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Therapeutic strategies for pediatric obesity and their effect in cardiovascular disease risk markers

Estratégias terapêuticas para a obesidade pediátrica e sua influência nos marcadores de risco cardiovascular

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ORIGINAL ARTICLE

ABSTRACT

Pediatric obesity is an important public health problem nowadays. Portugal is no exception, being one third of children and adolescent either overweight or obese. The behavioral approach is the basilar stone of obese treatment nowadays. It focuses in change lifestyle, substituting unhealthy habits by new, healthier, ones. A great number of strategies have been studied to try to respond to this growing problem, with varying results. The heterogeneity present in the scientific literature is likely to be explained by different study designs and targeted populations. Nevertheless, the results, in general, support that improvements in diet and increase in physical exercise pattern are associated with improvements in risk factors for cardiovascular disease, namely an atherogenic lipid profile, insulin resistance and inflammation, besides the reduction in adiposity itself. The combination of diet and exercise in the same intervention appear to be beneficial and complementary. However, different types of diet and exercise might lead to different results. The use of pharmacological adjuvants in pediatric obesity treatment is very limited in clinical practice due, mainly, to the lack of adequate studies; However some options have demonstrated to contribute to a small, but consistent, improvement in adiposity. Surgery, on the other hand, is the last therapeutic option and should be considered only in the more severe cases. Pediatric obesity tends to track until adulthood, and is associated with increased risk of cardiovascular disease in the future. Acting as early as possible in an individual life, when health habits are easier to acquire, and likelier to be kept, is crucial. Governments, including the Portuguese, have been paying more attention to this issue in the last years. However, much more can be made in general policies to create a less obesogenic environment and make the healthy choices the easier ones.

Keywords: pediatric obesity, intervention, cardiovascular disease

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ARTIGO ORIGINAL

RESUMO

A obesidade pediátrica é actualmente um problema de saúde pública crescente. Portugal não é excepção sendo que um terço da população pediátrica apresenta excesso de peso ou mesmo obesidade. A abordagem comportamental é a pedra basilar dos tratamentos da obesidade, focando-se em alterações do estilo de vida e substituição de hábitos nefastos por outros saudáveis. Um elevado número de estratégias foram estudadas para responder a este problema crescente apresentando, contudo, resultados variáveis. A heterogeneidade de resultados apresentada na literatura científica pode ser explicada por diferentes desenhos de estudo e de populações alvo. Não obstante, os resultados apontam no sentido de que melhorias na dieta e no padrão de actividade física estão associados com melhorias nos factores de risco cardiovascular, nomeadamente do perfil aterogénico lipídico, resistência à insulina, inflamação, para além da redução da própria adiposidade. A combinação de dieta e exercício na mesma intervenção parece ser benéfica e complementar. No entanto, diferentes tipos de actividade física e de dieta podem levar a resultados diferentes. O uso de adjuvantes farmacológicos no tratamento da obesidade pediátrica é altamente limitado na prática clínica, especialmente devido à falta de estudos adequeados; contudo algumas opções demonstraram contribuir para uma pequena mas consistente melhoria da adiposidade. A cirurgia é uma solução de último recurso e para casos extremos. A obesidade pediátrica tende a manter-se até à idade adulta e está associada a um aumento do risco cardiovascular futuro. Uma actuação tão precoce quanto possível, quando é mais fácil a aquisição de hábitos adequados, é crucial. Os governos estão a prestar cada vez mais atenção a este assunto. Contudo, muito mais pode ser feito em termos de políticas globais, no sentido de criar um ambiente menos propício à obesidade e favorável à escolha de opções mais saudáveis.

Palavras-chave: obesidade pediátrica, intervenção, doença cardiovascular

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INTRODUCTION

Obesity is increasing worldwide in recent years, both in developed and in developing countries, leading many authors to refer to obesity as the pandemia of the 21st century. In fact, obesity is now considered as a disease with its own complexity, and has been deeply studied in the last years. The modern lifestyle, characterized by increased energy intake and reduced energy expenditure, is at the basis of the obesity phenomena[1].

Pediatric obesity is accompanying the adult trend and has reached high rates in many countries. In Portugal around one third of the children are overweight or obese[2,3].

