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Article

Inflammatory and Regenerative Responses of the Epididymis Following Local Anesthesia: An Immunohistochemical Study

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Abstract: This experimental study evaluated immunohistochemical changes in epididymal tissue following different methods of local anesthesia using lidocaine and novocaine. A white outbred rat model was used with markers of inflammation (CD45) and regenerative potential (CD56). Intratesticular administration was associated with increased inflammatory activity (↑CD45) and reduced regenerative capacity (↓CD56), with the most pronounced effects observed after novocaine injection. In contrast, conduction anesthesia, particularly with lidocaine, showed lower CD45 expression and relative preservation of CD56-positive cells. A combined approach (lidocaine conduction anesthesia with microdose intratesticular novocaine) reduced inflammation while maintaining regenerative potential. These findings demonstrate that the route of anesthetic administration critically influences the immunomorphological response of epididymal tissue and support the use of less traumatic combined protocols in scrotal interventions.

Keywords: Local Anesthesia, Epididymis, Immunohistochemistry, CD45, CD56, Inflammation, Regeneration.

Introduction

Local anesthesia is widely used in urological and andrological practice for scrotal procedures, as well as in experimental models. However, the choice of anesthetic administration method (intratesticular, conduction, or combined) can determine not only the effectiveness of pain relief but also the severity of local tissue damage, followed by an inflammatory response and epididymal remodeling. Given the crucial role of the epididymis in sperm maturation and transport, even moderate inflammatory and degenerative changes in this area can impact reproductive function and lead to chronic post-traumatic changes [1].

According to the literature, intratesticular administration of lidocaine and other local anesthetics is used in clinical, veterinary, and experimental practice; however, a number of studies indicate the risk of a more pronounced local tissue reaction due to direct contact of the solution with the parenchyma, microvascular structures, and interstitial elements [2]. At the same time, conduction anesthesia (spermatic cord block) is considered a gentler pain relief option, capable of reducing the degree of direct tissue trauma and potentially reducing the inflammatory cascade [3]. Comparative morphoimmunological evaluation of various routes of anesthetic administration remains relevant,

since it is important for the practicing physician not only to achieve analgesia, but also to minimize late damaging effects [4].

In recent years, immunohistochemical verification of tissue reaction has been actively used in morphological studies, allowing for the objectification of inflammatory and reparative components. CD45 is a universal pan-leukocyte marker reflecting the intensity of inflammatory infiltration and immune activation [5]. CD56 (NCAM), in addition to its role as a NK cell marker, is associated with the regulation of cellular interactions, tissue repair processes, and tissue remodeling under conditions of injury [6]. Therefore, a comparison of CD45 and CD56 expression allows us to assess the balance between inflammation and the regenerative potential of epididymal tissue under various anesthesia techniques.

Thus, a comprehensive study of immunohistochemical indices (CD45, CD56) during intratesticular, conduction, and combined administration of lidocaine and novocaine represents a significant scientific and practical task. The obtained results can serve as a morphological justification for the selection of the safest methods of local anesthesia in andrological and urological practice, as well as in the setting up of experimental models associated with interventions on the scrotal organs [7].

Purpose of the study: To evaluate the inflammatory and regenerative tissue response of the epididymis under various methods of local anesthesia based on immunohistochemical analysis of the expression of CD45 and CD56 markers [8].

Materials and Methods

The study was performed as an experimental controlled randomized trial on 90 white mongrel male rats (weight 250-300 g). The animals were divided into 6 groups of 15 animals: control; intratesticular administration of 1% lidocaine (L-IT); conduction anesthesia with 1% lidocaine (L-CB); intratesticular administration of 1% novocaine (N-IT); conduction anesthesia with 1% novocaine (N-CB); combined technique (N-IT + L-CB) [9].

Epididymal tissue samples were collected 24 hours, 7 days, and 14 days after the procedure (five animals in each group per day). Morphological examination was performed on paraffin sections (4–5 μm) stained with hematoxylin and eosin and van Gieson staining.

Immunohistochemical evaluation was performed using the markers CD45 (leukocyte infiltration) and CD56 (reparative/regenerative activity). Expression was determined as the percentage of CD-positive cells in the epithelium and interstitium (at least 5 fields of view ×400 per animal).

Statistical data processing was performed in Microsoft Excel 2021 and Statistica 12.0 using the Student's t-test, χ^2, and Pearson correlation analysis; differences were considered significant at $p<0.05$ [10].

Results and Discussion

The control group showed a physiologically low level of CD45-positive cells, reflecting the absence of a pronounced inflammatory reaction in the epididymal tissue. Immunohistochemical analysis (DAB, ×400) revealed a single CD45-positive cellular infiltration predominantly in the interstitial areas (Fig. 1) [11].

