy are penicillins (beta-lactams, amoxicillin) as the first therapeutic line, classified as **B** FDA category and macrolides (erythromycin, azithromycin), cephalosporins as the second line [8]. Clindamicin is another effective and safetly antibiotic used in the moderate-severe acne of the pregnant woman. Precautions for its administration are required due to the risk of diarrhea and pseudomembranous colitis [9, 10].

Oral corticosteroids may be used in severe or fulminant acne resistant to antibiotic therapy.Prednisone is allowed after the first trimester of pregnancy, it belongs to FDA pregnancy category C. Dexamethasone is a long-acting synthetic corticosteroid increasly indicated during the perinatal and neonatal period [11, 12].

Topical anti-acne treatment is mandatory both at pregnant and non-pregnant women and it can control alone the mild clinical forms. It is much more accepted for pregnant women considering the usual absence of side effects on the fetus It consists in appropriate skin cleansing and the application of a topic agent such as azelaic acid, benzoyl peroxide, antibiotic preparations (erythromycin, clindamycin, metronidazole, dapsone) or with sulfacetamide and sulphur, salicylic acid , glycolic acid or iodine solution [13].

Given the severity of the case and the precautions for the administration of classic anti-acne products in pregnancy, we chose for topical treatment a combination between an antibiotic preparation (metronidazole) and an antiseptic one, potassium iodide solution named also iodine solution or Lugol's solution.

Potassium iodide (KI) is a salt composed of 76% of iodine and 23% of potassium which presents itself as transparent or white hexahedral crystals. It's solubility is variable depending on the solvent used, but it is higher soluble in water. One gram (1g) of potassium iodide is soluble in 0.7 ml of water. The iodine solution has neutral to alkaline properties. Lugol's is available in various strengths from 1% to slightly less than 13% iodine (wt/v). The most commonly-used 15% solution consists of elemental iodine (I_2) and 10% potassium iodide (KI) mixed in distilled water, and has a total iodine content of 126.5 mg/mL (fig. 4). Lugol's solution contains three chemical species: free elemental iodine, triiodideand iodide. Free iodine reacts with water to [11-13] make Lugol's solution brown, triiodide's weaker yellow color is not visible and iodide is colorless [14, 15].

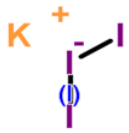

Fig. 4. Iodine solution chemical structure

Lugol's solution is a very old pharmaceutical product, first made in 1829 by the French physician Jean Lugol. It is part of the World Health Organization's List of Essential Medicines, the most effective and safe medicines needed in a health system. Initially, was used only in the therapy of thyroid diseases. Over time, was proved the benefit of iodine solution for treating inflammatory, immunemediated or infectious pathologies.Taking into account the dermatological area, Lugol's solution was an therapeutical option for psoriasis, eczema, lupus and syphilis. Also, it is recognized the benefit of topical treatment with iodine solution in inflammatory dermatoses such as granuloma annulare, erythema multiforme, erythema nodosum, subacute nodular migratory panniculitis and neutrophilic dermatoses (Sweet's syndrome, pyoderma gangrenosum). Iodine solution is also successfully used for certain fungal infections including cutaneous and lympho-cutaneous sporotrichosis**,** cutaneous cryptococcosis, human pythiosis, lymphocutaneous nocaria brasilliensis and entomophthoramycosis [16, 17].

There are various hypothesis regarding the mechanism of action for topical administration of iodine solution. Various studies showed that iodide has anti-inflammatory effect given by the ability to downregulating the free oxygen radicals generated by polimorphonuclears cells activation [18]. Another hypothesis about its anti-microbial role is based on the participation of iodide in halogenation reactions mediated by myeloperoxidases, which are mandatory for phagocytes function [19].

Iodine solution used for topical treatment makes skin brown and evaporates fast. One application loses 50% free iodine within two hours, 80% within two days and by the third day 88% has evaporated. No further evaporation takes place. Therefore 12% of any one application gets into skin tissues as iodide. Covering with plastic minimizes evaporation and helps the tissue regeneration rate.

Topical use of iodine solution has mild to moderate side effects. This may occur due to excesive iodine applications. In such cases can appear local intolerance manifested by pruritus, redness, smartness and, extremely rare uticaria or angioedema. Major side effects can occur when iodine is administrated orally, especially in pregnant women or at those patients with a history of kidney or thyroid disease. In our case, there were not side effects [20].

