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Review

Skin and obesity in childhood: an update

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Abstract: Overweight and obesity have grown in children in the last decades and are now an epidemic, leading to significant public health issues in developed and underdeveloped nations. Obese children have a higher prevalence of skin lesions than normal weight children. The present study is an updated-on state of the art of studies describing the association between childhood obesity and related skin lesions. The most frequent obesity-associated dermatological complications in children are acanthosis nigricans and acrochordons, atopic dermatitis, skin infections, and endocrinological changes including hyperinsulinism and hyperandrogenism. Other common skin manifestations associated with obesity are striae distensae and plantar hyperkeratosis. Although the causes of the majority of the skin lesions associated with obesity are not known, the larger mass of adipose tissue and the secretion of peptides (cytokines, hormones, etc.) from enlarged fat cells due to obesity could lead to skin lesions. Therefore, the prevention of obesity is essential to avoid most skin-associated lesions.

Keywords: skin lesions; children; obesity

1. Background

Overweight and obesity have grown in children in the last decades and are now an epidemic, leading to a significant public health issue in developed and underdeveloped nations [1,2]. In the United States, between 1980 and 2017, the rate of obesity in elementary school children increased from 6.5% to 18.4% [1]. In Argentina, the prevalence of overweight and obesity in elementary school children is approximately 40% [2]. Poor lifestyle behaviors are one of the main reasons for childhood obesity. These include sweetened beverage consumption, skipping breakfast, low milk, vegetable and fruit intake, and increased sedentary habits [2,3]. Children with obesity are more prone to becoming obese adults and having long-term cardiometabolic diseases [4], type 2 diabetes [5], and cardiovascular morbidity and mortality later in life [6]. Other complications include dermatologic (atopic dermatitis,

acanthosis nigricans) [7], sleep apnea, orthopedic (genu valgus, epiphysiolysis), and gastrointestinal/hepatic diseases (nonalcoholic hepatic disease). In addition, an increased prevalence of skin lesions has been observed in recent decades due to the increase in obesity in children [1,7].

However, the consequences of obesity in the skin are underestimated. The most frequent obesity-associated dermatological complications are acanthosis nigricans and acrochordons, atopic dermatitis, skin infections, and endocrinological changes including hyperinsulinism and hyperandrogenism [7]. In addition, the larger mass of adipose tissue and the secretion of peptides (cytokines, hormones, and paracrine transmitters) from enlarged fat cells due to obesity lead to skin lesions. These peptides can also lead to various disorders such as hyperinsulinemia, excess androgens, and inflammation [8]. In this way, obesity can modify the epidermal barrier of the skin with increased transepidermal water loss and dry skin [8]. Therefore, an up-to-date understanding of the evidence and research related to the association between childhood obesity and skin diseases is important. The present study reviews state-of-the-art studies describing the association between childhood obesity and related skin lesions. A systematic review of the literature, including articles in English, was undertaken using MEDLINE, EMBASE, and Google scholar. Informed consent obtained for the picture listed. A large population study including approximately 250,000 children and adolescents aged 5–17 showed that the highest prevalence of skin lesions in obese children was: acanthosis nigricans (in the insulin-resistance disorders), acne (in the androgen excess category), atopic dermatitis (in the inflammatory category), and polycystic ovary syndrome (in the endocrine category) [9]. Furthermore, bacterial and fungal infections and mechanical changes were also seen in obese children [9]. As shown in Figure 1, the concept is summarized.

The present review describes each category below.

