



REVISIONES

Diabetes mellitus in pediatric patients with cystic fibrosis

Diabetes mellitus en pacientes pediátricos con fibrosis quística

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ABSTRACT:

Introduction: Cystic Fibrosis (CF) is a hereditary recessive disease that affects several organs, mainly within the respiratory and digestive systems. Cystic Fibrosis Related Diabetes (CFRD) is one of its main complications.

Objectives: To study the specific complications of pediatric patients suffering from CFRD and how they affect a patient's quality of life. To compare the mortality rates of pediatric patients with CF and with CFRD. To highlight the importance of nurses in the management of pediatric patients with CFRD.

Methodology: A systematic bibliographic review was conducted. We included studies, in English and Spanish, published over the last 10 years, which analysed a population aged between 0 and 9 years old with CF and/or CFRD.

Results: Four databases were used for the systematic search. We analysed 10 articles to address the objectives.

Conclusions: The complications caused by CFRD and the care that patients require affect the patient's quality of life. Progress both with diagnosis and with treatment has improved the quality of life of patients, and has contributed to reductions in the difference between the mortality rates of patients with CF and without CFRD. Nurses who care for children with CFRD are essential as an information resource for patients and their families. Nurses must convey the importance of therapeutic adherence to achieve a better quality of life.

Key words: Cystic Fibrosis, Diabetes Mellitus, new-born, child, quality of life, nursing care.

RESUMEN:

Introducción: La Fibrosis Quística (FQ) es una enfermedad hereditaria recesiva que afecta a varios órganos, fundamentalmente de los aparatos respiratorio y digestivo. La Diabetes Relacionada con la Fibrosis Quística (DRFQ) es una de sus principales complicaciones.

Objetivos: Estudiar las complicaciones específicas de los pacientes pediátricos que padecen DRFQ y cómo afectan a su calidad de vida. Comparar las tasas de mortalidad de los pacientes pediátricos con FQ y con DRFQ. Poner de manifiesto la importancia del personal de enfermería en el manejo de los pacientes pediátricos con DRFQ.

Metodología: Se llevó a cabo una revisión bibliográfica sistemática. Se incluyeron estudios publicados, en inglés y castellano, durante los últimos 10 años, y que analizaban una muestra de población de entre 0 y 9 años con FQ y/o DRFQ.

Resultados: Se utilizaron 4 bases de datos para la búsqueda sistemática. Se analizaron 10 artículos para la resolución de los objetivos.

Conclusiones: Las complicaciones que provocan la DRFQ, y los cuidados que requieren afectan a la calidad de vida de los pacientes. La progresión del diagnóstico y los tratamientos ha hecho que mejore su calidad de vida y que la diferencia de mortalidad entre los pacientes con FQ y con DRFQ se reduzca. El personal enfermero que atiende a los niños con DRFQ es un recurso de información esencial para los pacientes y sus familias. Las enfermeras deben transmitir la importancia de la adhesión a los tratamientos para conseguir una mejor calidad de vida.

Palabras clave: Fibrosis Quística, Diabetes Mellitus, recién nacido, niño, calidad de vida, cuidados de enfermería.

INTRODUCTION

Rare illnesses are defined as those with a low prevalence in the Community (less than five cases per 10,000 inhabitants). Their prevalence is greater among adults than among children, because of the high mortality rates that some pediatric illnesses present. At present, there are known to be around 7,000 rare illnesses ⁽¹⁾.

Cystic Fibrosis (CF) is both a genetic and a chronic illness (autosomal recessive inheritance), which implies a serious health problem ⁽²⁾. It occurs because of a mutation in the CFDR gene in the long branch of chromosome 7. Its incidence varies between 1 out of 3000 and 1 out of 8000 live births. One out of every 25 people is a healthy carrier of this illness ⁽³⁾.

CF is a pathology that affects various organs, mainly the respiratory tract and the digestive system ⁽⁴⁾.

A sticky mucus that is produced in the respiratory tract is the cause of damage to the lungs and their infection, inflammation and the progressive deterioration of their functions ^(4,5).

