

Cyproheptadine as an appetite stimulant in children. Is it safe?

Ciproheptadina como estimulante do apetite em crianças. É seguro?

Ciproheptadina como estimulante del apetito en niños. ¿Es segura?

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Cyproheptadine prescription in children

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The article is relevant in the local Ecuadorian context, because it provides evidence that may support public policies to combat child malnutrition.

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The article presents a synthesis of evidence that proves the safety of Cyproheptadine for the treatment of children.

ABSTRACT

Background: Cyproheptadine as an appetite stimulant in children. Is it safe? This drug has been used to increase appetite in pediatric patients, regardless of their sex or the presence of pathological conditions. The effectiveness of this drug in terms of weight gain and growth is still a matter of interest. **due to the diversity of conclusions regarding its mechanism of action and therapeutic results. Methods:** This bibliographic review of the scientific literature focused on research in order to obtain results around scientific articles related to the use of cyproheptadine as an appetite stimulant in pediatric patients. **Results:** all the articles analyzed concluded that cyproheptadine is an effective medication for weight gain in pediatric patients, based on appetite stimulation, totally independent of sex and the presence of pathological states. **Conclusions:** Cyproheptadine is a safe medication, and adequately tolerated in all pediatric patients. It is possible to measure the improvement in weight and growth indices in patients under twelve years of age, if consumption is for at least four consecutive weeks.

Keywords: cyproheptadine; child development; appetite; weight gain.

RESUMO

Antecedentes: Ciproheptadina como estimulante do apetite em crianças. É seguro? Este medicamento tem sido utilizado para aumentar o apetite em pacientes pediátricos, independentemente do sexo ou da presença de condições patológicas. A eficácia deste medicamento em termos de ganho de peso e crescimento ainda é motivo de interesse, devido à diversidade de conclusões sobre seu mecanismo de ação e resultados terapêuticos. **Métodos:** Esta revisão bibliográfica da literatura científica teve como foco a pesquisa a fim de obter resultados em torno de artigos científicos relacionados ao uso da ciproheptadina como estimulante do apetite em pacientes pediátricos. **Resultados:** todos os artigos analisados concluíram que a ciproheptadina é um medicamento eficaz para ganho de peso em pacientes pediátricos, baseado na estimulação do apetite, totalmente independente do sexo e da presença de estados patológicos. **Conclusões:** A ciproheptadina é um medicamento seguro e adequadamente tolerado em todos os pacientes pediátricos. É possível medir a melhora nos índices de peso e crescimento em pacientes com menos de doze anos de idade, se o consumo for de pelo menos quatro semanas consecutivas.

Palavras-chave: ciproheptadina; desenvolvimento infantil; apetite; aumento de peso.

RESUMEN

Antecedentes: Ciproheptadina como estimulante del apetito en niños. ¿Es segura? Este medicamento ha sido utilizado para el aumento de apetito en pacientes pediátricos, independientemente de su sexo o la presencia de cuadros patológicos, La efectividad de este medicamento en lo que tiene que ver a aumento de peso y crecimiento es aún un tema de interés, esto debido a la diversidad de conclusiones en cuanto a su mecanismo de acción y resultados terapéuticos. **Métodos:** La presente revisión bibliográfica de la literatura científica, se centró en la investigación con el fin de obtener resultados en torno a artículos científicos relacionados con el uso de la ciproheptadina como estimulante del apetito en pacientes pediátricos. **Resultados:** la totalidad de los artículos analizados concluyeron que la ciproheptadina es un medicamento efectivo para el aumento de peso en pacientes pediátricos, en función de la estimulación de apetito, totalmente independiente del sexo y la presencia de estados patológicos. **Conclusiones:** La ciproheptadina es un medicamento seguro, y adecuadamente tolerado en la totalidad de pacientes pediátricos. Es posible medir la mejoría en cifras de peso y crecimiento en pacientes menores de doce años, si su consumo es por al menos cuatro semanas de forma consecutiva.

Palabras clave: ciproheptadina; desarrollo infantil; apetito; aumento de peso.

INTRODUCTION

Cyproheptadine is a serotonin 5-HT₂ and histamine H₁ antagonist that also blocks calcium channels. It was first introduced to treat allergic conditions, but for the past two decades, research has focused on its efficacy in increasing appetite and its direct effects on weight (Harrison et al., 2019). In surveys, it is also reported to have an effect on the linear growth of individuals under 12 years of age, which leads to a growth process that implies a continuous increase in high dimensional measurements for a constant period (Kim et al., 2021).