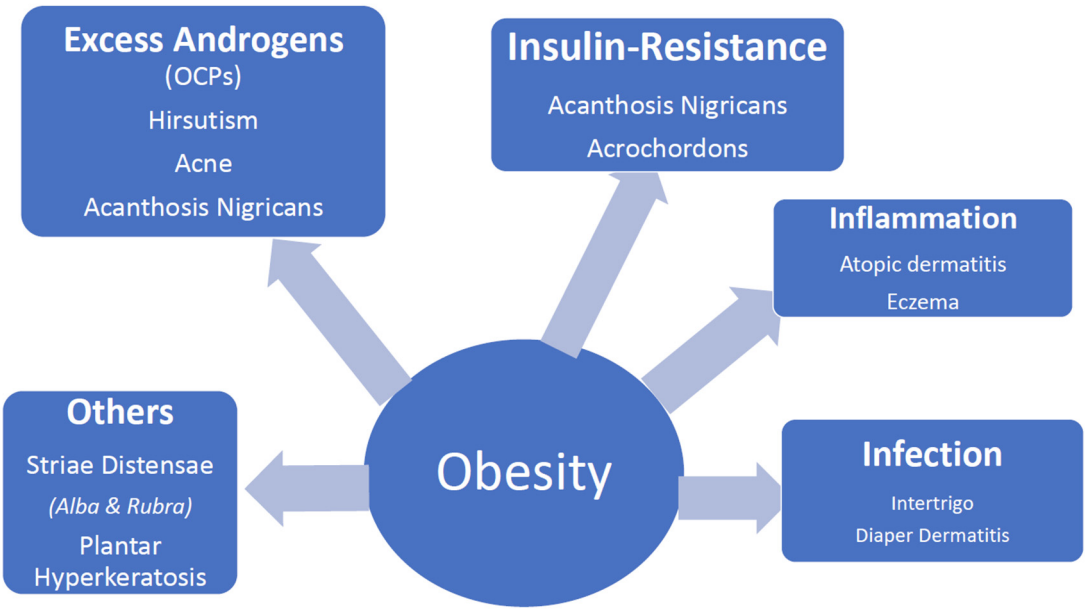

Figure 1. Summarize concept.

2. Insulin resistance disorders

The main skin lesions associated with obesity in this category are acrochordons and acanthosis, also related to diabetes, female sex, age ten and older, and non-white race [9]. As shown in Figure 2 acanthosis nigricans is characterized by a hyperpigmented, velvety, cutaneous thickening affecting localized areas of the skin in obese individuals [9]. It is located mainly in the neck, in the skin folds, and knuckles of the hands. Even though acanthosis nigricans is described as a sign of insulin resistance, our group found that BMI, but not insulin resistance, was associated with acanthosis in obese adolescents, suggesting that acanthosis might only reflect increased obesity [10]. In contrast, acanthosis nigricans was found to be associated with polycystic ovary syndrome, as a sign of insulin resistance, in obese adolescent girls [11].

The acrochordons are small growth forms in folds, such as the neck, armpits, and groin. Although generally small, acrochordons of greater than one centimeter have been found [12], and they are believed to be caused by skin-on-skin friction.

2.1. Excess androgens

Although the mechanisms are not fully understood, the leading skin lesions associated with excess androgens are acne vulgaris, hidradenitis suppurative (acne inversa), and polycystic ovarian syndrome (hirsutism, acne, acanthosis nigricans).

2.2. Acne

Acne is a chronic inflammatory skin disease. The obstruction of pilosebaceous units causes the formation of comedones (noninflammatory), followed by inflammation with papules, pustules, nodules, and cysts [13]. Acne during childhood comprises five groups according to age: neonatal, infantile, mid-childhood, preadolescent, and adolescent. Neonatal acne affects 20% of babies of less than six weeks, disappears by four months, and rarely needs medication [14]. Mid-childhood (between 1 and 7 years) acne is uncommon [14]. However, mid-childhood acne in 1–3-year-olds can be associated with overweight or obesity [15]. Acne in prepubertal ages may be the first physical sign of pubertal maturation. Acne is common in puberty and is considered an abnormal reaction to normal testosterone levels [16]. It usually appears on the face, neck, shoulders, upper back, and chest. Acne is associated with modified sebum levels, alterations in keratinization, and bacterial spread on the pilosebaceous units on the face and upper torso [16]. A multicenter study found that obesity was strongly associated with acne in children (65%) [17]. In contrast, a survey of young soldiers suggested that acne was not associated with obesity [18]. However, in pubertal adolescent girls, acne might be associated with obesity, acanthosis nigricans, hirsutism, seborrhea, androgenic alopecia, and insulin resistance, all components of the polycystic ovary syndrome [19]. Acne generally decreases over time and tends to disappear after puberty [19].