The most important digestive symptom is pancreatic insufficiency (85-90% of cases), which can affect both exocrine and endocrine pancreatic functions. Alteration of the exocrine function means that the stool has specific properties (Steatorrhea) ^(4,5). Alteration of the endocrine function can result in Diabetes Mellitus ^(4,5). Between 10 and 20% of new-borns with CF present an intestinal obstruction, which on occasions requires a post-birth operation ⁽⁴⁾. A digestive complication of less importance can occur in the biliary tract. The secretion of biliary juices is obstructed or prevented, causing their accumulation in the bile ducts, which can even provoke biliary cirrhosis ⁽⁵⁾. All these digestive system complications (hepatic, pancreatic, and of the intestinal wall ...) mean that patients with CF present poor nutrient absorption, accompanied by weight loss ^(6,7).

Men with CF have problems bearing children as a consequence of the obstruction of the deferent conduits and the epididymis. Women with CF present fewer complications. Fertility is diminished, and although the arrival of spermatozoid to the ovule is not prevented ⁽⁵⁾ women may need assisted reproduction treatments.

Digestive problems, the nutritional state and the reduction of physical activity means a progressive reduction of bone calcium, which increases the likelihood of fractures with age. A small number of people with CF present inflammation in some articulations ⁽⁵⁾.

In addition, these patients present salty sweat that can lead to salt loss and dehydration ⁽⁵⁾.

The objective of the diagnosis and the screening tests is for the earliest possible detection of people living with CF ⁽⁸⁾. Early diagnosis of CF is important to achieve a better quality and a longer life expectancy. To do so, the implementation of pre-natal diagnosis, the blood spot test or heel prick test, and the sweat test are all necessary ⁽⁹⁾. Prenatal diagnosis is based on the study of mutations in patients with CF who wish to bear children ^(3,8). The heel prick test (neonatal diagnosis) is practiced on new-borns within 48-72 hours of life. It tests for the presence of immunoreactive trypsinogen (IRT) in blood samples from the heel ⁽⁹⁾. The sweat test results provide diagnostic confirmation. Patients tested positive in the IRT test must have their chloride and sodium sweat levels tested. Two positive results (> 60 mmol/L) are necessary to confirm a diagnosis of CF ^(8,10).

The three fundamental pillars of treatment for patients with CF are antibiotherapy, respiratory therapy and correct nutrition ⁽⁶⁾. Antibiotherapy is one of the conclusive factors for improvements in the prognosis of CF. This therapy is employed to fight against chronic bronchial infections and exacerbation ⁽⁶⁾. Respiratory physiotherapy is based on daily bronchial cleansing to prevent the accumulation of mucosity in the bronchia and to avoid infection. There are different respiratory physiotherapy techniques such as postural drainage, percussion (or clapping) and the active cycle ^(6,7). Treatment has to be individualized for correct nutrition depending on the degree of affection. In general, it is recommended that patients with CF increase their energetic intake by 120-150% dependant on age and sex, for which purpose a high calory diet is advised such as butter, mayonnaise, sauces ... In the case of pancreatic exocrine insufficiency, it would at first be necessary to ingest pancreatic enzymes half-way through the meal. Insulin should be administered to treat pancreatic insufficiency. In addition, increased salt intake would be fundamental, due to the important losses of chloride and sodium, due to sweating and especially in summer, and in dry climates ^(6,7).

In the following table, the principal clinical symptoms of CF are shown alongside their treatment (Table 1).

Diabetes Mellitus refers to a group of physiological symptoms of different etiology and physiopathology, characterized by metabolic glucose imbalance, among which is found Cystic Fibrosis Related Diabetes (CFRD) ⁽¹¹⁾. With the progression of CF, a reduction in insulin secretion takes place, which leads to an imbalance of carbohydrate in the metabolism that can evolve into diabetes. This complication is at a later stage of the illness, in such a way that the percentage of patients with CF and affected by Diabetes increases with age ^(4,5,11,12). Although CFRD has aspects in common with other types of Diabetes, it has important differences that must be considered for its correct diagnosis and treatment (Table 2) ^(13,14).

