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EPIDERMMOLYSIS BULLOSA: A COMPREHENSIVE APPROACH ON ITS ETIOPATHOGENESIS, CLINICAL IMPLICATIONS AND TREATMENT

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Abstract: Introduction: Epidermolysis Bullosa (EB) is a congenital, rare, chronic, systemic, serious, non-contagious and autoimmune condition, considered a mechano-bullous dermatosis. Characteristically, affected individuals develop vesicles or blisters on the skin and mucous membranes, spontaneously or after minimal trauma. Therefore, EB appears to be a relevant topic for scientific investigations. **Objective:** Understand the pathophysiological aspects, causes, symptoms, diagnosis and treatment of epidermolysis bullosa, as well as its clinical implications. **Methodology:** The present study is a bibliographic review article related to Epidermolysis Bullosa, carried out between June and August 2024, 9 articles were selected, in which the review of articles was carried out in the electronic library database Scientific Eletronic Library Online (SCIELO), Journal of the USP School of Nursing, Latin American and Caribbean Literature in Health Sciences (LILACS), ``*Revista de Enfermagem do Centro-Oeste Mineiro*``, Estima–Brazilian Journal of Enterostomal Therapy, ``*Revista Portuguesa de estomatologia*``, Dental medicine and Maxillofacial Surgery, Electronic Annals, IX EPCC–International Meeting of Scientific Production UniCesumar and PubMed Central (PMC). The following selection criteria were defined: full texts, books, analysis and systematic reviews, between 2008 and 2021, in Portuguese and English. Results: EB is a disease associated with skin fragility, which is why its sufferers generally present vesicles or blisters on the skin and mucous membranes, spontaneously or after minimal trauma. It appears that the main manifestations are oral, ranging from the formation of blisters on the mucosa to erosions and denudation of the tongue and mucous membranes. For this reason, it is essential that dental follow-up is carried out early in patients with EB, so that it occurs in a preventive and resolutive manner. However, its treatment is not restricted to dentists alone, it occurs in a multidisciplinary manner, involving psychologists, nutritionists, physiotherapists, hematologists, dermatologists and nurses. In it, palliative measures are used to minimize risks such as infection, formation of exudate, foul odor, and ineffectiveness in preventing future wounds on delicate skin. It is also known that the better the treatment, the better the quality of life of those with EB. Regarding the prognosis, it varies according to the type of EB, the time for diagnosis and the correct treatment. In general, individuals with EB have a normal life expectancy. **Conclusions:** It is concluded that EB has multiple and major impacts on the lives of its sufferers and therefore requires early diagnosis and adequate and effective treatment in order to reduce its complications and improve the quality of life of patients.
Keywords: Epidermolysis Bullosa, mechano-bullous dermatosis, genodermatosis

INTRODUCTION

Epidermolysis Bullosa (EB) is a congenital, rare, chronic, systemic, serious, non-contagious and autoimmune condition, considered a mechano-bullous dermatosis. Characteristically, affected individuals develop vesicles or blisters on the skin and mucous membranes, spontaneously or after minimal trauma and, in more severe cases, they affect mucous membranes such as the mouth and esophagus. In other words, it comprises a group of diseases characterized by skin fragility, and can also affect mucous membranes and other organs of the body.

Rare diseases are generally triggered by genetic mutations that lead to pathophysiological changes in the body and are characterized by low prevalence. EB affects approximately one in every 50,000 births and several distinct clinical phenotypes

(more than 30) are observed, all according to the level of cleavage and its clinical and molecular characteristics. In Brazil, there are no consistent epidemiological data on this important disease. According to data from the national registry of the National Association on EB (DEBRA) from 2018, there are 794 reported cases of EB throughout the country, with Bahia being the third state with the highest number, surpassed only by São Paulo and Minas Gerais.

EB is considered a serious pathology if not diagnosed and treated early, as it has a high risk of infection and a high mortality rate in the neonatal period. It occurs in all races present in different countries and its incidence is equal between males and females.

EB is classified according to its type of genetic inheritance, plus the anatomical distribution of the lesions, plus the association of morbidity associated with the lesions, distinguishing three main groups, which are: Epidermolysis Bullosa Simplex (EBS), Epidermolysis Bullosa Junctional (EBJ) and Dystrophic Epidermolysis Bullosa (EBD) which is subdivided into dominant (EBDD) and recessive (EBDR). Two other types are also worth highlighting, namely: Kindler Syndrome (KS) and Acquired Epidermolysis Bullosa (EBA).