The use of therapeutic strategies for tackling obesity in pediatric ages aims at weight normalization and reduction of the future risk of cardiovascular disease (CVD). A behavioral approach, towards lifestyle modification, is the main pillar of obesity treatment, both in children and adults. The main objectives are to increase physical activity and improve diet in order to improve the energy balance. Two strategies are usually used: non-interventional programs, involving nutritional counseling and motivation to exercise; and interventional programs, involving the use of diets and/or physical exercise programs. Pharmacological drugs have also been tested as adjuvants in the treatment, with limited but consistent results[4-7].

Usually, childhood obesity is treated by a regular pediatrician. As obesity increases, and comorbidities or psychological consequences appear, a multidisciplinary approach becomes necessary, including a nutritionist, a behavior modification specialist, a psychologist and an obesity specialist pediatrician[4-7].

The treatment of obesity is a long process presenting different phases that should not be hurried. In the beginning of the treatment, several visits might be necessary, to build the trust between the doctor/team and the child. It is beneficial for the children to be followed by the same doctor throughout the treatment[8].

By improving weight other metabolic derangements present in obesity also tend to improve. The International Diabetes Federation (IDF) 2007 recommendations for the prevention and treatment of metabolic syndrome (MS) in children and adolescents, for example, focus on weight improvement and management, thus, tackling obesity as a MS underlying cause. IDF recommendations are not much different from other organizations such as the World Health Organization (WHO), the American Association of Pediatricians (AAP), and the Associacíon Española de Pediatría (AEP)[4,6,9,10].

Obesity reduction programs in children should be adapted to age, degree of obesity and presence (or not) of comorbidities. The treatment should start immediately and not wait for older ages[4,6,8,11]. Children and young adolescents have a linear growth potential that can help on body mass index (BMI) normalization and should be considered when defining a treatment strategy[4,7,8].

Depending on the age and the levels of adiposity, children with a BMI higher than the 85th percentile and lower than the 95th percentile (overweight children), or above 95th percentile but without comorbidities (obese children without complications), could follow 3 basic options[6,7,11]:

- Slow the rate of weight gain – used in very young children (2-4 years old), as they present a very rapid growth rate that might lead to BMI normalization;
- Weight maintenance – used for children over 4 years;
- Gradual weight loss (1 to 2 kg/month) to improve BMI, in older children and adolescents.

For children with BMI above the 95th percentile with comorbidities, an approach based on the severity of the situation should be used. Weight loss is usually necessary but, even in severe obesity, the weight loss program should be gradual for several reasons[7,8,11,12]:

- It should be used a goal that the children can achieve to avoid demotivation;
- Even slow weight gain involves a great reduction on habitual caloric intake, especially if the children is still growing;
- Treatment of weight excess is a long term process and gradual weight loss is easier to be sustained for longer periods;
- Even small improvements of adiposity markers are already associated with a reduction of CVD risk factors (e.g. atherogenic lipid profile).

Adolescents who have reached growth limit and have a BMI higher than 30 Kg/m^2 should be submitted to a program similar to that used for obese adults, to minimize CVD risk[5, 11].

It is necessary to approach the child/adolescent in his culture, social and family environment, as it would be harder to tackle childhood obesity without the help of parents and caretakers[5-7, 11, 13].

The Portuguese National Child and Adolescent Health Program (NCAHP) provide guidelines and check points to follow the pediatric development that, if correctly followed, might help to identify obesity and associated comorbidities while still in early stages, when the chances for a successful treatment are higher[14]. It also focuses on the promotion of healthy lifestyle habits, improving diet and increasing physical activity. A gradual responsabilization, first of the parents and, afterwards, of the child/adolescent, by their health maintenance and success of therapy should be done[14].

In Portugal, there are no clear guidelines on how the pediatric obesity should be approached, only general recommendations are given for a healthier lifestyle. Nevertheless, many hospitals in Portugal have specialized pediatricians and provide obesity appointments to which children can be referred. The obese appointments usually involve, besides the medical doctor, a visit to a nutritionist.