Table 1: Principal clinical symptoms of Cystic Fibrosis and its treatment.
CF: Cystic Fibrosis

Affected system	Clinical Symptoms	Treatment
Respiratory tract	Accumulation of mucus Infection of the respiratory tract	Respiratory physiotherapy Antibiotherapy
Digestive system	Exocrine pancreatic insufficiency. Endocrine pancreatic insufficiency	Pancreatic enzymes Insulin Surgical intervention

	Intestinal obstruction Weight loss	Increased energetic requirements
Reproductive system	Reduced fertility in men	Assisted reproduction techniques
Locomotive system	Reduction of serum calcium levels	Increased ingestion of calcium-rich foods. Physical exercise
Excretory system	Chloride and sodium loss	Increased salt intake

Table 2: Comparison between Diabetes Mellitus 1, Diabetes Mellitus 2 and Cystic Fibrosis Related Diabetes. DM: Diabetes Mellitus. CFRD: Cystic Fibrosis Related Diabetes

	DM Type 1	DM Type 2	CFRD
Start	Acute	Insidious	Insidious
Autoimmune etiology	Yes	No	No
Insulin secretion	Severe reduction	Slight reduction	Moderate reduction
Treatment	Insulin	Diet, oral medication and insulin	Insulin
Microvascular complications	Yes	Yes	Yes, but less
Macrovascular complications	Yes	Yes	No

As commented earlier, patients with CFRD have a significantly reduced quality of life and their diagnosis and treatment require the coordinated work of various medical disciplines. The great burden of care for patients with CFRD, above all in the case of pediatric patients, and the need for education in self-administered care in the family requires trained nursing professionals.

The absence of hospital protocols and specialized scientific publications led us to a bibliographic review with the following objectives: 1) To study the specific complications and how they affect the quality of life of pediatric patients with CFRD. 2) To compare the mortality rates among pediatric patients with only CF and pediatric patients with CFRD. 3) To highlight the importance of nursing staff in the management of pediatric patients with CFRD.

MATERIAL AND METHOD

The bibliographic review was carried out in the months of May and June, 2017.

Database searches for the selection of the information were conducted on the following platforms: Dialnet, Cuiden, Medline, SciELO, Enfispo, Biblioteca Cochrane Plus, PubMed and Google Académico with the following terms taken from structured vocabulary and trilingual DeCS (Health Science Descriptors): Fibrosis Quística, Diabetes Mellitus, recién nacido, lactante, preescolar, niño, calidad de vida, cuidados

de enfermería, Cystic Fibrosis, Diabetes Mellitus, new-born, infant, preschool, child, quality of life and nursing care. Results were only found on the following databases: Dialnet, Biblioteca Cochrane Plus, PubMed and Google Academic.

The selection criteria defined to carry out the search established as criteria for inclusion: articles published between 2008 and 2017, written in Spanish or in English. The exclusion criteria rule was that at least one of the principal descriptors would not appear (Cystic Fibrosis or Diabetes Mellitus) in the titles of the publications and that the age of the population under study was equal or older than 10 years old.

