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IMPROVING THE DIAGNOSIS AND TREATMENT OF GESTATIONAL TROPHOBLASTIC DISEASE: CHALLENGES AND PERSPECTIVES

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Abstract: Goal: Investigate gestational complications associated with Gestational Trophoblastic Disease (GTD), as well as explore effective diagnostic, therapeutic and preventive strategies. Method: A bibliographic review was carried out using the PubMed - MEDLINE database. 42 articles were initially identified, of which12were selected based on strict inclusion and exclusion criteria. The inclusion criteria covered articles published between 2014 and 2024 that dealt with topics related to DTG. Duplicate articles, publications only in summary format, and works that did not directly address the topic investigated or that did not meet other inclusion criteria were excluded. Result: The analysis concluded that the beta-HCG test is recommended as an initial diagnostic method due to its simplicity and cost-effectiveness. Early diagnosis proved to be crucial for the clinical improvement of patients, allowing early therapeutic interventions. However, despite not reducing the incidence of subsequent gestational trophoblastic neoplasia (GTN), early diagnosis is associated with a better prognosis when neoplastic complications arise. Final considerations: Continuous training of healthcare professionals is essential to implement these evidence-based practices, thereby improving the quality of care and outcomes for patients affected by GTD.
Keywords: gestational Trophoblastic Disease; Early diagnosis; DTG treatment.

INTRODUCTION

The DTG represents a pathological condition characterized by an exacerbated proliferation of trophoblasts. This condition can be classified into benign categories, such as hydatidiform mole, which can be partial (MHP) or complete (CHM), and malignant categories, such as gestational trophoblastic neoplasms (GTN). Early diagnosis and adequate follow-up are crucial for a favorable

prognosis, with high cure rates when treated appropriately and in a timely manner (Heller, 2017).

For early diagnosis, it is essential to evaluate the patient's clinical and symptomatic conditions, including the exacerbated increase in beta-human chorionic gonadotropin (B-HCG) and the presence of vaginal bleeding. Furthermore, histopathological and radiological examinations are essential for both the diagnosis and monitoring of the disease, enabling appropriate management and ensuring good results (Akakpo et al., 2017).

Although the probability of favorable results is almost 100% for DTG, it is imperative to make the diagnosis correctly and early. It is necessary to initially determine whether the condition is of benign or malignant origin and, based on this assessment, immediately initiate appropriate treatment. Treatments can range from chemotherapy interventions to surgical procedures, in addition to including longitudinal monitoring of the patient after the implementation of therapeutic resources (Heller, 2017).

The diagnosis of GTD, which develops from an abnormal proliferation of trophoblastic cells in the placenta, is made through the patient's clinical history, which involves symptoms such as vaginal bleeding during the gestational period and elevated B-HCG. Due to the low incidence of GTD cases, diagnosis can be challenging and subject to confusion with other differential diagnoses, such as epithelioid trophoblastic tumor (ETT), which can be misdiagnosed as an ectopic pregnancy. B-HCG measurement, combined with ultrasound and Doppler, is essential for the diagnosis and monitoring of TET (Akakpo et al., 2017; Fang et al., 2014).

Therefore, the aim of this literature review is to comprehensively and critically examine the existing literature to understand the pregnancy complications associated with GTD, exploring diagnostic, therapeutic and preventive strategies, and providing a detailed overview of the risks and challenges faced by women with this condition.

METHODOLOGY

This narrative bibliographic review was structured according to the criteria of the PVO strategy, which encompasses the Population or research problem, the Variables under study, and the expected Outcome. The study was guided by the question: "What are the main challenges faced in the early diagnosis and longitudinal monitoring of Gestational Trophoblastic Disease, and how can the most recent evidence in the literature guide more effective clinical approach strategies?"

To collect relevant data, searches were carried out in the PubMed - MEDLINE (Medical Literature Analysis and Retrieval System Online) databases, using search terms combined with the Boolean operators "AND" and "OR". This initial search resulted in the identification of 42 articles.

The inclusion criteria defined for the review were: articles written in English, published between 2014 and 2024, that addressed topics related to Gestational Trophoblastic Disease. Specific types of studies were selected, including randomized clinical trials, original articles, case reports, and systematic reviews, all available in full. The exclusion criteria applied included duplicate articles, those published only in abstract form, and those that did not directly address the problem investigated or that failed to meet the other inclusion criteria.

After careful application of the inclusion and exclusion criteria, 12 articles were selected to form the collection of this study. This careful selection ensured the inclusion of relevant and up-to-date literature, allowing an in-depth analysis of the challenges in

diagnosing and monitoring Gestational Trophoblastic Disease, and facilitating the identification of effective clinical approaches based on the most recent evidence.