Clearer guidelines regarding obesity and overweight treatment and prevention should be provided worldwide, and particularly in Portugal. It seems unreasonable that the NCAHP focus on dyslipidemia, hypertension and oral health programs, known comorbidities of obesity, while obesity is only referred twice along the 121 pages of the document.

In this paper we aim to shortly review some therapeutic strategies regarding pediatric obesity and the influence of those therapeutic options in the reduction of cardiovascular risk factors.

DIET

Unbalanced diet and increased energy intake is a common problem nowadays and a major contributor to the epidemic obesity. A healthy diet is more expensive than other unhealthy options, creating a problem for lower income families[5,10,11].

Some interventional programs, in order to better control energy intake, choose to provide at least one balanced meal per day. Although this is a good strategy, it has the predictable logistic, children compliance and financial problems, particularly in longer studies[9].

To design a healthy diet the children's nutritional habits and their socio-cultural reality should be considered. The basic idea of the diet in the obese pediatric patient is to adjust the energy intake to their necessities, in order to allow the correct development, as children and adolescents are in a period of constant changes, both physical and psychological. Thus, providing an adequate nutrition, to allow the child to reach his full development potential is essential[7,9,11]. The traditional recommendations are, usually, overestimated in obese, due to the decreased physical activity, and should be adjusted[9].

The first approach in obese children and adolescents is to reduce the usual nutritional mistakes. Over the last decades it has been observed a trend to increase the caloric density of foods, the percentage of fat and carbon hydrates (CH), and to reduce the content of

micronutrients and fibers. Thus, there is an absolute and relative increase in fat and CH intake. It is known that skipping breakfast increases the incidence of obesity and decreases school performance[17]. Other common mistakes include an excessive amount of candies and pastries as snacks, and an excessive intake of soft drinks with a high concentration of CH[5,7,9)]. The substitution of this type of snacks by other healthier options, e.g. fruits, is beneficial[8].

Not only the type of food is inadequate, but also the number of meals, the daily energy distribution, the serving sizes and their weekly basis[8,9]. In western cultures there is an excess of meat intake, especially red meat, with a reduction of fish based meals. The intake of meat should be reduced to 3 times a week, preferably lean meat (e.g. turkey, chicken), and the intake of fish should be of at least of 2-3 meals per week[9]. Fruit and vegetables intake usually do not reach the recommended 4-5 portions per day[6,9] and the consumption of whole grains is also reduced[9]. Due to the reduced intake of fruits, vegetables and cereals there is a lower intake of fibers, a macronutrient that is associated with the reduction of obesity and with other beneficial effects, as the regulation of intestinal function and reducing the risk of colon-rectal cancer[9]. In adolescents, the importance of alcohol ingestion in the energy balance should be considered[9].

Other healthy changes in food habits include the reduction of serving sizes and the increase in the time reserved for meals as, by prolonging the length of the meal, there is an increase in satiation through the release of anorexigenic and satiation mediators, as some gastro-intestinal peptides (e.g. Y peptide)[8].

The way food is prepared is important to stimulate children to eat healthy. Cooking with less fat and the substitution of frying by grilling and baking help to reduce fat intake[7, 9]. It is also important to reduce the use of oil and industrial sauces (e.g. mayonnaise, ketchup). The use of salt should be limited, as many of the obese children have increased BP; aromatic herbs are a good substitute. Food presentation should not be forgotten, as it motivates children to eat better and forget that they are in a diet, if that is the case[9].

The majority of the diets target changes in the amount and percentage of macronutrients. When the approach to reduce nutritional mistakes in overweight and moderated obesity is not successful, a nutritionist can prescribe a hypocaloric diet, with the reduction of daily energy intake of about 30%. A balanced hypocaloric diet might also involve the increase in fiber intake, the reduction of CH with high glycemic levels and the substitution of saturated by mono and poly-unsaturated fats[7,9]. Hypocaloric diets and low CH diets have shown similar results in short term studies[8].

In the last years a great number of fast diets and supplements have become available to help weight loss. The scientific data supporting these treatments are scanty and they should not be used by pediatric patients. Adolescents are a particular vulnerable group due to their autonomy to make some decisions[8].