This condition presents an important clinical challenge, both in terms of diagnosis and treatment, making it a relevant topic for scientific investigations due to its prevalence and complexity. In this literature review article, we will explore EB in depth, addressing its pathophysiological aspects, causes, symptoms, diagnosis and treatment, as well as its clinical implications. Through this investigation, we seek to contribute to a more comprehensive understanding of this condition and provide relevant information that can benefit both healthcare professionals and patients facing this medical challenge.

Additionally, we will discuss the long-term prognosis for patients with EB and how appropriate treatment can positively influence quality of life.

REVIEW OF LITERATURE:

Regarding the epidemiological data on EB, it is noted that this condition occurs in all races around the world and has the same incidence in males and females. (ANGELO, Marla Monica Fagundes Cardoso et al., 2012). It affects different age groups, generally starting at birth or in childhood and evolving with age. (BEGA, Aline Gabriela et al., 2015). The term EB refers to mechanobullous genodermatoses, that is, skin trauma of different intensities that can give rise to blisters, the severity of which will depend on the mutation involved in the pathogenesis. It commonly manifests itself in childhood, when babies are carried by their parents. (BENÍCIO, Claudia Daniella Avelino Vasconcelos et al. 2016)

The etiopathogenesis of EB is associated with the degeneration of proteins and lipid deficiency, making the basal cells fragile, which, when ruptured, allow hyaluronic acid to fill the spaces produced, triggering the formation of blisters, as they are characterized by epidermal detachment. complete layer or one of its layers, due to changes in keratin and collagen, in regions with friction or sudden changes in temperature. Therefore, the blisters can be superficial or deeper, and can be painful and bloody. (ANGELO, Marla Monica Fagundes Cardoso et al., 2012).

The diagnosis of EB is generally made soon after birth, through biopsy and histopathological study, in addition to clinical and laboratory analysis, that is, mapping through immunofluorescence, mutational analysis and electronic microscopy, the latter being considered the gold standard. Furthermore, it is important to diagnose the subtype and to do so, consider the phenotypic characteristics, such

as the specific extracutaneous manifestations and the mode of genetic inheritance, the types of mutations, the target protein and its relative expression in the skin. (RODRIGUESA, Naiara Santana et al., 2021). Furthermore, there is a lack of knowledge among professionals about the disease, as well as a lack of contact with it, a challenge in defining the diagnosis and initiating care. (XAVIER, Livia Maria Batista, 2020).

As it is an uncommon disease, little known and with a great variation in the clinical picture of the different subtypes, it is important that health professionals know the main classifications of EB, which are: Epidermolysis Bullosa Simplex (EBS), Junctional Epidermolysis Bullosa (EBJ), Dystrophic Epidermolysis Bullosa (EBD) which is subdivided into dominant (EBDD) and recessive (EBDR), these being hereditary, Kindler Syndrome (KS) and Acquired Epidermolysis Bullosa (EBA). (DA SILVA, Ronaldo Antonio et al., 2020).

EBS occurs in the majority of cases, its inheritance is autosomal dominant in which intra-epidermal cleavage occurs in the lower portion, due to alteration of the keratin determined by chromosomal mutation of genes 5 or 143, resulting in lesions that do not leave scars or cause nail or nail changes. dental. (BEGA, Aline Gabriela et al., 2015).

EBJ has an autosomal recessive origin, generally due to a mutation in the laminin gene, in which cleavage is located in the dermoepidermal junction of the lamina lucida of the basement membrane zone. This variation produces serious effects, with the occurrence of anemia, synechiae, growth retardation, dysproteinemia, cicatricial alopecia, palmoplantar hyperkeratosis, and can be fatal. In fact, laryngeal involvement, when it occurs, is generally in this subtype. (ANGELO, Marla Monica Fagundes Cardoso et al., 2012).

Dominant or recessive EBD is autosomal in nature with mutations in type IV collagen in general. The EBDR subtype is more mutilating, the cleavage is dermoepidermal with a defect in the structure of partial or total collagen VII and in the cellular release of synthesized collagen. This form leads to the appearance of synechiae on the feet and hands with functional uselessness, esophageal stenosis, causing anemia, growth retardation, dysplastic teeth and atrophic scars on the scalp. The patient usually does not reach adulthood. Esophageal bubbles generally evolve into scars and strictures, causing dysphagia and this being one of the biggest problems in EBDR. In EBDD, the cleavage is dermoepidermal below the lamina densa of the basement membrane zone.