Hidradenitis suppurativa, commonly known as acne inversa, is a progressive inflammatory disease that mainly affects adolescent women and is caused by the inflammation of the hair follicles in the friction areas of the body, such as armpits, groin, perineum, and thighs. Therefore, it is commonly associated with pediatric obesity since it contributes to inflammation and friction [19–22].

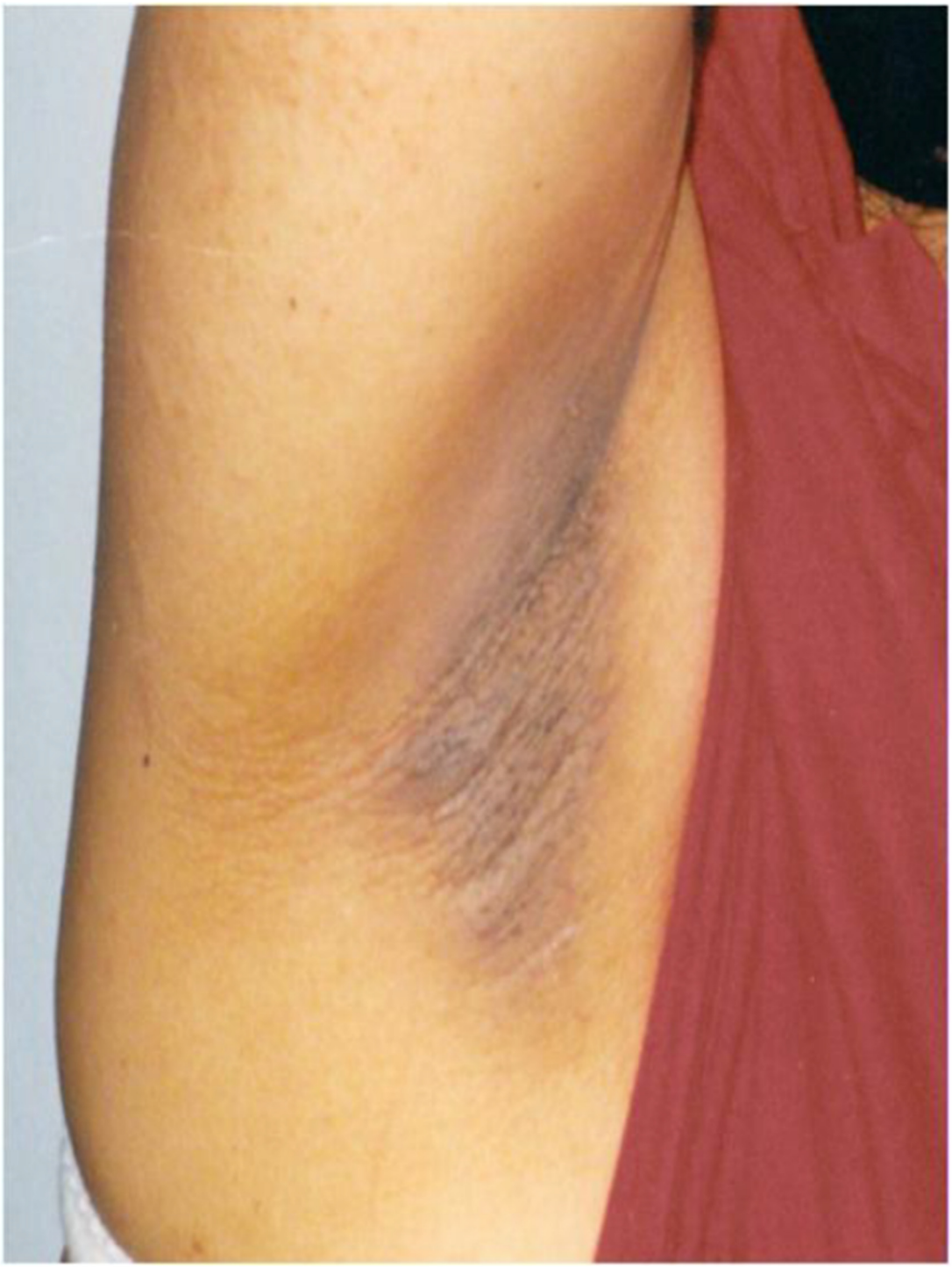

Figure 2. Acanthosis Nigricans in a 13-year-old adolescent with obesity. Source: Dr. Hirschler V.

The predisposition to obesity with a central or android distribution is now known to be the expression of anovulation and insulin resistance [19–22]. Hyperandrogenism is the most prevalent characteristic of polycystic ovary syndrome in adolescents [23]. The current diagnostic criteria are: a-Menstrual cycles longer than 90 days at least one year after menarche, menstrual cycles persistently under 21 or greater than 45 days at least two or more years after menarche, no menstrual cycles by the age

of 15, or at least two to three years after thelarche [24]. b-Hyperandrogenism is defined as hirsutism, acne, or biochemical hyperandrogenaemia lab-confirmed [25,26]. The presence of polycystic ovarian morphology is not a reliable marker during the eight years after menarche [26]. Adolescent girls with obesity with polycystic ovary syndrome have higher free testosterone and free androgen index and lower sex hormone-binding globulin than normal-weight girls [27].

Polycystic ovary syndrome symptoms resulting from excess androgen production can be mitigated by treatment normalizing menstruation and hirsutism [28]. The first recommendation should be the prevention and treatment of obesity. For girls with hirsutism, cosmetic hair removal combined with medical management should be offered. Furthermore, excess androgen production symptoms should be medicated with oral contraceptive pills and/or metformin, which can effectively manage hirsutism and anovulation [28].

3. Inflammation

