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PSORIASIS AND BILIARY PATHOLOGY: FEATURES OF THE COURSE AND THERAPY

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Abstract: Diseases of the gallbladder (GB) and biliary tract (GDT) are a very pressing problem for modern medicine, due to their extremely wide prevalence and great difficulties for clinicians in differentiated recognition and treatment of this pathology. In the overall structure of gastroenterological morbidity, they account for more than 40% and have a clear tendency towards progressive growth. Currently, in Russia, the incidence of gallbladder and gallbladder pathology ranges from 29.4 to 45.5 cases per 1000 adult population, and in most cases, loss of ability to work occurs many times during the year. Chronic acalculous cholecystitis (CAC) occupies a central place among biliary pathologies, diagnosed in 55-63% of cases. Timely diagnosis of chronic bile duct disease with recognition of the biliary dysfunctions that invariably accompany it is a necessary guarantee of the effectiveness of individual etiotropic treatment of patients. However, the treatment of chronic biliary tract and dysfunctional disorders is not a solved problem for clinicians, since the diagnostic techniques used do not allow one to clearly differentiate the pathology of the biliary tract.Among the large arsenal of laboratory and instrumental research methods, the method of fractional duodenal intubation (FDS) with subsequent study of the physico-chemical composition of bile is a distinctive feature of the entire diagnosis of chronic bile duct disease. This is practically the only method that allows you to objectively assess not only the kinetic ability of the gallbladder and the tone of the sphincter apparatus, but also to identify pathology at the level of changes in the microscopic and biochemical parameters of the resulting bile. The biochemical composition of bile is a highly informative indicator of the state of the hepatobiliary system, allowing one to diagnose not only the stage of the developed disease, but also to identify pre-disease. Mathematical calculation of FDZ graphs using the method of N.G. Kamaeva and M.E. Semendyaeva (1979), significantly improved the diagnostic capabilities of classical duodenal intubation, since the quantitative characteristics of choledynamic processes made it possible to more accurately differentiate various forms of dyskinetic disorders, determine the degree of bile deficiency and differentiate individual pathogenetic therapy.
Key words: It must be emphasized that given the abundance of official bile secretory and choleretic drugs, as well as highly mineralized natural waters, their use is of an empirical nature and in the available literature there is no data on their effect on the pathogenetic links of the bile excretion process using mathematical analysis of fractional duodenal intubation graphs.

The purpose of this work was to study the nature of clinical, biochemical and functional disorders of bile secretion in patients with chronic biliary disease with secondary biliary dysfunctions and to evaluate the influence of some herbal remedies (decoction of cultivated chicory root, hepatofalk-plant) on the functional state of the hepatobiliary system in experiment and clinic.

The problem of improving the treatment of psoriasis remains relevant today, which is due to the stable, high level of morbidity in people of working age and the significant frequency of detection of comorbid conditions in patients with psoriasis. According to clinical and statistical data, psoriasis affects from 3 to 7% of the world's population; the population frequency of psoriasis in Central

European countries ranges from 2 to 4.7%. The proportion of psoriasis among other skin diseases is high; cases of severe forms of this dermatosis, difficult to treat in patients with concomitant pathologies, and often leading to disability, have become more frequent.