To help children learn the best nutritional options, different strategies have been used, as the traffic light diet. In this diet the foods are classified according to their content in fat. The foods labeled green are low in fat and could be consumed freely, while the consumption of food of the red group, high in fat, should be limited. Similar campaigns have been used in Portugal with interesting results[8].

When a weight-losing diet is followed, besides the decrease in fat mass, a decrease in lean mass also occurs. Thus, it is important to add protein sources of high biological value to the diet and to increase physical exercise levels, in order to maintain and improve the lean mass throughout the diet[9].

In overweight and moderately obese younger children the main objective is to maintain the body weight without compromising the normal body development, as the BMI, usually norma-

lizes with height increase[7,9]. Also, the energy restriction should be moderate, in a way that it can be sustained in time[8]. Very low caloric diets (500-600 kcal/day) and the use of liquid formulas to substitute entire meals should not be used in children and adolescents, and are only recommended in cases of increased health risk and morbid obesity[9]. In fact, some centers specialized in the treatment of morbidly obese or obese with comorbidities have successfully used that approach [(8)]. These diets need special attention to avoid the development of acidosis, through an adequate CH intake, and to prevent the extensive loss of lean mass, by controlling the protein ingestion[8,9].

BIOCHEMICAL OUTPUTS OF DIET

Diet restriction is associated with improvements in adiposity and in lipid profile, namely a reduction in total cholesterol (TC) and low density lipoprotein cholesterol (LDLc). The influence of diet in high density lipoprotein cholesterol (HDLc) and triglycerides (TG) appears to be limited, presenting physical exercise more pronounced effects[18]. This fact might be explained by a small impact of diet on insulin resistance (IR)[18].

An improvement in inflammation, following diet-induced weight loss has also been reported. In fact, following a diet restriction program, total adiponectin levels (an anti--inflammatory mediator) were increased, while inflammatory mediators such as leptin, interleukin (IL)-15, and IL-18, were reduced[19,20]. A cumulative effect of diet and physical exercise on the improvement of the inflammatory status was reported[19], however, there are conflicting results[20].

The use of specific components in the diet, besides the energy restriction, might lead to different outcomes regarding metabolic changes. The different types of fats, for instance, are associated with different effects. Increased fat intake is associated with a reduction of adiponectin[21], while children receiving n3 fatty acids supplementation presented an improvement of the inflammatory status (increased adiponectin and reduced TNF-α and leptin). The improvement in inflammation is probably on the basis of the reduction in IR[22].

The type of diet recommended, its caloric content, and individual components should be defined according to the individual degree of obesity, presence or not of comorbidities and specific metabolic risk profile, in order to obtain the expected benefit from it.

PHYSICAL ACTIVITY

Southern European countries, including Portugal, present lower physical activity levels, among children and adolescents, than countries from Central and Northern Europe. Part of the increased prevalence of obesity in the Southern countries might be related to this fact[23].

An inadequate energy intake accompanied by reduced physical activity is very likely to result in weight excess. An increase of the physical activity levels is mandatory in obesity treatment and has multiple benefits. To achieve an improvement, two points should be considered: to reduce the time spent on sedentary behaviors and to increase physical activity levels.

The daily energy expenditure is calculated by the sum of the energy expended in rest, the diet induced thermogenesis and the energy expended on physical activities[9].

Strategies and interventional programs to increase the physical activity among pediatric populations have flourished in the last years. School based programs might be particularly interesting as they take advantage of children availability and school sports equipment[5,9]. However, programs involving physical exercise should choose stimulating and new activities, especially for the younger children, as their interest is harder to maintain[7,11]. The simple increase of the hours spent on curricular physical exercise do not present significant improvements[11].

The guidelines for physical activities in children and adolescents state that 30 to 60 min a day should be dedicated to moderate or intense physical activity[5,6,9,11]. Physical activities should be adequate for age and gender. The general recommendations have to be adjusted for each children and the exercise plan adequate to their socio-cultural-economic background[5-7, 9,11].

