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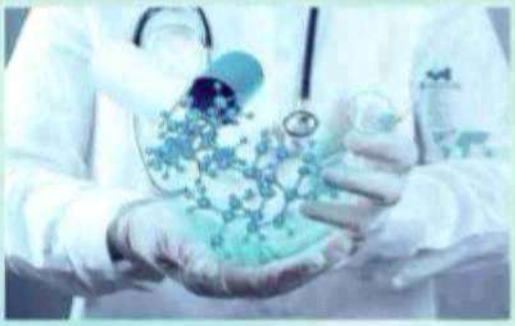

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NEW DAY IN MEDICINE

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IMMUNOLOGICAL INDICATORS OF THE DEVELOPMENT OF HEPATORENAL SYNDROME IN LIVER CIRRHOSIS

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✓ ***Resume***

Hepatorenal syndrome (HRS) is a serious complication of liver cirrhosis characterized by progressive renal failure, leading to high morbidity and mortality rates. The underlying mechanisms of HRS involve complex interactions between hemodynamic changes, systemic inflammation, and immune dysregulation. Immunological factors, particularly pro-inflammatory cytokines and immune cell alterations, play a crucial role in the pathogenesis of HRS by exacerbating renal dysfunction and systemic vasodilation.

Findings indicate that HRS patients exhibit significantly elevated levels of IL-6 and TNF-α, along with increased regulatory T-cell populations and monocyte activation markers. Elevated CRP and procalcitonin levels correlate with worsening renal function, emphasizing the role of systemic inflammation in HRS progression.

Keywords: Hepatorenal syndrome, liver cirrhosis, immunological markers, inflammation, cytokines, endotoxemia, renal dysfunction.

ИММУНОЛОГИЧЕСКИЕ ПОКАЗАТЕЛИ РАЗВИТИЯ ГЕПАТОРЕНАЛЬНОГО СИНДРОМА ПРИ ЦИРРОЗЕ ПЕЧЕНИ

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✓ ***Резюме***

Гепаторенальный синдром (ГРС) является серьезным осложнением цирроза печени, характеризующимся прогрессирующей почечной недостаточностью, что приводит к высоким показателям заболеваемости и смертности. Основные механизмы ГРС включают сложные взаимодействия между гемодинамическими изменениями, системным воспалением и иммунной дисрегуляцией. Иммунологические факторы, в частности провоспалительные цитокины и изменения иммунных клеток, играют решающую роль в патогенезе ГРС, усугубляя почечную дисфункцию и системную вазодилатацию.

Результаты показывают, что у пациентов с ГРС наблюдаются значительно повышенные уровни ИЛ-6 и ФНО-α, а также повышенные популяции регуляторных Т-клеток и маркеров активации моноцитов. Повышенные уровни СРБ и прокальцитонина коррелируют с ухудшением функции почек, подчеркивая роль системного воспаления в прогрессировании ГРС.

Ключевые слова: гепаторенальный синдром, цирроз печени, иммунологические маркеры, воспаление, цитокины, эндотоксемия, почечная дисфункция.

JIGAR SIRROZIDA GEPATORENAL SINDROMI RIVOJLANISHINING IMMUNOLOGIK KO'RSATKICHLARI

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✓ ***Resume***

Gepatorenal sindromi (GRS) jigar sirrozining jiddiy asorati bo'lib, surunkali buyrak yetishmovchiligi bilan tavsiflanadi. Bu esa yuqori kasallanish va o'lim ko'rsatkichlariga olib keladi. GRS ning asosiy mexanizmlari gemodinamik o'zgarishlar, tizimli yallig'lanish va immunitetning buzilishi o'rtasidagi murakkab o'zaro ta'sirlarni o'z ichiga oladi. Immunologik omillar, xususan, yallig'lanishga qarshi sitokinlar va immunitet hujayralarining o'zgarishi buyrak funksiyasining buzilishi va tizimli tomirlarning kengayishini kuchaytirib, GRS patogenezida hal qiluvchi rol o'ynaydi.

Izlanishlar shuni ko'rsatadiki, GRS bilan og'rigan bemorlarda IL-6 va TNF-a ning sezilarli darajada yuqori darajalari, shuningdek, tartibga soluvchi T-hujayra populyatsiyasi va monosit faollashuv belgilari ko'paygan. Yuqori SRO va prokalsitonin darajalari buyrak funksiyasining yomonlashishi bilan bog'liq bo'lib, GRS rivojlanishida tizimli yallig'lanishning rolini ta'kidlaydi.

Kalit so'zlar: Gepatorenal sindrom, jigar sirrozi, immunologik belgilar, yallig'lanish, sitokinlar, endotoksemiya, buyrak disfunksiyasi.

Relevance

Liver cirrhosis is a chronic condition leading to severe systemic complications, including hepatorenal syndrome (HRS). HRS is primarily a functional renal failure resulting from profound vasodilation in the splanchnic circulation, leading to reduced renal perfusion [1-3]. Increasing evidence suggests that immune system alterations contribute significantly to the pathogenesis of HRS. This study examines immunological indicators associated with HRS progression.

Pathophysiology of HRS and Immunological Involvement: HRS is categorized into Type 1 (rapidly progressive) and Type 2 (chronic and less severe). Immunological disturbances play a crucial role in HRS development, including:

Pro-inflammatory cytokines: Elevated levels of tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-1 beta (IL-1β) are observed in patients with cirrhosis and HRS, indicating systemic inflammation [4].

Endotoxemia and Bacterial Translocation: Increased intestinal permeability in cirrhotic patients facilitates bacterial translocation, leading to endotoxin-induced immune activation [5].