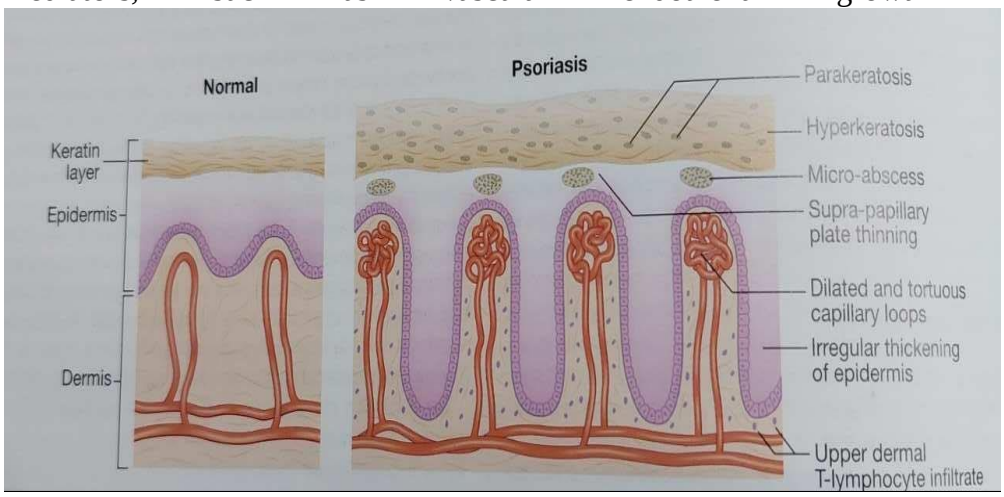
Currently, psoriasis is defined as a chronic dermatosis of a multifactorial nature, which is characterized by hyperproliferation of epidermal cells, impaired keratinization, an inflammatory reaction in the dermis, as well as changes in various organs and systems. The disease is characterized by a variety of factors that influence its development and the occurrence of exacerbations: stress, infections, alcoholism, smoking, as well as the frequent presence of comorbid conditions such as hyperlipidemia, obesity, diabetes mellitus, in which psoriatic manifestations are the result of a long-term inflammatory process accompanied by the development of complex immunopathological and metabolic disorders associated with increased tissue destruction and uncontrolled epidermal proliferation. With psoriasis as a systemic pathology, changes are noted in the state of the hepatobiliary system and the digestive system, which negatively affects the course of dermatosis. A number of authors emphasize the need to diagnose and treat pathology of the liver and biliary system in patients with psoriasis to optimize standard antipsoriatic therapy and prevent unwanted side effects. At the same time, there is insufficient data in the literature on methods for screening biliary pathology in patients with psoriasis and on the presence of "trigger" factors that contribute to both the exacerbation of the psoriatic process and the formation of pathological changes in the biliary system; about the frequency and nature of these disorders in patients with manifestations of dermatosis of varying severity, there is practically no data on the detailed characteristics of the clinical and functional state of the gallbladder and biliary tract, the biochemistry of bile and blood serum in patients with psoriasis, there are insufficient recommendations for therapy in patients with psoriasis with various types of comorbid biliary pathology. The listed aspects of the problem served as the basis for formulating the purpose and objectives of this study.

Psoriasis is a chronic inflammatory, hyperproliferative skin disease. It is characterised by well-defined, erythematous scaly plaques, particularly affecting extensor surfaces, scalp and nails, and usually follows a relapsing and remitting course Psoriasis affects approximately 1.59% -3% of popula tions of European ancestry but is less common in Asian, South American and African populations. It occurs equally in both sexes and at any age: although it is uncommon under the age of 5 years, more than 50% of patients present before the age of 30 years. The age of onset follows a bimodal distribution, with an early-onset type in the teenage or early adult years, often with a family history of psoriasis, a more severe disease course and strong HLA association. The later-onset type is typically seen between 50 and 60 years, usually without a family history and with a less severe disease course.

Both genetic and environmental factors are important. Twin studies show concordance rates of 60%-75% and 15%-20% for psoriasis arising in monozygotic and dizygotic twins, respectively. The age at onset and severity of disease are often similar in familial cases. If one parent has psoriasis, the chance of a child being affected is about 15%-20%; if both parents have the disease, this rises to 50% and the risk is increased further if a sibling also has the disease.

Variants of the HLA-C region within the major histocompatibility complex (MHC) on chromosome 6 account for almost half of the heritability of psoriasis. However, at least 70 other loci are implicated, with susceptibility variants that lie within or close to genes involved in regulating epider- mal barrier function, antigen presentation, cytokine production, notably IL-13 and IL-23, T-cell differentiation (especially Th-1 and Th-17 subsets) and nuclear factor kappa B (NFxB) signalling. Some of the loci that pre- dispose to psoriasis overlap with those implicated in Crohn's disease,ankylosing spondylitis and psoriatic arthritis. Although the theory is controversial,stress may exacerbate psoriasis in susceptible individuals and psoriasis is itself a cause of psychological stress.Likewise,there is a higher incidence of smoking and heavy alhocol consumption in patients with psoriasis but unclear whether this is cause or effect.There is also an association between psoriasis and metabolic syndrome.

The main features are: keratinocyte hyperproliferation and abnormal differentiation,leading to retention of nuclei in the stratum corneum; inflammation, with a T-cell (mainly activated Th-1 and Th-17) lym- phocytic infiltrate and release of cytokines and adhesion molecules, such as interleukins (including IL-17, IL-23 and IL-12), TNF-α, IFN-y and intercellular adhesion molecule (ICAM)-1; vascular changes, with tortuosity of dermal capillary loop vessels and release of mediators, such as vascular endothelial growth factor (VEGF).



The initiating event for psoriasis is unknown. Disordered cell prolifera- tion is a key feature: this was previously thought to be the primary event but is now considered to be secondary to inflammatory change. The transit time for keratinocyte migration, from basal layer to shedding from stratum corneum, is shortened from approximately 28 to 5 days, so that immature cells reach the stratum corneum prematurely. Proliferation rate is also increased in non-lesional skin but to a lesser extent. Similarly, even the clinically unaffected nails of patients with psoriasis grow more quickly than those of controls.

