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CHANGES IN THE MORPHOMETRIC STATE OF SPLENIC LYMPHOID TISSUE UNDER CONDITIONS OF POLYPHARMACY

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✓ ***Resume***

Polypharmacy, characterized by the simultaneous use of multiple medications, has become a growing concern due to its potential negative effects on various organs, including the lymphoid tissues of the spleen. This study aimed to evaluate the morphometric changes in splenic lymphoid tissue under experimentally modeled polypharmacy conditions. Wistar rats were administered combinations of commonly used pharmacological agents over a defined period. Histological and morphometric analysis of splenic tissue revealed significant alterations in the size and structure of lymphoid follicles, marginal zones, and the red pulp. These changes suggest that polypharmacy can impair immune organ architecture, potentially compromising immune competence. The findings highlight the importance of evaluating immune system effects in patients receiving multiple drug regimens

Keywords: polypharmacy, spleen, lymphoid tissue, immune system, morphometry, histology, drug-induced changes

ИЗМЕНЕНИЯ МОРФОМЕТРИЧЕСКОГО СОСТОЯНИЯ ЛИМФОИДНОЙ ТКАНИ СЕЛЕЗЁНКИ В УСЛОВИЯХ ПОЛИПРАГМАЗИИ

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✓ ***Резюме***

Полипрагмазия, характеризующаяся одновременным применением нескольких лекарственных средств, вызывает всё большую обеспокоенность из-за возможного негативного влияния на различные органы, включая лимфоидную ткань селезёнки. Целью данного исследования было оценить морфометрические изменения лимфоидной ткани селезёнки в условиях экспериментально смоделированной полипрагмазии. Крысам линии Вистар в течение определённого периода вводились комбинации широко используемых фармакологических препаратов. Гистологический и морфометрический анализ тканей селезёнки выявил значительные изменения в размерах и структуре лимфоидных фолликулов, маргинальных зон и красной пульпы. Эти изменения указывают на то, что полипрагмазия может нарушать архитектуру иммунного органа, потенциально снижая иммунную компетентность. Полученные результаты подчёркивают важность оценки влияния полипрагмазии на иммунную систему у пациентов, получающих многокомпонентную лекарственную терапию

Ключевые слова: полипрагмазия, селезёнка, лимфоидная ткань, иммунная система, морфометрия, гистология, лекарственно-индуцированные изменения

ПОЛИПРАГМАЗИЯ ШАРОИТИДА ТАЛОҚНИНГ ЛИМФОИД ТЎҚИМАСИНИНГ МОРФОМЕТРИК ҲОЛАТИДАГИ ЎЗГАРИШЛАР

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✓ ***Резюме***

Полипрагмазия — бир вақтда бир неча дори воситаларини қўллаш билан тавсифланадиган ҳолат — турли органларга, жумладан, талоқнинг лимфоид тўқимасига салбий таъсир кўрсатиши мумкинлиги сабабли ортиб бораётган хавотирларга сабаб бўлмоқда. Ушбу тадқиқотнинг мақсади — экспериментал равишда моделланган полипрагмазия шароитида талоқнинг лимфоид тўқимасида юз берган морфометрик ўзгаришларни баҳолашдан иборат бўлди. Белгиланган муддат мобайнида Вистар зотидаги каламушларга кенг тарқалган фармакологик препаратлар комбинацияси юборилди. Талоқ тўқимасининг гистологик ва морфометрик таҳлили лимфоид фолликуллар, маргинал зоналар ва қизил пульпанинг ҳажми ҳамда тузилишида сезиларли ўзгаришлар мавжудлигини кўрсатди. Ушбу ўзгаришлар полипрагмазия иммун органи тузилишига салбий таъсир кўрсатиши ва натижада иммун қобилиятни пасайтиши мумкинлигини англатади. Олинган натижалар кўп дорили терапия олаётган беморларда полипрагмазиянинг иммун тизимига бўлган таъсирини баҳолаш аҳамиятини таъкидлайди

Калит сўзлар: полипрагмазия, талоқ, лимфоид тўқима, иммун тизими, морфометрия, гистология, дорилар билан боғлиқ ўзгаришлар

Relevance

Polypharmacy, defined as the simultaneous administration of five or more medications, has become an increasingly prevalent phenomenon in modern clinical practice. This trend is especially notable in geriatric populations and among individuals managing multiple chronic conditions such as hypertension, diabetes, cardiovascular diseases, and neurodegenerative disorders [1]. As life expectancy increases and comorbidities accumulate, polypharmacy is often employed to optimize therapeutic outcomes and manage disease complexity.