Oxidative Stress and Nitric Oxide Dysregulation: Reactive oxygen species (ROS) and excessive nitric oxide (NO) production contribute to vasodilation and renal hypoperfusion.

Altered Immune Cell Function: Impaired neutrophil, monocyte, and T-cell responses result in ineffective bacterial clearance and chronic inflammation.

Renal failure is a common complication of patients with cirrhosis, occurring in 1 in 5 patients with cirrhosis, and 20-50% of hospitalized patients have renal dysfunction. It is decompensated of cirrhosis the most serious from complications one and death or liver to transplantation take will come [10]. Sharp kidney deficiency short time inside glomerular filtration decrease in speed (GFS). is considered This is the liver cirrhosis with hurt in patients wide spread out and heavy is a complication. In cirrhosis sharp kidney deficiency diuretics too much except a lot use, from the stomach and intestines blood leaving is big in volume paracentesis, bacterial infections and others because of surface coming acute kidney failure. AKF was in serum creatinine exceeding 1.5 mg/ l with determined. But blood in serum creatinine of the amount change cirrhosis has been in patients common muscle of mass decrease and this disease with hurt of patients fed up not eating as a result surface the arrival also for AKF sure diagnostic important have it's not [9]. That's why for in cirrhosis hepatorenal syndrome (HRS) and kidney of deficiency the term his diagnosis criteria changed. Last data that's it showed that it is cirrhosis has been in patients cytokines level increase kidney deficiency with depend. In cirrhosis kidney lack of interleukin-18 (IL-18), interleukin-6 (IL-6), interleukin-20 (IL-20) of biomarkers use this complication reasons to differentiate help will give and disease consequences forecast about information gives [8]. Cytokines a lot functional proteins is a cell inside molecules as important role plays.They are immune cells, that's it including T- cells and macrophages by work is released and interleukins IL-1, IL-2, IL-6, IL-12, IL-17, interferon- (IFN-) g, tumor necrosis - (TNF-) α , factor own into takes, of these all of them inflammation strengthens or to inflammation against activity shows - IL-4, IL-10, IL-11 and IL-13. Interleukin (IL-6) liver in homeostasis, for example, from an injury after of hepatocytes increase and in recovery important role plays. Hepatocytes proliferation promotion of ARD development prevention get for IL-6 levels balancing the most efficient of methods one IL-18 liver cirrhosis and portal

hypertension in development pathogenetic role plays and with HCV depends cirrhosis for invasive didn't happen from markers is one [10].

The aim of the study: To study the immunological indices of the development of hepatorenal syndrome in liver cirrhosis.

Materials and Methods

A prospective observational study was conducted on 100 cirrhotic patients, divided into two groups: those with HRS (n=50) and those without HRS (n=50).

Inclusion Criteria

- Patients diagnosed with liver cirrhosis based on clinical, laboratory, and imaging findings.
- Patients fulfilling the diagnostic criteria for HRS.

Exclusion Criteria

- Patients with chronic kidney disease unrelated to cirrhosis.
- Patients with active infections or malignancies.

Immunological Parameters Evaluated

- Cytokine profile: Interleukin-6 (IL-6), Tumor Necrosis Factor-alpha (TNF-α), and Interleukin-10 (IL-10) were measured using ELISA.
- Immune cell populations: CD4+ and CD8+ T cells, regulatory T cells (Tregs), and monocyte activation markers were assessed using flow cytometry.
- Inflammatory markers: C-reactive protein (CRP) and procalcitonin levels were determined.

Statistical Analysis

Data were analyzed using SPSS software. Continuous variables were compared using t-tests or Mann-Whitney U tests, while categorical data were analyzed using the chi-square test. Correlation analyses were performed to identify relationships between immunological markers and renal function parameters.

Results et discussion

The mean age of the study population was 55 ± 10 years, with a male-to-female ratio of 3:2. There was no significant difference in baseline liver function between the two groups.

Immunological Findings

1. Cytokine Levels:
   - IL-6 and TNF-α were significantly elevated in HRS patients compared to cirrhotic patients without HRS ($p<0.001$).
   - IL-10 levels were paradoxically increased in HRS patients, indicating an anti-inflammatory compensatory mechanism.
2. Immune Cell Alterations:
   - CD4+ T cell counts were reduced in HRS patients, whereas CD8+ T cells showed no significant difference.
   - Treg populations were significantly increased in the HRS group ($p<0.05$), suggesting immune suppression.
   - Monocyte activation markers were upregulated in HRS patients, correlating with disease severity.
3. Inflammatory Marker Correlation:
   - CRP and procalcitonin levels were higher in HRS patients and showed a strong inverse correlation with glomerular filtration rate (GFR) ($r=-0.72$, $p<0.001$).

The results highlight a distinct immunological profile in cirrhotic patients with HRS. Elevated pro-inflammatory cytokines (IL-6, TNF-α) contribute to systemic inflammation, while increased IL-10 and Tregs suggest a compensatory immunosuppressive response. These findings support the hypothesis that immune dysregulation plays a critical role in HRS pathogenesis.

Early identification of immunological markers may provide a prognostic tool for predicting HRS development in cirrhotic patients. Furthermore, targeting immune pathways could be a potential therapeutic approach to mitigate HRS progression.

Conclusion

HRS is a life-threatening condition in cirrhotic patients, with immune dysregulation playing a significant role in its pathogenesis. Identifying immunological markers could aid in early diagnosis and personalized treatment strategies. Further research is needed to develop targeted immunotherapies for improving patient outcomes.

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