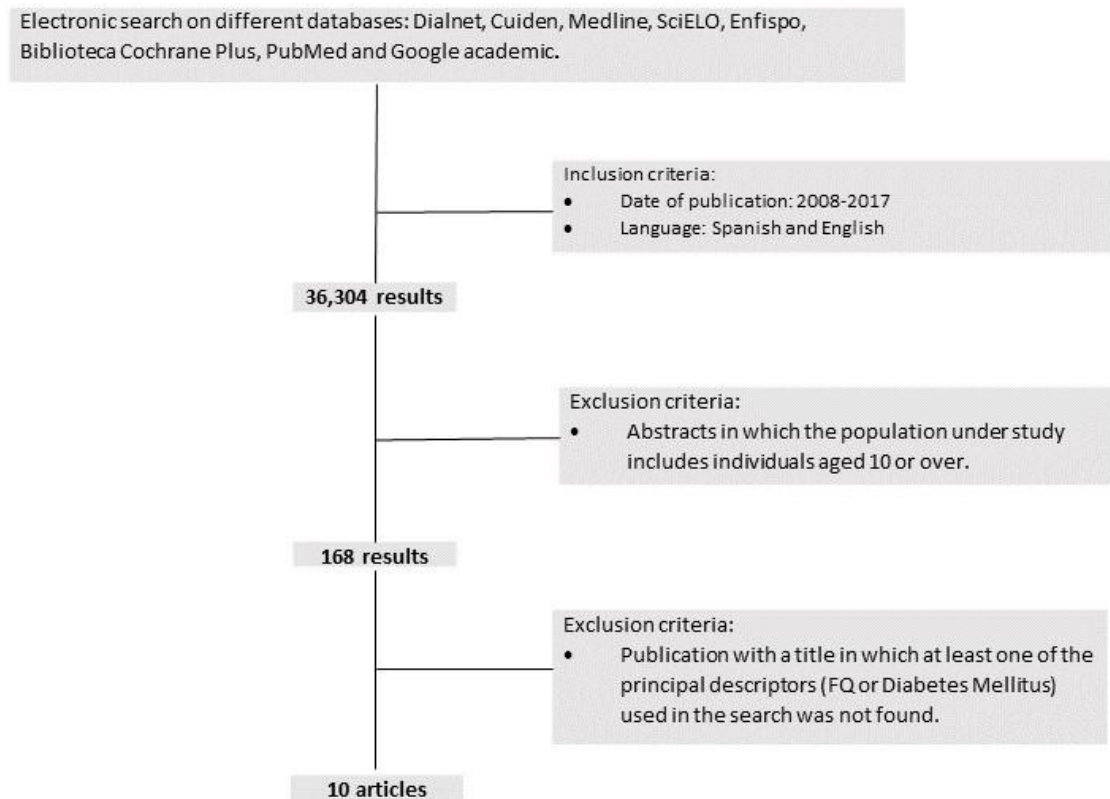
The search in the different databases returned a total of 36,304 results (Figure 1). The authors conducted a critical reading of all the titles, discarding those without at least one of the principal descriptors (Cystic Fibrosis or Diabetes Mellitus) obtaining a total of 168 publications. After reviewing the summaries, 158 articles were excluded because they centred on the study of individuals over 9 years in age. Finally, a total of 10 studies were selected for the literature review (Figure 1).

RESULTS

In this planned review, ten studies were analysed that complied with the previously established selection criteria. From among the selected studies, seven were narrative reviews, two were systematic reviews and one was a retrospective cohort study. The characteristics and the principal results of the studies under review are summarised in Table 3.

When studying the specific complications and their effect on the quality of life of pediatric patients with CFRD, the bibliographic review highlights that a five-year presence of Diabetes is usually necessary before microvascular complications are evident, for which reason their appearance among pediatric patients is rare. Among the microvascular complications, retinopathy affects approximately 10-23% of patients with CFRD and, although rarely serious, they should receive a dilated eye exam every year. Early nephropathy is usually characterized by microalbuminuria. An isolated sample of urine has to be collected and its albumin/creatinine ratio tests to conduct the test. Finally, the peripheral neuropathy has to be controlled each year, through a neurological examination and an examination of the feet ⁽¹³⁾. The amount of time that the patients should pass to perform these tests means that their quality of life is negatively affected.

Figure 1: Flow diagram of the selection process of the articles for the systematic review



Another specific complication of patients with CFRD is diabetic ketoacidosis, although it is not frequent in the child population with CFRD, as children still show a degree of endogenous insulin secretion. Insulin-induced hypoglycemia has also been reported, at all times related with increased administration⁽¹⁵⁾. Hyperglycemia can occur during acute illness or due to systematic treatment with glucocorticoids, which means that the need for insulin increases abruptly, by a factor of approximately two-to-four^(13,14,16). The need for regular self-administration to control glycemia, learning a proper self-administration technique, and knowing what action to take when faced by these complications are additional factors that deteriorate the quality of life of these patients.