This drug has been used in studies evaluating its efficacy by focusing on specific disease groups with marked weight loss due to disease progression (Pais, 2019). Among the main diseases on which scientific research is focused are various types of cancer in adults and children, human immunodeficiency syndrome (AIDS), anorexia nervosa (AN) and capsular fibromas (Mohammadi et al., 2021). Although it is considered that strategies focused on weight gain in patients of all ages have taken multidisciplinary paths, it is important to analyze the effectiveness of cyproheptadine, this being a drug approved by the main pharmacological regulatory bodies, in which it can be test the direct effects on weight gain (Acosta & Pirez,

There is a pathological entity that affects a specific age group, with the highest incidence of cases between eight and sixteen years of age. This is food intake avoidance/restriction disorder (TERIA), defined as an inadequate and persistent modification of eating behaviors due to external influences that directly affect the perception of food as a positive source of energy input. and nutrients (Badr & Naguy, 2022). Cyproheptadine has been reported to be effective in the treatment of primary restrictive symptoms, but it has been stressed that it should not be the only form of treatment in cases of avoidance as it can worsen symptoms with totally adverse results (Turcott et al., 2022).

Regarding the use of this medication for the treatment of children diagnosed with malnutrition and low weight, it has been observed in various investigations that it has beneficial effects in terms of weight gain to different degrees, this is conditioned by the demographic and socioeconomic situation of each of the study subjects (Harrison et al., 2019). Similarly, cyproheptadine has a beneficial effect on growth, provided treatment is maintained for at least three months, that is, when individual results can be objectively assessed (Grunert et al. Associates, 2021).

The evaluation of changes in appetite is inconclusive with respect to this drug because objective evaluations were not performed to obtain results. It is important to mention that it is considered a safe drug in children and adolescents, since the most frequently reported side effect is sedation, which gradually disappears with subsequent exposure to the drug (Gupta et al., 2023).

In the case of children diagnosed with diseases that cause appetite and weight gain, cyproheptadine has been shown to directly affect this anthropometric index in patients with chronic disease (Villarroya et al., 2021). The patient has been exposed for more than 9 months, and the results may be conditioned by adherence to the medication, the prescription of other compounds, or decreased effectiveness (Childs & Jatoi, 2019). There are no objective conclusions based on the analysis of the variation in appetite, however, in this specific population group, no adverse effects that modify the state of health have been reported from the beginning of its consumption.

The objective of this research work is to evaluate the effectiveness of cyproheptadine in weight gain, inform about its safe use and the ability to act as an appetite stimulant, in turn analyze the side effects of its consumption in groups of children with characteristics heterogeneous.

METHODS

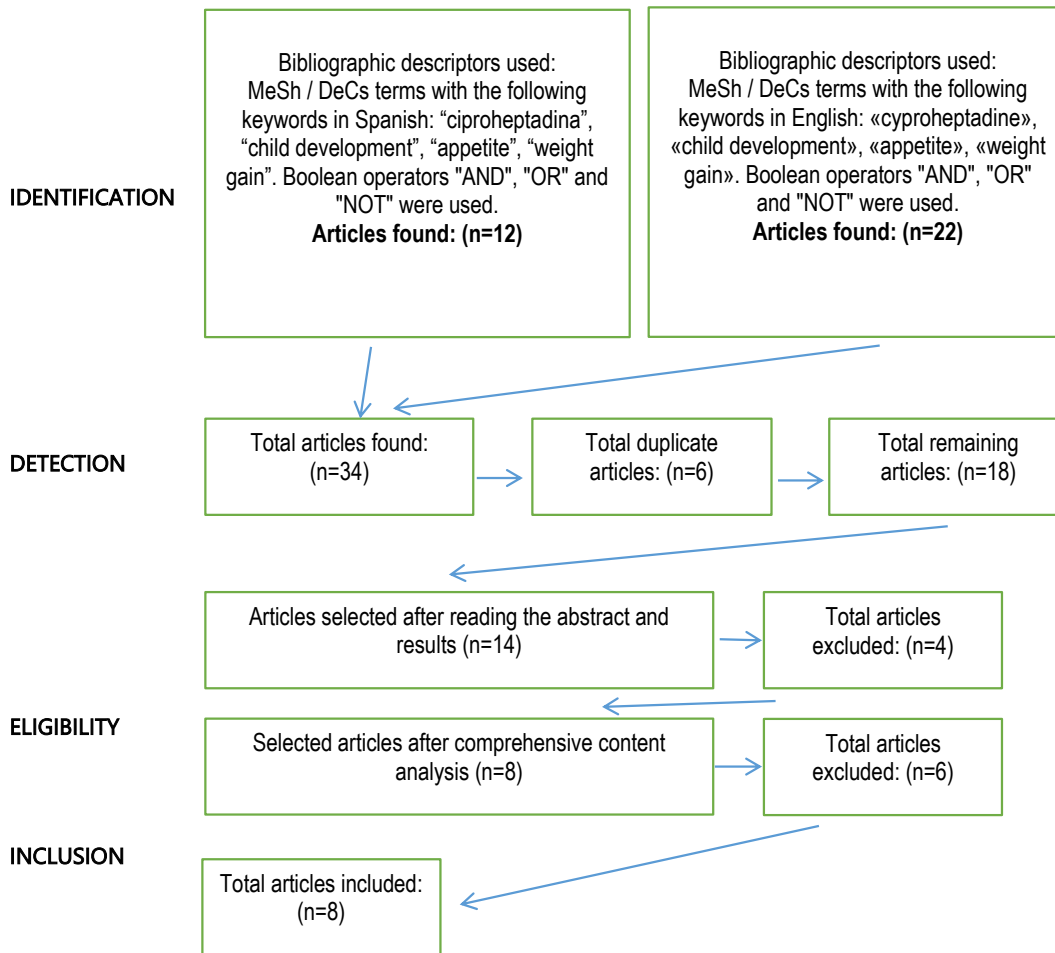
This bibliographic review of the scientific literature focused on research in order to obtain results around scientific articles related to the use of cyproheptadine as an appetite stimulant in pediatric patients. Papers published during the last five years, from 2017 to 2023, were taken into account within the research process. The search for information focused on analyzing the articles that contained relevant information on the use of this drug and the direct effects in pediatric patients. regarding increased appetite, weight gain, and possible side effects.