Conclusions

The treatment of severe acne during pregnancy is really challenging because the anti-acne medications, dermatocosmetics and physical procedures have not been tested in pregnant patients and the pathophysiological changes specific to gestation (hormonal and immunological changes) persist until birth. Severe acne, refractory to systemic antibiotics, with a psychosocially significant impact, as in our patient, benefit from strictly supervised short cure with oral corticosteroids and local maintenance therapy with iodine solution. This may improve inflammatory symptomatology and the iodine's antimicrobial effect is powerful and safe both for mother and fetus.

The purpose of the therapeutic measures applied in the severe acne of the pregnant woman is mainly to control the disease and not to cure it, the full safety of the fetus being primordial. We conclude that iodine solution, a traditional formula used for more than 150 years, it is a timely method, safe and efficient for the treatment of severe acne at pregnant woman.

References

1.DRENO B, BLOUIN E, MOYSE D, BODOCH I, KNOL A, KHAMMARI A. Acne in pregnant women:A French survey. Acta Derm Venereol 2014; 94(1): 82-3.

2.AWAN S.Z., LU J.Management of severe acne during pregnancy:A case report and review of the literature. Int J of Women's Dermatol 2017; 3: 145-150.

3.SMITH J.B., HANSEN C.D., ZONE J.J. Potassium iodide in the treatment of disseminated granuloma annulare. J Am Acad Dermatol 1994; 30: 791-792.

4.CHIEN A.L, QI J, RAINER B, SACHS D.L., HELFRICH Y.R. Treatment of acne in pregnancy. J Am Board Fam. Med. 2016; 29(2): 254-262.

5.KAPTANOGLU A.F., MULAZIZ D. Acneiform Eruptions and Pregnancy. Acne and Acneiform Eruptions 2017; 83-91.

6.KUBBA R, BAJAJ A.K., THAPPA D.M., SHARMA R, VADAMURTHY M, DHAR S, CRITON S. Acne in pregnancy. Indian J Dermatol Venereol Leprol. 2009; 75(1):59.

7.KONG Y.L., TEV H.L. Treatment of acne vulgaris during pregnancy and lactation. Drugs 2013; 73(8): 779-787.

8.PADBERG S., SCHAEFER C, PETERS P, MILLER R.K. et al. Anti-infective agents. Drugs during pregnancy and lactation: treatment options and risk assessment 2015; 3rd ed: 116-162.

9.ROMOREN M, LINDBAEC M, NORDENG H. Pregnancy outcome after gestational exposure to erythromycin: a populational-based register study from Norway. Br J Clin Pharmacol. 2012; 74: 1053-1062.

10.SARKAR M, WOODLAND C.C., KOREN G, EINARSON A.R. Pregnancy outcome following gestational exposure to azithromycin. BMC Pregnancy Childbirth 2006; 6:18.

11.HOREV L. How to treat acne in pregnant women? Curr Derm Rep. 2014; 3: 135-140.

12.LEACHMAN S.A., REED B.R. The use of dermatologic drugs in pregnancy and lactation. Dermatol Clin 2006; 24(2): 167-197.

13.KHODAENI E, FOULADI R.F., YOUSEFI N, AMIMIA M, BABAEINEJAD S, SHOKRI J. Efficacy of 2% metronidazole gel in moderate acne vulgaris. Indian J Dermatol. 2012; 57(4): 279-281.

14.SWEETMAN S. Martindale: the complete drug reference. United Kingdom, Ed. Pharmaceutical Press; 2009: 2169-2170.

15.KIRK T.G. The Merck index. 12th ed.New York: Merck & Co; 1996: 7809.

16.STERLING J.B, HEYMANN W.R. Potassium iodide in dermatology: a 19th century drug for the 21st century uses, pharmacology, adverse effects, and contraindications. J Am Acad Dermatol 2000; 43: 691-697.

17.ROSANE O.C., ALINE C., PRISCILA M.M., ANDREA REIS B.E. Use of potassium iodide in Dermatology: updates on an old drug. An Bras Dermatol. 2013; 88(3): 396-402.

18.HONMA K, SAGA K, ONODERA H, TAKAHASHI M. Potassium iodide inhibits neutrophil chemotaxis. Acta Derm Venereol 1990; 70: 247-249.

19.DERRY D.M., Regeneration of Human Scar Tissue with Topical Iodine:A Preliminary Report-Part 1. Thyroid Science 2008; 3(6): 2-9.

20.HEYMANN W.R. Potassium iodide and the Wolff-Chaikoff effect: relevance for the dermatologist. J Am Acad Dermatol. 2000; 42:490-492

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