In addition to the above, patients with CFRD present the most severe form of pulmonary illness, that is due to a reduction of the forced inspiratory volume in the first second (FEV1), increased pulmonary exacerbation, and increased prevalence of the pathogens *Pseudomona aeruginosa* and *Burkholderia cepacia* in the sputum^(13,17). The health-care team, the family and the patient all have to be very aware that lung illness is the principal cause of death among these patients, which makes it necessary to practice exercises and respiratory physiotherapy, so that the pulmonary function is not affected. They should therefore spend lengthier periods of time on those specific health-care exercises.

All these complications have a prominent influence on the quality of life of pediatric patients affected by CFRD, due to the amount of care that they need to prevent those complications, to delay their effects for as long as possible, and when they do appear, to perform the best possible follow up, to avoid serious complications.

In various studies the mortality rate between pediatric patients with only CF and pediatric patients with CFRD is compared: the mortality rate between people with CFRD is around four-to-six times higher than those patients with only CF ^(13,18,19). In a retrospective cohort study completed in the United Kingdom between the years 1996 to 2005, with an average population monitoring time of over 2.9 years, the mortality rate of a population of study of 5,892 people with CF and CFRD, aged between 0 and 65 years old, was studied. According to this study, the mortality rate increased with age, in both groups. In the group of children, as in the other age groups, the mortality was slightly higher among patients with CFRD (of the 2,161 children commencing the study, the number of deaths at the end of the follow up was 14 children) ⁽¹⁹⁾.

The presence of CFRD, in both pediatric and adult patients, provoked a deficient pulmonary function, weight loss, protein catabolism and a poor nutritional condition, all of which led to an increase in morbidity and death ^(13-16,20).

Although mortality has continued to be higher among children with CFRD than among children with only CF, over recent years, a constant reduction in the mortality rate among patients with CFRD has occurred, probably attributable to early diagnosis and treatment ^(13,14,21).

Finally, in some of the studies under review, the importance of the role of nursing staff is highlighted in the management of pediatric patients with CFRD. The patients with CFRD should be treated and advised by a multidisciplinary team familiar with the physiopathology of CFRD. However, the great number of care practices that have to be administered to these patients, such as teaching the measurement of glycemia, appropriate food, respiratory exercises ..., means that the role of the nurse is fundamental for improvements to the quality of life ^(13,17).

The nursing staff that treat these patients should be properly trained and knowledgeable of the care that they will deliver and to do so they should continually refresh their knowledge ^(16,22).

The nurse should educate the patient and the family in proper glycemic control, and insulin dosing and administration, because optimal glycemic control is fundamental over time, to diminish the risk of microvascular complications. Specific recommendations are also necessary that will teach them to relate the dosages of insulin with the carbohydrates present in the food, because it is essential that children maintain a proper weight and Body Mass Indice (BMI) ⁽¹⁵⁾.

In short, the nursing staff must educate, support, advise, and motivate not only the patients, but also their parents and close family, so that they are an important and a good source of support for the patients and so that they gain greater awareness of the illness ^(13,14).

Table 3: Selected characteristics of the articles included in the study. I.F.: Impact Factor