Clinically, nails may appear dystrophic or absent, with the presence of hypochromic and atrophic macules (albo-papuloid lesions), milia, hypertrophic scars and mild oral involvement. (ANGELO, Marla Monica Fagundes Cardoso et al., 2012).

KS is a mixed type with several types of cleavage with bleb formation generally occurring in the lucid layer, and can clinically simulate the three types of congenital EB. It is characterized by the formation of acral blisters, fusion of fingers and toes, poikiloderma and photosensitivity. (SECCO, Izabela Linha et al., 2019).

Regarding EBA, it appears that the clinical manifestations differ from those mentioned previously and are milder. It is a rare autoimmune form that occurs due to autoantibodies in the lamina and sublamina densa. Blisters develop in adulthood in areas of trauma that leave atrophic scars and milia. (XAVIER, Livia Maria Batista., 2020).

The findings of subtype genes have a practical role in the development of accurate prenatal diagnoses and gene therapy. (XAVIER, Livia Maria Batista., 2020).

As seen, most of the time it is a hereditarily transmitted disease. Therefore, the consanguinity of the parents and the history of similar diseases in the family are factors to be taken into consideration. (XAVIER, Livia Maria Batista., 2020).

In general, the places most affected by EB are: the extensor surface of the elbows, knees, ankles, hands and buttocks. Among the most common signs and symptoms are cutaneous: blisters, ulcerations, large scars on the surface of the body, cicatricial baldness and dystrophic folds. Extracutaneous findings can involve organs such as the eyes, oral mucosa, teeth, esophagus, gastrointestinal tract and genitourinary tract. (BEGA, Aline Gabriela et al., 2015).

More broadly, we can classify the manifestations of EB into:

General clinical manifestations: vary according to the severity of the disease, the most common being atrophic scars, bacterial infections, nail dystrophy, syndactyly, hand and foot deformities, hyperpigmentation, milia formation, alopecia, ankylosis, facial deformity and early development of skin cancer. It is worth mentioning that squamous cell carcinoma of the skin develops more frequently in patients with EBDR, when compared to other types. Furthermore, a multifactorial complication that can occur mainly in EBDR and EBJ is anemia that can occur due to iron deficiency, due to blood loss that occurs with the rupture of blisters or due to inflammation, associated with the healing of chronic wounds, resulting in in circulating cytokines that probably inhibit erythropoiesis and reduce the efficiency of iron utilization. (ANGELO, Marla Monica Fagundes Cardoso et al., 2012).

Manifestations of the gastrointestinal tract (GIT): dysphagia, odynophagia, choking, intestinal constipation, laryngeal stenosis and nasal vestibule stenosis may occur, and any part of the GIT can be injured, with the exception of the pancreas and liver. It is worth mentioning that the most serious complication is esophageal stenosis. (FANTAUZZI, Rodrigo Santana et al., 2008).

Urinary tract manifestations: the most common clinically are hematuria, dysuria and urethral meatus stenosis. In very serious cases urinary sepsis may occur. (ANGELO, Marla Monica Fagundes Cardoso et al., 2012).

Ophthalmological manifestations: can occur acutely such as conjunctival hyperemia, redness, tearing, blisters, vesicles and erosions on the cornea, associated with acute inflammation or damage to the surface of the eye and chronically such as scars on the cornea, formation of symblepharons. (ANGELO, Marla Monica Fagundes Cardoso et al., 2012).

Oral manifestations: EB affects all oral surfaces and is the target of the greatest commitments and challenges encountered by people with EB. They can range from the formation of blisters on the mucosa to erosions and denudation of the tongue and mucous membranes. Furthermore, ankyloglossia, microstomia, changes in the development of occlusion, atypical swallowing, muscle imbalance, maxillary atrophy and mandibular prognathism, predisposition to the development of oral carcinoma, impacted and supernumerary teeth may occur. In EBJ, the occurrence of enamel hypoplasia is common, a characteristic that is pathognomonic of its subtypes. In EBDR, the dentition is severely damaged and enamel hypoplasia is common. (ANGELO, Marla Monica Fagundes Cardoso et al., 2012).

As it was evidenced, changes in the oral cavity are the most common and cause the most pain for patients. For these reasons, oral health ends up being neglected and hygiene is not carried out correctly. Simply using toothbrushes can lead to blisters and gum inflammation. Furthermore, patients who

have deformities in their hands and fingers due to EB have greater difficulty with oral hygiene. In this context, the appearance of cavities, the presence of biofilm and even the development of severe periodontal diseases is common, often leading to partial or total edentulism. (RODRIGUESA, Naiara Santana et al., 2021).