In order to make the research process effective in the bibliography, databases that include scientific articles validated by the research community related to health issues were used. Among the databases that were taken as a research resource were: ProQuest, Medline, SciFinder, Lilacs, Scopus and PubMed. Articles in Spanish, English and Portuguese were accepted in the final results of the research.

When processing the articles resulting from the investigation, the PRISMA method was applied, suitable for processing results related to bibliographic reviews of the scientific literature in terms of health issues. In addition, articles that

are incomplete or that their research work is still in progress, without having a definitive conclusion, were not taken into account.

Figure 1. PRISMA method application flowchart.



Note. This graph presents the steps related to the PRISMA method, allowing the systematic processing of the information resulting from the investigative process. Self-made figure.

RESULTS AND DISCUSSION

The expected growth rate in children under 12 years of age is conditioned by the state of nutrition, and will directly affect the assessment in growth tables for sex and age. Up to 10% of pediatric outpatient visits are related to growth retardation in children. Treatment of non-organic growth failure will focus on behavior modification to stimulate appetite and increase oral food intake. The use of stimulants, such as cyproheptadine, can promote weight gain in healthy children and those with medical conditions. This drug has two possible mechanisms of action, directly activating the hypothalamic appetite center and generating effects on serotonin 5-HT_{2C} and histamine H₁ receptors (Lin et al., 2021).

For their part, Harrison et al. (2021), investigated various population groups and their response to the effect of cyproheptadine. In children under 12 years of age with low weight, an improvement was shown in terms of increased appetite, with a greater positive effect related to exposure to the compound greater than three months. In most studies, cyproheptadine was well tolerated, with no information on significant adverse effects in children. In this age group, the most common side effect was sedation, although it was observed that this improved after the start of the medication.

In the investigation carried out by Razzaghy et al., (2018), came to the conclusion that the use of the drug cyproheptadine generated height growth in patients diagnosed with growth hormone insensitivity syndrome, therefore, it was considered that this compound represents an alternative for the use of the factor growth factor type 1 (IGF-I) in this type of complex cases. It was possible to measure the increase in appetite in the patients, but the important outcome was height growth, which increased significantly.

Lemoine et al. (2018), in their research in the pediatric population with Silver-Russell syndrome, established that cyproheptadine is a drug that is effective for this specific group of patients, with significant improvements in growth rate and nutritional status. Prior to initiation of treatment with the target study compound, the research subjects had stagnant weight gain for at least 6 months. These are considered to be favorable results in pediatric patients with a pathological diagnosis, but the need for prospective studies regarding each entity is also stressed.

Grünert et al. (2021) developed a study that focused on analyzing the efficacy of cyproheptadine in increasing appetite in cases of pediatric patients diagnosed with cystic fibrosis. Cystic fibrosis is a multi-organ hereditary genetic pathology that leads to progressive lung disease and nutrient malabsorption. No specific dose-response terms were observed, weight gain could be observed in patients who were exposed to the use of the drug. There was also a trend towards an improvement in lung function during the 12 months of treatment compared to the previous 12 months. In the investigation they concluded that cyproheptadine is effective in improving the nutritional status of pediatric patients with cystic fibrosis with suboptimal nutrition.