Author/ Year	Design	I.F.	Selected results
Laguna T.A, Nathan B.M, Moran A. (13) 2010	Narrative Review	6.71	<ul style="list-style-type: none"> * The impact of CFRD increases with age, but cases of CFRD have been diagnosed in children younger than 3 months. * Mortality rates are higher among patients with CFRD than among patients with CF without Diabetes Mellitus. Early diagnosis and proper treatment reduce the mortality rates among patients with CFRD. * Among the possible vascular complications, patients with CFRD present microvascular complications (retinopathy and nephropathy), but no macrovascular complications. The microvascular complications do not develop until 5 years have passed since the onset of Diabetes. * CFRD should be monitored by a multi-disciplinary team of health professionals knowledgeable of CF, Diabetes and CFRD.
O’Riordan S.M.P, Robinson P.D, Donaghue K.C, Moran A. (14) 2009	Narrative review	3.48	<ul style="list-style-type: none"> * CFRD principally affects patients that present the most serious mutations of CF. * According to a study of the University of Minnesota (U.S.A.), the prevalence of CFRD, in a sample of 61 children between 5 and 9 years old, was 9%. * Patients with CF and without Diabetes present variable levels of insulin sensitivity, but the patients with CF and with Diabetes are resistant to insulin. * The diet of patients with CFRD should have higher amounts of calories, a high fat content, a high protein content and salt intake should be increased in accordance with the needs of the patient. * During an acute illness, the patient will require large doses of insulin, as much as even four times the previous dosage of insulin. * Parents and family are essential and should be included in the management plan to guarantee acceptable levels of care at home.

<p>Ode K.L, Moran A. (15) 2013</p>	<p>Narrative review</p>	<p>19.74</p>	<ul style="list-style-type: none"> * CFRD is a more common complication than CF. * Fluctuation of glucose levels that usually precede Diabetes are more common in children younger than 10 years old. * Although cases have been described of Diabetes in very small children with CF, diabetes rarely occurs in 10-year-old children. The prevalence in this age range was approximately 1-5% and was higher among girls than among boys (in a sample of 63 children aged between 0-9 years old; the prevalence among girls was 3% and among children was 0%). * The prevalence of CFRD increases with age.
<p>Moran A, Brunzell C, Cohen R.C, Katz M, Marshall B.C, Onady G, et al. (16) 2010</p>	<p>Narrative review</p>	<p>5.79</p>	<ul style="list-style-type: none"> * The presence of CFRD is associated with an increase of morbi-mortality, characterized by a state of insulin deficiency, protein catabolism, weight loss, increased frequency of pulmonary exacerbations and reduction of the pulmonary function. * A multidisciplinary team of health professionals, which has experience with both CF and Diabetes, is fundamental to conduct good follow up of patients with CFRD. * Proper communication between professionals and between professionals and patients is essential, as poor communication leads to stressful situations. * The role of the nursing team is to centre on stimulating and supporting the patient and their family.
<p>Cohen Cymber-knoh M, Shoseyov D, Kerem E. (17) 2011</p>	<p>Narrative review</p>	<p>2.69</p>	<ul style="list-style-type: none"> * CFRD affects 9% of children. It has been linked to a reduction of the pulmonary function and a higher risk of death associated with respiratory insufficiency. * The glucose oral tolerance test is used for early diagnosis of CFRD. * The multidisciplinary team, in charge of follow up and control of patients with CFRD, should have an experienced endocrinologist, as an integral member of the team. * The difference between the mortality of

			patients with CF and with and without Diabetes is diminishing.
Kelly A, Moran A. (18) 2013	Narrative revision	4.72	<ul style="list-style-type: none"> * CFRD occurs with greater frequency in serious mutations of CF and is related to exocrine pancreatic insufficiency. * The mortality rate among patients with CFRD is almost six times higher than it is among patients with CF without diabetes. * The improvement of survival is related to early identification and treatment. * The worsening of the pulmonary function is linked to the presence of CFRD, regardless of patient age.
Chamnan P, Shine B.S.F, Haworth C.S, Bilton D, Adler A.I. (19) 2010	Retro- spective cohort study	5.79	<ul style="list-style-type: none"> * The monitoring period was 2.9 years. There were 2,161 children between 0 and 9 years of age with both CF and CFRD; the mortality in this group is notably higher among the children with CFRD than among those patients with only CF. * The mortality rates among patients with CFRD increased with age. * Diabetes is linked to a four-fold increase in the risk of death in relation to those patients with no Diabetes.
O'Riordan S.M.P, Dattani M.T, Hindmarsh P.C. (20) 2010	Narrative review	1.72	<ul style="list-style-type: none"> * CFRD is usually asymptomatic and can remain undetected up to four-years before the diagnosis. * CFRD, as well as affecting people with serious mutations of CF, is also related with exocrine pancreatic insufficiency. * The onset of CFRD is insidious and can be asymptomatic for years. * Following the recommended treatment depends on the complexity and the duration of the treatment.
Moran A, Dunitz J, Nathan B, Saeed A, Holme B, Thomas W. (21) 2009	Systematic revision	5.79	<ul style="list-style-type: none"> * The pulmonary function is significantly affected among individuals with CFRD, for which reason the treatments in use today are much more aggressive than in the past. * The early diagnosis and the proper treatment of CFRD have played an important role in the increase of survival among patients. * Mortality rates among both different sexes was notably reduced and almost disappeared.
Illán Noguera	Systematic review	0,12	<ul style="list-style-type: none"> * Nursing care should be dedicated to improving the quality of life of the