Increasing activity levels with everyday activities, as gardening, walking to school, riding a bicycle and traditional children games, as hide and seek, might be effective in increasing the metabolic level and should be encouraged[7,8,11]. On the other hand, sports groups, although helpful, may not provide enough activity, due to the limited training period, weekly schedule, and the fact that level of engagement in the exercise vary between individuals[7,11]. The use of accelerometers is a good option for objectively control the level of physical activity, even during entire days. Its use has, however, considerable financial costs[6].

Moreover, the ingress in a sport group of an unfit obese child should be done carefully as an initial incapacity to perform requested exercises could lead to demotivation and an eventual bulling by the peers, what could cause the child to withdraw. Thus, group sports could be postponed until the patient has reached minimum skills[7, 11].

There are conflicting results regarding the success of interventional programs involving exercise alone or combined with diet. Doubts exist, particularly regarding the long term effectiveness on weight maintenance[9,11]. Further studies on the influence of less "aggressive" programs following (e.g. a motivational approach towards the improvement of lifestyle habits) would be important[12].

Regarding sedentary behaviors, such as screen time, parents should define the period of duration and its content, while outdoor playing should be encouraged, if safeness is granted[8].

Once again, each obese individual is a particular case and should be addressed in that way. The child should be challenged and motivated to increase physical activity gradually and to achieve realistic goals. Unpleasant situations should be avoided.

BIOCHEMICAL OUTPUTS OF PHYSICAL EXERCISE

An adequate performance of physical exercise presents several beneficial effects. For instance, there is an improvement of the lipid profile, with the reduction of TG and the increase of HDLc. A key factor underlying this improvement seems to be the increase in insulin sensitivity that follows the increased physical fitness. In fact, the improvement of the hepatic insulin sensitivity is associated with changes in the lipoproteins produced by this organ towards the production of a less atherogenic profile[24-27]. Nevertheless, there are still some contradictory results[28]. Diet, on the other hand, seems to have limited impact on HDLc and insulin sensitivity[18].

The increase in regular physical activity is also associated with an improvement of the inflammatory status, with the reduction of inflammation markers, such as IL-6, CRP, leptin and TNF-α[28-3] and the increase in anti-inflammatory adiponectin[32,33]. In fact, the exercise-related improvement in IR is likely to be associated with this enhancement of the pro/anti-inflammatory balance[34,35]. However, there are still some controversies regarding changes in inflammatory mediators levels with physical exercise and weight loss, particularly on which markers vary and in the extent of the modification[36-38].

The variation in the training protocol used in an intervention program can lead to different results. Although both aerobic training (AT) alone, and aerobic combined with resistance training (ART) improved adiposity measures, as BMI, BMI z-score, visceral fat and subcutaneous fat, and were effective in reverting MS in obese individuals, the improvement achieved with ART were bigger than with AT[39].

Cardiorespiratory fitness (CRF) is inversely associated with CVD risk markers and total mortality[40], and one of the main determinants of the physical activity levels in children and adolescents[23]. In fact, a lower CRF is related to increased sedentary behaviors and weight gain[41]. Although CRF has a considerable genetic background, it increases with exercise[23]. The use of training protocols aiming to increase CRF, as well as the use of CRF as an outcome of exercise programs, might be a good strategy to control the effectiveness of interventional programs.

Some studies suggest that improvements in IR, lipid profile (e.g. HDLc) and inflammatory status are only present in the case of a substantial improvement in BMI (e.g. a reduction of BMI z-score > 0.5)[30,31,42], while others state that even moderate reductions are already characterized by improvements[12].

Besides the weight reduction that might accompany the increase in physical exercise, a key factor to explain the metabolic changes that occur, are the changes in the body composition, particularly the reduction in central adiposity, known to be associated with worsening of the risks factors for CVD[43-45]. Thus, some of the conflicting results regarding the effects of physical exercise and diet on metabolic parameters might be related to the effective changes in body composition. More than considering only changes on weight or BMI to evaluate the success of an interventional program, the analysis of markers of adiposity distribution, such as waist circunference, waist circunference-to-height ratio, skin folds and DEXA, would be a better option.

Study the impact of small reductions of adiposity on CVD risk markers would be important. Smaller improvements might be a more realistic target, which could be more easily achieved and sustained, avoiding the loss of motivation in longer, stricter programs.