DISCUSSION

ADVANCES IN EARLY DIAGNOSIS OF GESTATIONAL TROPHOBLASTIC DISEASE

Despite recent advances in the treatment of GTN, this pathology remains rare and little known globally, which often leads to late diagnoses and suboptimal treatments for affected patients. In this context, the use of the beta-hCG (human chorionic gonadotropin hormone) test is recommended as the initial diagnostic method due to its simplicity, cost-effectiveness and ability to detect the disease early, in addition to monitoring treatment and monitoring possible recurrences (Braga et al., 2019).

Burny et al. (2016) proposed a classificatory method based on hCG measurements to assess the risk of developing GTN in women after performing curettage or suction due to a hydatidiform mole. This method stratifies risk into three levels: low risk, with follow-up for up to 21 days; intermediate risk, requiring active monitoring for more than 21 days before any therapeutic decision; and high risk, where treatment is necessary after 21 days of follow-up.

Furthermore, to refine GTN therapeutic approaches, immunohistochemistry and tissue DNA genotyping emerge as valuable diagnostic tools. These techniques are particularly useful for differentiating the histopathological types of tumors, offering more precise insights for treatment (Hui, 2019). However, research such as that by Sun et al. (2015) suggest that the development of GTN may be intrinsic to the nature of complete mole and therefore would not be significantly affected by early diagnosis. This study proposes that, although early diagnosis may influence clinical presentation, the incidence of postmolar GTN appears not to be impacted by early detection of complete hydatidiform mole.

In most cases, the diagnosis of GTD is made in the first trimester of pregnancy, predominantly through ultrasound. The typical "honeycomb" sonographic feature indicative of a complete mole is rarely observed during this period. Commonly, there is an absence of fetal parts and a cystic appearance of the placenta, which can make diagnosis difficult. Therefore, it is essential that molar pregnancies are confirmed by histological examination after evacuation for a miscarriage or when a molar pregnancy is suspected (Ngan et al., 2021).

After diagnosis, close monitoring of the patient is crucial due to the risk of progression to GTN. In a study carried out by Gueye et al. (2016) in low-income countries, the FIGO 2000 criteria were slightly modified to include: persistence of stable high β-hCG levels for two consecutive tests within four weeks; 10% increase in β-hCG level in two consecutive tests within two weeks; any elevation in β-hCG level for six months after mole expulsion; and histopathological diagnosis of choriocarcinoma.

It is essential to highlight that GTN can arise from any type of pregnancy, including miscarriage, ectopic pregnancy, full-term/pre-term pregnancy and, most notably, after a hydatidiform mole. GTN must also be considered in cases of metastatic neoplasia in women of reproductive age with an unknown primary site, especially if there is a history of recent pregnancy. Furthermore, it is important to remember that a simple hCG test can be decisive not only to diagnose this neoplasm, but also to monitor treatment, confirm cure and detect recurrences early, enabling effective rescue therapy (Braga et al., 2019).

EVOLUTION AND CHALLENGES IN THE MANAGEMENT OF GESTATIONAL TROPHOBLASTIC TUMORS

Malignant phenomena associated with gestational trophoblastic disease can manifest years after the initial gestational event, with significant variations depending on the different subtypes. Invasive moles, for example, are known to occur approximately six months after a previous molar. In contrast, it is believed that choriocarcinoma may have a potential for malignancy after a prolonged period, extending for years or even decades after the initial event (Silva et al.). Placental Site Trophoblastic Tumors (PSTT) and epithelioid trophoblastic tumors, rarer subtypes, have a higher rate of resistance to chemotherapy treatment. The presence of a gestational history of more than 48 months and stage 4 of the disease are considered relevant prognostic markers (Hancock; Tidy., 2020).

The need for specialized assistance in histopathology reference centers is fundamental and contributes to improving health indicators. Traditionally, gestational trophoblastic disease is considered to have a good prognosis, conditioned by the quality of diagnosis and treatment and strict surveillance in the post-remission period. Studies carried out in Morocco revealed that 72% of patients were cured within a one-year follow-up period. However, late diagnosis resulted in less favorable prognoses (Kachani; Alami; Bezad., 2017). Furthermore, abandonment of post-treatment follow-up represents a significant challenge to the continuity of medical care. Strategies such as reminders via text messages and phone calls have been implemented to improve adherence to follow-up (Kachani; Alami; Bezad., 2017).

FINAL CONSIDERATIONS

The rarity of GTD often complicates early diagnosis, which can be mistakenly confused with other medical conditions. Despite significant progress in treatment, GTD remains a rare and often underdiagnosed condition, which often leads to late diagnoses and treatments that are not fully adequate. This situation highlights the critical importance of future studies focused not only on improving diagnostic tools, but also on educating healthcare professionals about the peculiarities of this condition to ensure more effective identification and management. Greater awareness and understanding of DTG is essential, aiming to improve the quality of care provided and, consequently, the quality of life of patients.

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