C.R, Álvarez Martínez M.C, Martínez Rabadán M, Pina Díaz L.M, Guillén Pérez F, Bernal Barquero M, et al. (22) 2014			children and, to strengthening adherence to treatment. * Nurses are the principal source of support for patients and their families. * Nurses should be the source of support and information for children and parents. They should help patients to understand that treatment is basic in order to have a better quality of life.
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DISCUSSION

Most of the articles reviewed in this study coincide in so far that Cystic Fibrosis Related Diabetes (CFRD) is the most common morbidity related condition of Cystic Fibrosis (CF) ^(13-18,20,21) present in around 20% of adolescents and 40-50% of adults diagnosed with CF ⁽¹³⁾.

Some of them make the point that CFRD occurs mainly in patients that present the most serious CF mutations ^(13,14,18,20) -i.e. classes I, II and III ⁽¹³⁾. These mutations are related to pancreatic insufficiency ^(13,14,18).

Some of the works highlight that the prevalence of CFRD increases with age ^(14,15,20,21), but there are discrepancies in the data between the different studies. The prevalence of CFRD among American children is 9% ^(14,20) while among Danish children it is 3% ⁽¹⁵⁾. Among American adolescents, the prevalence of CFRD is 26% ^(14,20) and among Danish adolescents it is 15% ⁽¹⁵⁾. With regard to the adult population, the data for the American population show prevalence values of 50% ^(14,20), and those of the Danish population fluctuate between 40 and 50% ⁽¹⁵⁾. These discrepancies are certainly due to markedly different social and cultural lifestyles between the North American and the Danish populations.

Some of the studies point out that CFRD develops in an insidious way meaning that the patients are asymptomatic over several years ^(13,16,18,20). The absence of symptoms should be no obstacle to the application of measures that permit early diagnosis and appropriate treatment, as both of these measures have contributed to an increasing life expectancy over the years ^(13,15,21). In this sense, various works recommend conducting the Oral Glucose Tolerance Test (OGTT) on children suffering from CF at an early age, but differ at the age they are practiced. The American Diabetes Association (ADA), Cystic Fibrosis Foundation (CFF) and International Society for Pediatric and Adolescent Diabetes (ISPAD) advise starting annual screening at the age of 10 years old, due to the appearance of diabetes at that age on rare occasions ⁽¹³⁻¹⁸⁾. In contrast, a study carried out by researchers at the University of Minnesota and another led by the researcher Katie Larson Ode advised starting the annual screening with OGTT earlier, at the age of 6 years old ^(15,18,21). The reason is that, based on those studies, CFRD progresses much earlier in children of 6-to-9 years old

that obtain abnormal OGTT results than it does in children with normal tolerance to glucose ⁽¹⁵⁾. The discrepancies between these studies ^(16,19,22) may be due to the cost/benefit balance. Advancing screening by 4 years would imply costs that are perhaps not justified in view of the small number of patients whose OGTT results might be abnormal and on which action could be taken to delay the development of Diabetes. Surprisingly, none of the studies examined this aspect. Even so, it is suggested that the recommendations from ADA, CFF and ISPAD be followed, because they are important institutions centred on the study of CF and diabetes.