In view of the above, it is essential that dental monitoring is carried out early in patients with EB. It is important that there is preventive treatment, with a qualified dentist and frequent consultations in order to provide guidance on correct and adapted hygiene, reduction of the consumption of cariogenic foods, frequent cleaning and application of fluoride, restoration of enamel and dentin defects and extractions of the most affected teeth in order to eliminate ongoing sources of oral infections. (ANGELO, Marla Monica Fagundes Cardoso et al., 2012).

Therefore, patients with EB require daily care from birth, where delay in diagnosis or lack of preparation by the healthcare team can have impactful consequences on the individual's life. Even after rapid diagnosis, the complexity of dealing with this type of rare disease requires specific care, although the mother assumes the role of main caregiver, family support is essential, as the birth of a child with EB is a traumatic event for a family, requiring individualized support to enable the provision of the best care for the baby, which has a major impact on the life of the patient and their family. as well as family members and caregivers, whether due to physical pain, emotional suffering or economic impact. Another complicating aspect in the care of patients with EB is the lack of knowledge on the part of health professionals regarding the particularities of the disease, the complexity of the dressing and the lack of communication between the multidisciplinary team and the family. This pathology causes much greater negative impacts when it comes to patients, who suffer from pain, fears about the use of medications, the non-acceptance of self-image and the limitation of specialist professionals in the area, which together promote an environment of distress to the patient. patient generating psychological problems, such as fear, anxiety, frustration, anger and depression, which often increases with age, due to the altered perception of body image and the increase in deformities in the extremities, which makes them increasingly incapacitated for their activities, with the presence of chronic pain and worsening wound healing, requiring psychosocial care and strengthening monitoring in PHC, the patient's gateway to the SUS.(DA SILVA, Ronaldo Antonio et al., 2020)

This way, specialist professionals, who are scarce, state the need for more planned and organized work, to facilitate decision-making. Among these professionals, those with the greatest knowledge about EB are doctors and nurses, as they provide direct assistance to the patient, but multidisciplinary support is essential, with psychologists, nutritionists, dentists, physiotherapists, hematologists, dermatologists, nurses, among others. others, for a better quality of individuals affected by EB. (ANGELO, Marla Monica Fagundes Cardoso et al. 2012)

EB has no cure, treatment consists of controlling the autoimmune nature of the disease through medications, such as corticosteroids and immunosuppressive drugs, however the use of products to treat wounds in EB has presented problems such as: risk of infection, formation of exudate, foul odor, and not effective in preventing future wounds on delicate skin. That is why palliative measures are used such as treating wounds, including appropriate dressings, puncturing blisters and using aluminum chloride to prevent sweating and the formation of too

much heat, preventing their spread and preventing infection.

In addition to guidance regarding the diet and care and contact at home, as simple tasks, such as crawling, walking, wearing certain types of clothes or shoes require effort and can cause the formation of blisters, therefore, it requires modifications to the environment such as the use of special beds, seats in bathtubs, wheelchairs, shoes, among others. Correct guidance for the family regarding the appropriate rupture of blisters is preferably done before bathing, using disposable needles or scissors with tips, duly disinfected. The use of non-adherent gauze must be part of these patients' daily lives to repair injuries. It is important to remember that the skin must also be cared for, using complexes of essential fatty acids to protect it. Over time, the appearance of blisters generally decreases, disappearing without leaving scars, which contributes to the average life expectancy of most of these patients being normal. (BEGA, Aline Gabriela et al. 2015)

Despite this, patients with epidermolysis bullosa can undergo standard anesthetic instrumentation, albeit with a greater risk of complications. It is important that every instrument that comes into contact with the skin and mucosa (face mask, laryngoscope and endotracheal tubes) must be well lubricated. Lubricated gauze would be recommended to fix the electrodes for cardiac monitoring, sphygmomanometer and venous access. Complications such as esophageal perforation, pneumomediastinum, pneumoperitoneum and mediastinitis must be diagnosed early, as they can be fatal. (FANTAUZZI, Rodrigo Santana et al.2008)