Obesity is a risk factor for the development of inflammatory skin lesions, such as atopic dermatitis, eczema, and psoriasis.

Atopic dermatitis, which typically develops in the first five years, is a frequent childhood inflammatory skin condition due to epidermal barrier alteration, pruritus, and cutaneous inflammation [29]. Atopic dermatitis is generally manifested by itchy, red, crusty patches of inflamed skin, appearing and disappearing cyclically. Although the reason for atopic dermatitis is unknown, it is believed to be associated with an alteration in the child's immune system [29]. Obesity has been shown to exacerbate the inflammatory state in early childhood [30]. Obesity induces inflammation through cytokines produced from adipose tissue [31]. Adipocytes secrete a variety of adipokines, including leptin, adiponectin, plasminogen activator inhibitor-1, interleukin-6, and tissue necrosis factor -α [32]. Increased production of cytokines and alteration of their catabolism would be associated with the inflammatory state of obesity [33]. However, the intimate molecular inflammatory mechanisms caused by obesity-associated with inflammatory skin diseases are not yet known.

A large retrospective study found that obese children younger than two were 15 times more likely (OR, 15.10) to have atopic dermatitis. In addition, obese children aged 2 to 5 years had two and a half times the likelihood (OR, 2.58) of having atopic dermatitis than normal-weight children [34]. Furthermore, the longer the duration of obesity in early childhood, the greater the risk of having atopic dermatitis [35]. Chronic sleep disruption is common in children with atopic dermatitis and is associated with poor school performance, low self-esteem, and familial stress [29]. Low self-esteem and familial stress are also associated with obesity, exacerbating the symptoms. Children with atopic dermatitis also have a higher risk of infections [29]. Immune dysfunction and barrier disruption make the skin more susceptible to bacterial infiltration, especially Staphylococcus Aureus, which is very common in children with atopic dermatitis [34].