In relation to the complications that these patients had, all the articles that were consulted and that refer to the complications coincide. With regard to the respiratory complications, the forced inspiratory volume in the first second (FEV1) was reduced as the pathogens in the respiratory tract and the pulmonary exacerbations increased ^(13,17). It was highlighted with regard to microvascular and macrovascular complications, in all the articles, that this type of patient only suffers from microvascular complications, such as retinopathy, nephropathy, and neuropathy ^(13,14,16,18,20).

It was affirmed in all the studies that compared the mortality rates of the population with CF and the population with CFRD that the mortality rates were higher among the population with CFRD ^(13,16,18,19). In addition, they maintained that early diagnosis and correct treatment is helping to reduce mortality rates among the patients with CFRD ^(13,17,21), which means that the difference between the patients with CF and the patients with CFRD is seen to diminish to the point where it is almost non-existence ⁽²¹⁾.

Finally, most of the studies highlight that people living with CFRD should be assisted by a professional multidisciplinary team that should have broad knowledge and experience in the treatment of Diabetes and CF ^(13,16,17). Among this group, the role of the nurse can be highlighted. This professional is in charge of providing much-needed support and appropriate care-related knowledge on care to both the patient and to the close family ^(16,20,22). Among these care services, the correct administration of medicine can be highlighted, such as antibiotics in the case of pulmonary exacerbations, in order to improve the respiratory function and insulin, as well as explanations on the importance of keeping to the course of treatment for their health and control of the illness. Nurses should also provide information on appropriate diets that should be followed, so that they maintain a good weight, a good nutritional state and optimum levels of glucose in the blood.

The selection criteria applied in the review might have given rise to certain limitations in the study. In the first place, the age that the population under study should have. The reference population is pediatric. In Spain, this population encompasses the new born child up until the child is 14 years old, but only children between 0 and 9 years old have been considered in this study. The reason is that in the review of the different studies, the age ranges were observed to be between 0 and 9 years old and between 10 and 20 years old, for which reason children aged between 10 and 14 years old were in the age range of the adolescent population.

In second place, the date of publication of the articles, which was limited to the past 10 years, might have supposed some loss of information. Even so, it was considered that earlier studies would be obsolete and would not provide up-to-date information for the review. It may also be highlighted that most of the studies employed for the completion

of this systematic review were other reviews, although a retrospective cohort study was also used.

Finally, the scarcity of current investigative studies on CFRD is notable and, if we centre solely on those conducted by Spanish health professionals, they are even still scarcer. It is therefore necessary to return to this line of investigation; increasingly so nowadays, as the life expectancy of these patients is longer, resulting in increasingly frequent cases of Diabetes Mellitus.

CONCLUSIONS

Having completed the systematic bibliographic review on Cystic Fibrosis Related Diabetes (CFRD) among pediatric patients (between 0 and 9 years in age), it can be concluded that CF damages the pancreas, negatively affecting the exocrine and endocrine function. As the pathology evolves, the endocrine function is notably affected, which ultimately provokes Diabetes Mellitus.

Patients with CFRD present a series of acute complications such as ketoacidosis diabetes (quite rare among children) and insulin induced hypoglycemia. They also present a series of chronic complications, such as microvascular complications, protein catabolism, weight loss and increased pulmonary exacerbations.

These complications and their care mean that patient quality of life is affected, but it is being improved, due to the advances in the diagnosis and the new treatments. These advances have also meant that the difference in mortality rates between patients with CF and patients with CFRD are narrowing.

The nursing team that attends to children with CFRD is the principal information resource for these patients and their families. Nurses have to help them understand that closely following their treatment is basic to having a better quality of life.

In short, education for health is fundamental in these patients, because, as well as everything related to other CF-related complications, it is necessary to teach patients how to use insulin, the proportions in which it is to be used, and a proper carbohydrate intake in the diet to satisfy that dietary requirement.

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