PHARMACOLOGICAL STRATEGIES

Pharmacological strategies to improve weight loss in pediatric obese patients have been proposed. Nevertheless, these strategies must be always an adjuvant to lifestyle changes, including diet and increased physical exercise. The weight loss obtained by the use of drugs is, usually, small but significant[5, 9,46].

The use of an adjuvant pharmacologic therapy should be considered carefully and in specific cases, when the relation risk/benefit is favorable. Patients that could be considered for pharmacological therapy include obese individuals that do not respond to behavioral treatments or present comorbidities, and overweight children presenting comorbidities. Overweight or obese children with a strong family history of T2DM or CVD should also be considered, even when comorbidities are not present[5, 9, 46].

The drugs used have specific actions and can be included in the following groups: drugs reducing energy intake (anorexigenics), drugs that interfere with dietary nutrients and drugs interfering with the metabolism[9,46]. Table 1 resumes some of the drugs that have been studied and/or used in pediatric obese patients, their mechanism of action and adverse effects.

In Portugal the only drug approved for the treatment of obesity is Orlistat, however it is not recommended for children and adolescents[47-49].

Other drugs have been used in adults with interesting results regarding weight reduction, however the information about their applicability in pediatrics is limited or absent. This list of drugs enclose bupropion (anti-depressive), lorcaserin (selective 5-HT2C receptor agonist), tesofensine (monoamine re-uptake inhibitor), pramlintide (amylin analogue), exenatide and liraglutide (GLP-1 analogs); other drugs, as acarbose (pseudotetrasaccharide), have still limited support, even in adults [46]. Rimonabant (CB1 cannabinoid receptor inhibitor), an apparently promising drug, was withdraw due to the association with an increased risk of suicide idealization and attempt[8].

Another therapeutic option for the treatment of obesity, available in Portugal, is a medical device called XL-S Medical®. The functional component of this device is Litramine, a complex of soluble organic and vegetal fibers that jellify in the stomach, capturing the lipids present in the meal, diminishing their absorption, with effects similar to orlistat (although the mechanism of action is different). Although it doesn't have a pharmacological action, its use in individuals under the age of 18 years should be done only under the supervision of a pediatrician[49,50].

Obesity is a multiorgan pathology, and weight control is mediated by a large number of mechanisms in the organism. In this way, the use of therapies combining different drugs, acting by different mechanism, to treat or prevent weight gain, such as the combination of peripheral and central acting drugs, can enhance the success of the pharmacologic therapy[5,46]. Some of the combinations used in adults are phentermine and topiramate (approved by the Food and Drugs Administration (FDA) for the treatment of obesity in adults, in 2012), bupropion and naltrexone (recommended for approval by FDA Metabolic Drugs Committee), amylin and leptin analogues, and pramlintide and phentermine or sibutramine[46]. None of these combinations are available in Portugal[47-49].

The use of pharmacologic treatment should always be considered with caution, particularly in pediatric patients, and faced as adjuvant of lifestyle modification strategies. Nevertheless, it should not be a taboo and, when a positive risk benefit balance is considered, the use of drugs can be a helpful tool. Portuguese and European regulatory agencies have adopted a particularly restrictive position towards possible pharmacological options, particularly when compared to the USA's FDA. As a direct consequence, off-label use is a growing reality in obese treatment. More flexible legislation and clearer guidelines would probably guarantee the safety and efficacy of obesity treatments. When considering the pros and cons of pharmacological options it is important to consider not only the comorbidities presented by the patient, but also the risk for future obese-related complications. Thus, the balance between the benefits and risks of controlling adiposity, especially in young ages, is very important, as obesity is a chronic condition that tracks into adulthood. Moreover, the drugs to treat obesity, both in adults and in children, have to demonstrate long-term safety and efficacy, particularly when treatment is started in pediatric ages[5,46].