In the study carried out by Kazemi et al. (2017), related the use of cyproheptadine with the treatment of patients with low weight and anorexia in the age group of 2 to 10 years. Being an antihistamine drug, it constitutes a medicine that has benefits beyond its purpose of creation. According to the findings of this study, there were no serious side effects related to cyproheptadine. Therefore, considering the acceptable safety of the drug to induce growth in underweight children, especially in pathological cases, the use of the drug in adequate doses is proposed.

A systematic analysis of the French pharmacovigilance database was carried out, where results were found in patients under 4 years of age treated with cyproheptadine. Within the investigation it was found that this drug caused mild important neurological symptoms such as: drowsiness, confusion, seizures, agitation and asthenia. Regarding the overdose, some patients presented anticholinergic syndrome, such as: urinary retention, tachycardia, facial flushing, hyperpyrexia, dry mucosa, dilated pupils, constipation, dizziness, confusion, agitation, seizures, athetosis, hallucinations and delirium, a few hours after cyproheptadine ingestion (Bertrand et al. 2021).

Regarding this topic, Costa et al. (2019), investigated in their investigation possible cases of cyproheptadine overdose. In the first instance, these findings were considered to depend on the practices of caregivers of pediatric patients based on the need for increased appetite and growth efficiency. In contrast, the study found that the majority of cases of poisoning were mainly due to the accidental ingestion of amounts higher than recommended, which mostly evolved adequately, without long-term complications. Most of the cases were related to the male sex, in addition to demographic characteristics, such as location within an urban area.

DISCUSSION

Pediatric patients who come to the clinic for poor growth, regardless of whether they have underlying medical conditions, report having no appetite and their parents express marked concern regarding this issue (Badihian et al., 2018). In this age group it is common to consume small amounts of food, but in this group of patients there is no demand at any time of the day for food rations, in addition to the fact that there is no variety of ingredients in cases of consumption (Kadkhoda et al., 2019). A selected group of pediatric patients can overcome this problem, psychological therapies and nutritional support tend to have a positive impact on the feeding process, supported by parents in this case (Spettigue et al., 2018). As opposed,

Treatment through the use of cyproheptadine has been beneficial in the pediatric population that has difficulties in their normal growth process, in addition to effectively increasing appetite (Cogings et al., 2019). This drug, previously known as an antiserotonergic and antihistamine agent, has been used as an appetite stimulant in patients younger than 12 years of age who were diagnosed with gastrointestinal, oncological, psychiatric, and autoimmune pathologies (Kaenkumchorn et al., 2022). Its mechanism of action is believed to be related to stimulating appetite through receptors in the ventromedial hypothalamus, this is related to its antihistamine and antiserotonergic function. Similarly,

Through investigations carried out over time, mainly in recent years, it has been possible to demonstrate that cyproheptadine is effective for the treatment of pediatric patients who present growth deficits and lack of appetite, which directly interferes with weight gain. (Waxmonsky et al., 2020). These results are independent of the sex of minors, in addition to the fact that it is safe in patients with comorbidities. Similarly, it has been possible to prove its safety and effectiveness in patients under two years of age, with satisfactory results. The adverse events of this medication are mild in the majority of patients, together with the fact that they are overcome with exposure to the compound for more than seven days. In isolated cases, adverse effects have been reported at the level of the nervous system,

The results of weight gain can be evidenced from four weeks of consumption, an assessment four months after the

start of treatment is necessary in each patient, this in order to assess the specific effectiveness in each case. The results are a function of adequate adherence to treatment, in addition to the fact that it has been shown that the most satisfactory weight gain results are in pediatric patients who have previously lost weight in an accelerated manner, which alerts caregivers to take decisive measures.

The drug cyproheptadine is established as an effective compound for the treatment of patients seeking weight gain and appetite, in addition to improving growth figures. We believe that it is still necessary to carry out research focused on recommending cyproheptadine as the first line of treatment in those children who are underweight, regardless of the cause related to this health problem.

CONCLUSION

1. Cyproheptadine is a safe medication and adequately tolerated in all pediatric patients. It presents mild adverse events, which do not threaten the lives of patients, there are isolated cases in which drowsiness, confusion and seizures may occur.

2. This compound is effective for the treatment of patients in need of increased appetite. Its consumption for at least four consecutive weeks can measure the improvement in weight and growth figures in patients under twelve years of age.

3. Satisfactory results are independent of the patient's sex. It is also important to mention that it is an effective medicine in patients who have been diagnosed with gastrointestinal, oncological, psychiatric and autoimmune pathologies.

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