Regarding oral health, periodic monitoring at the dental office is necessary, with the purpose of preventing, diagnosing and treating oral pathologies. Before starting dental treatment, it is essential to contact the clinical team responsible for the patient. This is because epidermolysis bullosa causes medical, physical and social limitations in the patient, making dental treatment difficult. Therefore, it is important that the patient's contact with the dentist occurs early so that careful prevention can be established, avoiding oral problems caused by poor oral hygiene. Although rehabilitative dental treatment is possible, it is quite exhausting, involving risks for the patient. Therefore, health promotion and prevention of oral diseases must be emphasized and started as early as possible. extreme care from the professional to avoid trauma and ulcerations. Even with the risks of bullous formations in the oral region, it is important that children are breastfed, the sucking movements, although slower, stimulate the anatomical structures, preparing children for the chewing act and establishing an efficient chewing process, swallowing will be able to be carried out appropriately and without compensatory pressure, reducing its impact on the patient. Because, during puberty, greater nutrition is required, if supplementation is not sufficient, gastrostomy feeding may be necessary, being a valuable tool for drug administration, but it is important that this procedure is carried out before the onset of growth retardation, so as not to harm the patient's quality of life. (ANGELO, Marla Monica Fagundes Cardoso et al. 2012)

The prognosis varies considerably and is based on the EB subtype and the patient's overall health. Patients with EBS have a normal life expectancy, however the existence of complications can compromise these data. Patients with EBJ have a high risk of neonatal death or death in the first years of life. Patients with EBD have a greater risk of death from the second decade of life, mainly due to metastasis from squamous cell carcinoma. (XAVIER, Livia Maria Batista; 2020)

CONCLUSION

It is concluded, therefore, that EB is a serious pathology that must be diagnosed and treated early, as it has a high risk of infection and a high mortality rate in the neonatal period. As it is a disease associated with skin fragility, sufferers generally present vesicles or blisters on the skin and mucous membranes, spontaneously or after minimal trauma. Regarding symptoms, it appears that the main manifestations are oral, ranging from the formation of blisters on the mucosa to erosions and denudation of the tongue and mucous membranes. For this reason, it is essential that dental follow-up is carried out early in patients with EB, so that it occurs in a preventive and resolutive manner.

EB has no cure, but there is treatment that consists of controlling the autoimmune nature of the disease. Treatment is multidisciplinary, involving psychologists, nutritionists, dentists, physiotherapists, hematologists, dermatologists and nurses. In it, palliative measures are used to minimize risks such as infection, formation of exudate, foul odor, and ineffectiveness in preventing future wounds on delicate skin.

Regarding the prognosis, it varies according to the type of EB, the time for diagnosis and the correct treatment. In general, individuals with EB have a normal life expectancy.

Therefore, it appears that EB has multiple and major impacts on the lives of its sufferers and therefore requires early diagnosis and adequate and effective treatment in order to reduce its complications and improve the quality of life of patients.

REFERENCES

ANGELO, Marla Monica Fagundes Cardoso et al. Manifestações clínicas da epidermólise bolhosa: revisão de literatura. **Pesquisa Brasileira em Odontopediatria e Clínica Integrada**, v. 12, n. 1, p. 135-142, 2012.

BEGA, Aline Gabriela et al. Epidermólise bolhosa: revisão de literatura. **Anais Eletrônico, IX EPCC–Encontro Internacional de Produção Científica UniCesumar**, 2015.

BENÍCIO, Claudia Daniella Avelino Vasconcelos et al. Epidermólise bolhosa: foco na assistência de Enfermagem. **Estima–Brazilian Journal of Enterostomal Therapy**, v. 14, n. 2, 2016.

DA SILVA, Ronaldo Antonio et al. A vivência do cuidado materno a uma lactente com epidermólise bolhosa. **Revista de Enfermagem do Centro-Oeste Mineiro**, v. 10, 2020.

FANTAUZZI, Rodrigo Santana et al. Manifestações otorrinolaringológicas e esofágicas da epidermólise bolhosa. **Revista Brasileira de Otorrinolaringologia**, v. 74, p. 657-661, 2008.

OLIVEIRA, Thais M. et al. Clinical management for epidermolysis bullosa dystrophica. **Journal of Applied Oral Science**, v. 16, p. 81-85, 2008.

RODRIGUESA, Naiara Santana et al. Epidermólise bolhosa–uma série de 33 casos. **Revista Portuguesa de Estomatologia, Medicina Dentária e Cirurgia Maxilofacial**, v. 62, n. 1, p. 35-41, 2021.

SECCO, Izabela Linha et al. Cuidados de enfermagem a neonato com epidermólise bolhosa: relato de caso. **Revista da Escola de Enfermagem da USP**, v. 53, p. e03501, 2019.

XAVIER, Livia Maria Batista. Epidermólise bolhosa: organização dos serviços de atenção à saúde e perfil epidemiológico dos pacientes atendidos em Salvador, Bahia. 2020.