SURGICAL TREATMENT AND OTHER OPTIONS

Surgical treatment in obese children and adolescents is controversial and the last therapeutic option, used only when the traditional approaches failed. It might be considered in case of extreme obesity (BMI > 40kg/m^2) with associated comorbidities (hypertension, dyslipidemia, IR, non-alcoholic fatty liver disease (NAFLD)…), and in case of BMI > 35 kg/m^2 with associated serious comorbidities (T2DM, sleep apnea, endocraneal hypertension or serious NAFLD)[8,9,11]. Moreover, as adolescents are still in development, bariatric surgery should be carefully considered. The recommendations for bariatric surgery include:

- A minimum Tanner stage of 4 or 5. Less mature individuals could be considered if severe comorbidities are present;
- Have reached at least 95 % of growth potential, especially if malabsorptive surgery is considered;
- Psychological maturity and capacity to understand the limitations that will follow the procedure:
- Dietary and activity changes;
- Family and social support;
- Exclusion of genetic or syndromic obesity[6-8];
- Failure of lifestyle intervention, with a duration of at least 6 months[8].

Bariatric surgery is also contraindicated

in adolescents with history of alcohol or drug abuse in the last year, pregnant or planning to get pregnant in the next 2 years, and in patients who did not correctly followed previous lifestyle treatment[7].

The most relevant bariatric techniques in pediatric obesity are gastric bypass, gastric banding and gastric balloon.

The gastric bypass in Y of Roux, due to its malabsorptive and restrictive nature, is one of the most used surgical options in obesity. In fact, it is the most used technique in the USA. This surgery consists of a reduction of stomach size and a reduction of intestinal absorptive capacity via the creation of a gastrojejunal anastomosis[6,8]. The gastric bypass allows the loss of 50-60% of the body weight, as well as improvements in several metabolic parameters, such as TG, TC and IR[6,8,9,11]. Side effects involve nutritional deficiencies, due to malabsorption. Patients submitted to this surgery need to be followed by a multidisciplinary team, including doctors, psychologists and nutritionists before and after surgery[6, 9,11].

The gastric banding is a less invasive surgical technique, when compared to gastric bypass. This option has increasing acceptance nowadays, due to its reversibility and lower number of side effects. The gastric banding is, in fact, the most used bariatric surgery in Europe for the treatment of obese adolescents, presenting a considerable success. It consists in the laparoscopic placing of a silicon ring around the proximal part of the stomach that will limit food ingestion. This ring can be regulated by introducing saline in a subcutaneous reservatory. However, the weight reductions are more limited than with gastric bypass, reaching around 20-30%, the side effects, as malabsorption, are less frequent and have less impact in the development of the adolescents[6,7,9].

The endoscopic implantation of a gastric balloon is the lowest invasive option, when compared to the other two. Similarly to the gastric banding this is a reversible technique with lower number of side effects. Achieved weight reductions are comparable to those obtained with the gastric banding (20 - 30% of weight reduction)[6-9].

The temporary nature of the gastric balloon, and the reversibility of gastric banding, come with the common problem of weight rebound, once the balloon or the banding are removed. A multidisciplinary team with psychologists and dietitians, beside pediatricians, need to follow the patient, before and during the whole process, with particular attention after the removal of the restrictive device[7].

CONCLUSION

Pediatric obesity is a public health problem. It is associated with increased risk of CVD in adulthood, besides other comorbidities that are present already in early ages, greatly affecting the quality of life. An adequate intervention in these ages, when healthy habits are more likely to be acquired and kept is, thus, crucial.

In fact, the literature presents a considerable amount of studies regarding the intervention on pediatric obesity, with varying results. Part of this variation could be explained by different study designs and population.

Nevertheless, changes in lifestyle, with the increase in physical activity levels and a healthier diet, are associated with improvements in cardiovascular risk factors, namely lipid profile, IR and inflammation.

The combination of diet and exercise in the same intervention appear to be beneficial. However, different types of diet and exercise might lead to different results.

The use of pharmacological adjuvants in pediatric obesity treatment is very limited in clinical practice due, mainly, to the lack of adequate studies; however some options have demonstrated to contribute to a small, but consistent, improvement in adiposity. Surgery, on the other hand, is the last therapeutic option and should be considered only in the more severe cases.

Obese children and adolescents would benefit from the development of a scientifically based standard protocol, involving changes in physical exercise levels and diet, through a behavioral approach. This protocol should be adapted to each individual cultural and socio--economic background.