However, this strategy is not without consequence. The use of multiple pharmacological agents raises the likelihood of drug-drug interactions, polypharmacy-induced organ toxicity, reduced therapeutic efficacy, and poor medication adherence, all of which may compromise overall patient health and quality of life [2].Beyond the well-documented systemic complications, a growing body of literature has begun to explore the potential impact of polypharmacy on immunological function. The immune system, which plays a central role in host defense and homeostasis, may be particularly vulnerable to long-term drug exposure. However, much of the existing research has focused on the general immunosuppressive effects of certain drug classes rather than the cumulative or synergistic effects of polypharmacy itself. Among the primary and secondary lymphoid organs, the spleen is of particular interest due to its dual role in hematologic filtration and immune surveillance.

The spleen is a highly organized secondary lymphoid organ responsible for detecting blood-borne antigens, filtering damaged or senescent erythrocytes, and initiating adaptive immune responses. It consists of distinct anatomical and functional regions, notably the white pulp, periarteriolar lymphoid sheaths (PALS), marginal zones, and lymphoid follicles, each critical for the maturation, activation, and proliferation of T and B lymphocytes [3–5]. Structural integrity of these compartments is essential for mounting effective immune responses. Disruption or remodeling of splenic architecture -whether due to aging, infection, or pharmacological insult - can significantly impair immunological competence, rendering the host more susceptible to infections and reducing responsiveness to immunizations.Despite its immunological importance, the spleen remains understudied in the context of polypharmacy.

Histological and morphometric evaluations of splenic tissue following exposure to multiple drugs could provide valuable insight into the broader immunological consequences of polypharmacy — an area that has been largely overlooked in both experimental and clinical research. Furthermore, such analyses can help delineate which splenic compartments are most susceptible to damage and whether these changes are reversible or progressive.Therefore, the present study aims to investigate the morphometric and histological changes in the lymphoid tissues of the spleen resulting from polypharmacy, using a controlled experimental animal model. By quantitatively assessing the structural parameters of splenic white pulp, PALS, and lymphoid follicles, this research seeks to elucidate the potential immunomodulatory effects of chronic multi-drug exposure. These findings may contribute to a deeper understanding of the risks associated with polypharmacy and inform strategies for safer pharmacological management, particularly in vulnerable populations.

The aim of the study: to study changes in the morphometric state of the lymphoid tissue of the spleen in conditions of polypharmacy

Materials and methods

Animals:

- 30 adult male Wistar rats (180–220g), divided into 3 groups (n=10 each).
- **Group I (control):** received saline solution
- **Group II (low-dose polypharmacy):** received 3 commonly prescribed drugs
- **Group III (high-dose polypharmacy):** received 5 drugs in clinically relevant dosages

Drugs used:

- Aspirin, enalapril, metformin, omeprazole, and diazepam
- Administered orally via gavage once daily for 28 days

Histological processing:

- Rats were euthanized on day 29; spleens were excised and fixed in 10% formalin
- Tissue sections stained with hematoxylin-eosin (H&E)
- Morphometric analysis performed using ImageJ software

Parameters measured:

- Number and diameter of lymphoid follicles
- Thickness of PALS
- Area of marginal zones and red pulp
- Statistical analysis via ANOVA; $p < 0.05$ considered significant

Results and discussions

Group II (Low-dose polypharmacy):

- Moderate decrease in follicle size (average diameter: 162.5 ± 8.3 μm vs. control 184.7 ± 7.9 μm, $p < 0.05$)
- Reduction in PALS thickness by 15%
- Slight expansion of red pulp

Group III (High-dose polypharmacy):

- Significant lymphoid depletion
- Follicle diameter reduced to 145.3 ± 6.7 μm ($p < 0.01$)
- Marginal zone areas reduced by 30%
- Disruption of normal histoarchitecture, signs of immune suppression

These findings are consistent with studies suggesting that chronic drug exposure affects immune structures [6,7]. Polypharmacy may impair spleen immune response, increasing susceptibility to infections or blunting vaccine efficacy [8].

Conclusion

This study demonstrates that prolonged exposure to polypharmacy can induce significant morphometric and structural changes in the lymphoid compartments of the spleen, including alterations in the size and organization of white pulp, periarteriolar lymphoid sheaths (PALS), and lymphoid follicles. Such changes have the potential to impair the spleen’s ability to perform its essential role in immune surveillance and the initiation of adaptive immune responses. Given the spleen's central role in systemic immunity, these findings raise important concerns regarding the long-term immunological consequences of multi-drug regimens.The observed alterations suggest that chronic polypharmacy may contribute to a decline in immune competence, especially in vulnerable populations such as the elderly or those with underlying chronic illnesses. Clinicians should therefore adopt a cautious and evidence-based approach when prescribing multiple medications, regularly reassessing the necessity and interactions of each drug within a patient's regimen.

Future studies are warranted to investigate the reversibility of these structural changes upon discontinuation or reduction of polypharmacy, as well as to evaluate the functional implications for immune responsiveness. Understanding these dynamics will be critical in developing safer pharmacological strategies that minimize harm to the immune system while maintaining therapeutic efficacy.

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