Eczema is an inflammation of the skin characterized by pruritus, skin dryness and erythema [36]. It is closely correlated with BMI. Furthermore, a large study with more than 15,000 children showed that excessive gestational weight gain was associated with 10% more risk for eczema [37]. Another large longitudinal cohort study of US children showed that higher weight gain during pregnancy associated with overweight during pre-pregnancy was related to a higher risk for atopic dermatitis [38]. High levels of inflammatory markers have also been associated with gestational weight gain [39].

These studies suggest that obesity prevention should start during maternal pre-pregnancy or pregnancy, as when prevention begins in childhood, it may already be too late.

4. Skin infections

The increased risk of skin infections in obese individuals is probably due to a proinflammatory state and decreased cell-mediated immune responses [35]. Obese individuals have larger skin folds, increased friction, and sweat more profusely than nonobese individuals [40]. This increased humidity heightens local inflammation, leading to skin lesions, such as intertrigo, with overgrowth of bacteria, Candida species, and dermatophytes [41]. Moreover, this could be worsened by a lack of exercise and inadequate hygiene [42].

One of the most common manifestations of skin infection in obese children is intertrigo [43], a skin flexural surface inflammation exacerbated by heat, friction, moisture, maceration, and poor ventilation [44]. Intertrigo is manifested by pustules on an erythematous base which may join and become patches lined by pustular lesions [4]. Furthermore, children present diaper (napkin) dermatitis at younger ages, which is an intertriginous dermatosis and one of the most common dermatologic diseases in infants and children [45]. Obese individuals have a larger surface area of skin folds and higher temperatures, increasing the risk of infections such as Candida Albicans [44,46]. Candida Albicans may colonize healthy individuals' gastrointestinal tract or oropharynx as part of their microflora, but it is not normal in the skin. A predisposing factor for skin candidiasis includes obesity [43].

Folliculitis is the inflammation of the hair follicle. Generally, hair follicles become inflamed after physical injury, and Staphylococcus Aureus can lead to infectious folliculitis [44]. Staphylococcus aureus infections are also more common in obese patients [47].

4.1. Other common skin manifestations associated with obesity

Striae distensae are thin scars located in areas of dermal alterations due to stretching of the skin [48]. Striae distensae are most common in puberty and obesity [39]. During puberty, striae distensae are associated with growth spurts. Although the etiology is unknown, causes include hormones, physical stretch, and structural alterations to the integument [48]. The initial form of striae distensae is called rubrae, which is erythematous and purple. These later lose their pigmentation and become an atrophic scar called striae alba [48].

A cross-sectional study performed in Korean adolescents showed that 83% presented striae albae, and only 27% rubrae [49]. In addition, there was a significant correlation between weight, height, and BMI and the severity grade of striae distensae in boys [49].

4.2. Plantar hyperkeratosis

A pilot comparative study showed that obesity in childhood changes foot shape [40]. Childhood obesity is often associated with foot pain or alterations due to greater weight bearing down on the small forefoot bones [50]. Furthermore, obese prepubertal children demonstrated physical changes in the foot structure with a lower footprint angle and a higher Chippaux-Smirak index [51]. These pressures on the foot may lead to plantar hyperkeratosis, a skin sign of severe obesity [52].