Governments, including the Portuguese, have been paying more attention to this issue in the last years. However, much more can be made in general policies to create a less obesogenic environment and make the healthy choices the easier ones.

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Table 1 - Pharmacological options for obesity treatment

Drug	Mechanism of action	Side effects
	Centrally acting anorexigenic	
Phentermine[a] and diethylpropion[a] [46-49]	Anorexogenic effects by increasing adrenergic tone, decreasing energy intake and increasing resting energy expenditure	Euphoria, palpitations, hypertension, cardiac arrhythmias, dizziness, blurred vision and abuse potential.
Fluoxetine, chlorphentermine[1], fenfluramine[b] and dexfenfluramine[b] [46-49]	Reduces appetite by increasing serotonergic release or inhibiting re-uptake	Cardiac valvulopathies, increased risk of primary pulmonary hypertension, headache, abdominal pain, drowsiness, insomnia, dry mouth, increased activity and irritability
Methylphenidate and dextroamphetamine[1] [46-49]	Anorexogenic effect by inhibiting dopamine reuptake	Agitation, insomnia, tachycardia, hypertension, hyperhidrosis and abuse potential
Sibutramine[2] [5, 6, 9, 11, 46-49]	Inhibits serotonin, norepinephrine and dopamine reuptake, presenting an anorexogenic effect and increasing energy expenditure	Cardiovascular events (myocardial infarction and stroke), hypertension, increased heart rate, headache, dry mouth, anxiousness, insomnia, depression, constipation and cholelithiasis
Leptin[a,c] [9,11,46-49]	Transmits information to hypothalamic centers of the adipocyte lipid reserves and of nutrients and energy of meals – satiation effect	Increased inflammation
Topiramate [5, 9, 46-49]	Anorexogenic effects by GABA-ergic stimulation	Psychomotor disturbances, difficulties with concentration, sedation, reduction of learning skills, paresthesias and taste impairment.
	Drugs affecting dietary nutrients	
Orlistat[d] [5, 6, 9, 11, 46-49]	Inhibits gastrointestinal and pancreatic lipases, reducing the absorption of ingested dietary fats	Intestinal gases, oily stools, oily spotting, oily evacuation, abdominal pain, fecal urgency, diarrhea and gallstones. Lipid soluble vitamins deficiency.
	Drugs affecting the metabolism	
Metformin [5, 6, 9, 11, 46-49]	Modulation of insulin action. Inhibits intestinal glucose absorption, reduces hepatic glucose production and increases peripheral insulin sensitivity by improving glucose uptake and utilization	Diarrhea, nausea, vomiting and flatulence. Vitamin B12 and folic acid deficiency
Octreotide[e] [5, 46-49]	Modulation of insulin action. Octreotide inhibits the release of the growth hormone, thyrotropin and corticotropin from the hypophysis; and of insulin and glucagon from the pancreas and ghrelin from the stomach.	Transient elevation of blood glucose, diarrhea, abdominal pain, discomfort, flatulence influenza-like symptoms, constipation, headache, fatigue, dizziness, nausea, anemia, hypertension, and gallstones
Growth hormone[f] [5, 46-49]	Modulation of lipolysis. Inhibits LpL, increases hormone-sensitive lipase levels and stimulates lipolysis in adipocyte, stimulates protein synthesis and increased fat-free mass	Increased risk of tumor, potential adrenal insufficiency, insulin resistance, increased risk of sleep apnea and increased cardiac diameter
Ephedrine combined with caffeine[a] [46-49]	Modulation of energy expenditure. Ephedrine increases catecholaminergic tone while caffeine acts by inhibiting phosphodiesterases. Ephedrine presents a thermogenic effect that is enhanced with the administration of caffeine	Cardiac effects, nausea, insomnia, tremor, dizziness and palpitations

a, not commercially available in Portugal. b, withdraw from Portuguese market. c, Used only to treat syndromic obesity related to lack of leptin production. c, only pharmacological option approved in Portugal. f, Used only for the treatment of patients with hypothalamic obesity. f, used only to treat syndromic obesity characterized by reduced synthesis of growth hormone – e.g. Prader Willi Syndrome.