While immunological factors clearly play a key role in psoriasis, the precise mechanisms of disease initiation and the sequence of events that lead to psoriasis are not fully defined. Therapeutic efficacy through targeted biological inhibition of the effects of key cytokines,notably TNF-a, IL-17, IL-23 and I-12,continues to provide major insight into the pathagenesis of psoriasis and the pathways and mechanisms involved. This is the most common presentation and usually represents more stable disease.The typical lesion is a raised,well-demarcated erythematous plaque of variable size.In untreaed disease,silver/white scale is evident and more obvious on scraping the surface,which reveals bleeding points(Auspitz sign).The most common sites arethe extensor surfaces,notably elbows and knees,and the lower back. Others include:

***Scalp:** involvement is seen in approximately 60% of patients. Typically, easily palpable, erythematous scaly plaques are evident within hair-bearing scalp and there is clear demarcation at or beyond the hair margin. Occipital involvement is common and difficult to treat. Less often, fine diffuse scaling may be present and difficult to distinguish from seborrhoeic dermatitis. Involvement of other seborrhoeicsites', such as eyebrows, nasolabial folds and the pre-stemal area, is not uncommon and again may be confused with seborrhoeic dermatitis. Temporary hair loss can occur but permanent less is unusual.

***Nails:** involvement is common, with thimble pitting, onycholysis, subungual hyperkeratosis and periungual involvement.

***Flexures:** psoriasis of the natal cleft and submammary and axillary folds is usually symmetrical, erythematous and smooth, without scale.

***Palms:** psoriasis of the palms can be difficult to distinguish from eczema.

Guttae psoriasis

This is most common in children and adolescents and is often the inital presentation. It may present shortly after a streptococcal throat infection and evolves rapidly. Individual lesions are droplet-shaped, small (usually less than 1 cm in diameter), erythematous, scaly and numerous. An episode of guttate psoriasis may clear sponta neously or with topical treatment within a few months, but UVB phototherapy is often required and is highly effective. Guttate psoriasis often heralds the onset of plaque psoriasis in adulthood.

Erythrodermic psoriasis

Generalised erythrodermic psoriasis is a medical emergency

Pustular psoriasis

Pustular psoriasis may be generalised or localised.Generalised pustular psoriasis is uncommon ,unstable and life-threating.It will often emergein the context plaque disease and the onset is usually sudden,with large numbers of small,sterile pustules on an erythematous background,often merging into sheets ,with waves of new pustules in subsequent days .The patient is usually febrile and systemically unwell,and this must be dealt with as a medical emergency.Unstable pustular psoriasis may be precipitated as a rebound phenomenon following either topical or systemic glucocorticoid use in a patient with psoriasis .Localised pustular psoriasisof the palms and soles(palmoplantar pustulosis) is more common,chronic and closely associated with smoking;small,sterile pustules and erythema develop and resolve with pigmentation and scaling.A localised form of sterile pustulosis of a few digits(acropustulosis) can also occur.It is unclear whether these localised forms of pustulosis are truly psoriatic.

Artropathy

Between 5% and10% of individuals with psoriasis develop an inflammatory arthropathy,which can take on a number of patterns.Joint involvement is more likely in patients with psoriatic nail disease.

Investigations

Skin biopsy is not usually required but may be performed if there is diagnostic doubt.An infection screen,particullary throat swab and/or serology for recent streptococcol infection,may be informative in guttate psoriasis.Assesment of impact on life using the DLQI and diesease extent using PASI(Psoriasis Area and Severity Index) is essential.Due to the association of psoriasis with metabolic syndrome,comorbidities and cardiovascular risk factors should be assessed and managed along usual lines.HIV testing should be considered in severe or recalcitrant psoriasis.

Conclusion: In patients with psoriasis, changes in the structural and functional state of the gallbladder wall and biliary system, motor disorders, impaired emptying of the gallbladder and biliary tract, and features of the biochemical and colloidal properties of bile, the severity of which correlated with the severity of the skin process, were identified for the first time. In patients with varying degrees of severity of psoriasis, the need for therapy taking into account comorbid disorders of the biliary system, inclusion of cholekinetic drugs (extract of fumaria, milk thistle fruits) in combination with a choleretic (artichoke extract) into the treatment complex, which helps optimize therapy (achieve clinical remission, improving quality of life, lengthening the period of remission and reducing the number of relapses). Bile flow is disturbed as a result of the gall bladder not working well. This process causes the intestines to rest. As a result of intestinal dysfunction, toxic substances are absorbed into the blood and cause psoriasis symptoms to appear on the skin.

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