5. Obesity prevention

Childhood obesity prevention is critical since although short-term treatment of obesity can be successful, long-term treatments are less effective. As mentioned earlier, prevention should start during pre-pregnancy and pregnancy, as exposure to maternal gestational diabetes has been associated with increased adiposity during childhood [53]. A study performed by our group found that children of mothers with central obesity had a higher prevalence of cardiometabolic alterations [54]. Furthermore, maternal waist circumference was the only significant independent risk factor for their children's obesity complications adjusted for confounding factors [54]. Children of mothers with overweight or obesity had larger birth weights and higher BMI than those of mothers with normal weight [55]. A large prospective study showed that children with higher birth weight were more likely to be obese during childhood and adolescence [55]. A study performed by our group on more than 2,500 schoolchildren in five Argentinean states showed that central obesity in 9-year-old children was significantly associated with high birth weight [56]. BMI acceleration in early childhood, 2–6 years of age, even in the absence of obesity, is the critical age for the development of ongoing obesity [55]. Monitoring BMI standard deviation scores in young children with maternal overweight or high birth weight may be vital in preventing future obesity [55]. A large prospective study showed that risk factors for obesity in children occur at an early age, principally those with obese parents and unhealthy lifestyle behaviors [57]. Children of mothers with overweight had longer daily screen time than those of mothers with normal weight [58]. In addition, 6-year old children with more than 30 minutes of daily screen time and with overweight mothers had significantly higher BMIs than those without overweight mothers [58]. We found that the prevalence of obesity in indigenous schoolchildren was significantly lower (3.6%) than in urban Hispanic children (13.6%) [59]. Consistently, 26% indigenous vs. 2.5% urban children ate ≥ 5 servings/day of fruits and vegetables, 30% indigenous vs. 59% urban children watched TV ≥ 2 h/day, and 8.2% indigenous vs. 13.1% urban children skipped breakfast; suggesting that healthier lifestyle was associated with lower prevalence of obesity [59]. Furthermore, we found that overweight and obesity were associated with low milk intake, skipping breakfast, and a family history of hypertension in 8-year-old schoolchildren from different Argentinean regions [2]. In addition, our group showed that as milk intake increases, waist circumference and insulin resistance decrease in apparently healthy Argentinean children from a low socioeconomic status [60]. Insulin resistance in the pediatric age is associated with obesity and also with physiological pubertal development. Thus, compared with adults, obese children might have higher insulin resistance than obese adults due to the insulin resistance associated with physiological pubertal development, probably increasing the risk of obesity complications at younger ages.

Another possible reason for childhood obesity is parents' lack of understanding about their children's excess weight, especially in low socioeconomic groups since it is the most vulnerable population [61]. Very few mothers of obese preschool children from low socioeconomic status believe that their children are obese and therefore are not concerned [62]. In addition, maternal misperception of shape and eating habits is associated with children's obesity [63]. Our group found a distorted perception of shape among mothers of obese preschool children [63]. Notably, 98% of mothers of obese children rated them as normal weight or thin [63]. In addition, mothers exhibited a poor overall ability to estimate how obese children ate [63]. Notably, 97% of mothers of obese children thought that their children ate correctly [63]. Most parents feel offended when told that their child is overweight, and many feel ashamed or stigmatized [64]. Therefore, if parents disagree that their children eat larger

portions or have high body weight, it will be challenging for health care professionals to deal with these families.

Encouraging healthy lifestyle behaviors, especially in children with mothers with gestational diabetes, obese mothers, or those born with high birth weight, may be important to prevent obesity complications. Healthy food intake is associated with a lower prevalence of obesity [65,66]. Increases in fiber, vegetable protein, and polyunsaturated fat intake are also associated with lower hepatic fat in youth [53]. Increased caloric intake, a lack of physical activity, and sedentary behavior are associated with childhood obesity [67]. A study performed by our group on 1,200 schoolchildren showed that overweight and obesity were associated with low milk intake, skipping breakfast, a family history of hypertension, and higher systolic blood pressure [2]. Efforts to prevent childhood obesity following intrauterine exposure to maternal gestational diabetes should target the prenatal or early life periods [68].

6. Obesity treatment

6.1. Lifestyle behaviors modifications

The treatment of obesity is based on healthy lifestyle behaviors. This includes eating 3–5 servings of fruits and vegetables per day, one serving of lean meat or chicken or fish per day, avoiding juices and sodas, avoiding foods rich in saturated fat, and occasionally junk food [69]. In addition, avoiding sedentary behaviors, limiting daily screen time, and stimulating daily physical activity should be encouraged [67].

Behavioral methods are often effective in children. Suggested strategies include: allowing the child to decide when he does not want to eat more and not insisting on finishing the meal since many parents have a distorted image of the portion that the child should eat; establishing schedules and family meals; respecting the food in front of the table with the right chair, the proper cutlery, and without the TV on. Meals available at home should be appropriate for daily consumption, avoiding junk food. Except when children sleep, they should not be sedentary for more than one hour per day. Children should be encouraged to engage in daily physical activity for 60 minutes. Choose toys that stimulate physical activity [47]. Plan a daily physical activity with the family and encourage the child to play outside.

6.2. Pharmacological treatment

Although healthy lifestyle behaviors should be a priority to treat childhood obesity, pharmacological interventions could be recommended after the failure of lifestyle changes. Unfortunately, many promising weight loss drugs have been withdrawn from the market due to life-threatening side effects [70]. Drugs that are currently approved by regulatory Agencies and available in many countries for the treatment of childhood obesity are orlistat, phentermine, and liraglutide.

Orlistat is a peripherally acting agent that inhibits gastric and pancreatic lipases by preventing triglycerides hydrolysis and reducing the absorption of dietary fats. A multicenter, randomized, double-blind trial including 539 severely obese adolescents showed decreased BMI in the orlistat arm [71]. Possible side effects are steatorrhea, flatus with discharge, and fecal incontinence, probably due to the non-absorbed fats in the intestine [70]. As orlistat can alter the absorption of lipid-soluble vitamins, supplementation of vitamins A, D, E, and K should be considered [70].

Phentermine its mechanism of action is not yet fully understood. Phentermine is a centrally acting agent that suppresses appetite by inhibiting the reuptake of norepinephrine by the SLC6A2 transporter in the hypothalamus and other regions of the central nervous system [72]. These effects increase the concentration of norepinephrine in the synapse with stimulation of beta 2-adrenergic receptors. A retrospective study of obese adolescents examined the effectiveness of phentermine added to changes in lifestyle behaviors and found that phentermine was associated with a more significant decrease in BMI than those treated with changes in lifestyle behaviors alone [73]. Paresthesia, dry mouth, constipation, insomnia, dysgeusia, anxiety, and depression are the main side effects [74].

GLP-1 receptor agonists significantly reduce BMI and body fat in adults, children, and adolescents. The mechanisms suggested are slow gastric emptying, postprandial fullness and satiety, decreasing appetite and food intake by working on the hypothalamus, limbic/reward system, and cortex, all of which can result in weight loss [70]. A follow-up study performed in approximately 250 obese adolescents who failed to modify lifestyle behaviors were randomized into two groups. One group received liraglutide daily and the other placebo plus lifestyle changes [75]. Forty-three percent of the adolescents treated with liraglutide decreased their BMI by at least 5%, compared with only 19% of those treated with placebo. In addition, gastrointestinal adverse events, including nausea, diarrhea, constipation, vomiting, and dyspepsia, were significantly more common in the liraglutide group [75,76]. However, long-term studies on the benefits of these drugs and possible adverse effects are lacking in the pediatric group.

7. Conclusions

Failure of lifestyle changes is expected in the treatment of obesity. Furthermore, very few drugs are approved in the pediatric ages. Therefore, the prevention of obesity is of utmost importance. In addition, when the children are obese, the treatment is chronic. Although the causes of the majority of the skin lesions associated with obesity are not known, it has been observed that their prevalence was higher in obese children. Unlike adults, a critical point to keep in mind is that parental understanding that children are at risk of obesity is essential to prevent obesity. It is very difficult, or almost impossible, to prevent or treat obese children in families who do not recognize that their children are obese. In addition, unlike adults, another possible mechanism linking childhood obesity and skin diseases is the presence of physiological insulin resistance during pubertal development that could be significantly higher than in adult obese patients. Therefore, the prevention of obesity is essential to avoid concomitant complications. Finally, it is crucial to note that when the child is obese, we are already late. The way to success is obesity prevention. With the prevention of obesity, most of its associated skin lesions could probably be avoided.

Conflict of interest

The author declares no conflicts of interest in this paper.

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