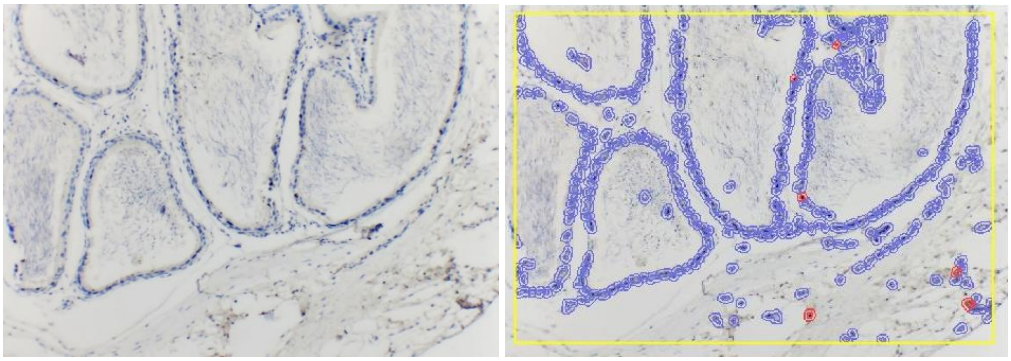

Figure 1. CD45 expression in the epididymis of the control group. DAB, ×400.

Total number of identified cells	326
Positive cells	6
Negative cells	320
Positive expression	1.84%
Total area	3337400 px^2

The total number of identified cells was 326, of which 6 were CD45-positive, which corresponds to 1.84%.

Thus, the control group is characterized by minimal activity of the inflammatory component, which can be considered as a basic morphoimmunological background.

In the tissues of the epididymis of the control group, the baseline level of CD56-positive cellular elements is determined, reflecting the physiological state of local immune regulation and reparative potential [12].

Immunohistochemistry (DAB, ×400) revealed a moderate number of CD56-positive cells in the interstitium and at the periphery of epithelial structures (Fig. 2).

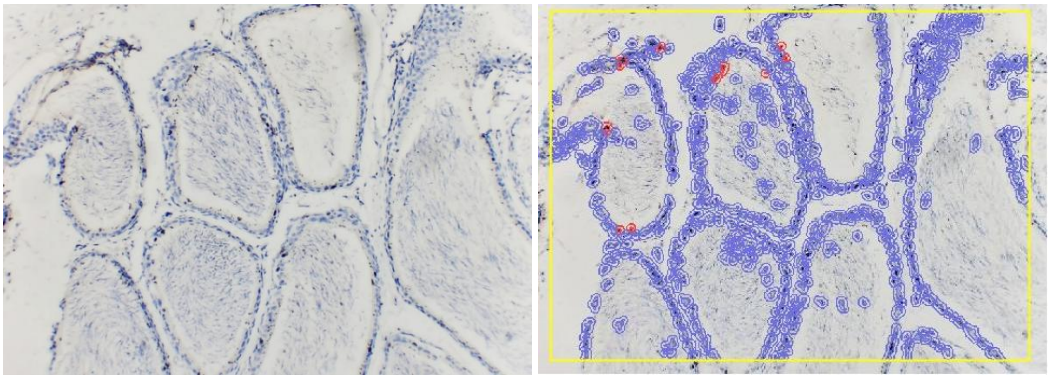

Figure 2. CD56 expression in the epididymis of the control group. DAB, ×400.

Total number of identified cells	474
Positive cells	10
Negative cells	464
Positive expression	2.1%
Total area	346380 px^2

Of the 474 identified cells, 10 were CD56-positive, representing 2.1%. These data can be considered an indicator of normal tissue activity associated with regenerative processes.

After intratesticular administration of a 1% lidocaine solution, a pronounced activation of the inflammatory component in the tissues of the epididymis is observed, which is manifested by a significant increase in CD45-positive cellular infiltration (Fig. 3) [13].

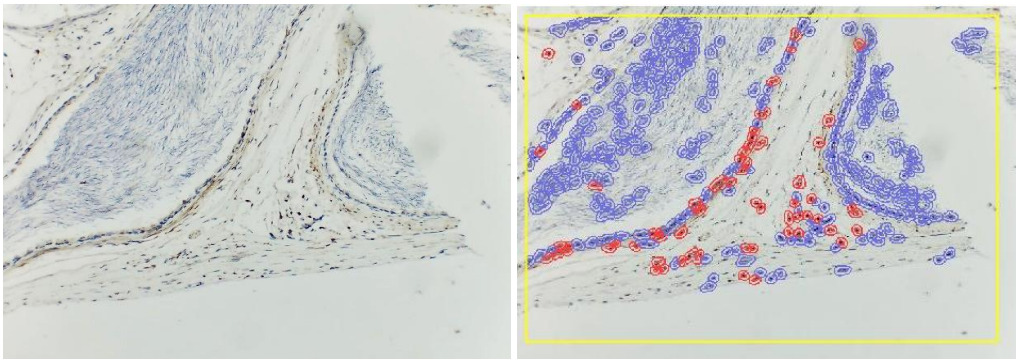

Figure 3. CD45 expression after intratesticular administration of lidocaine. DAB, ×400.

Total number of identified cells	320
Positive cells	62
Negative cells	258
Positive expression	19.34%
Total area	324951 px^2

Immunohistochemical staining (DAB, ×400) revealed multiple CD45-positive infiltrates in the interstitial space, with focal cell clusters around vascular structures. The total number of identified cells was 320, with 62 CD45-positive cells, representing 19.34%, or significantly higher than the control group (1.84%). Thus, intratesticular lidocaine administration is accompanied by a pronounced immunoinflammatory response, indicating a significant tissue reaction.

Intratesticular administration of a 1% novocaine solution is accompanied by a significant decrease in CD56 expression, which indicates suppression of the regenerative/reparative activity of the epididymis tissue.

Immunohistochemical examination (DAB, ×400) reveals extremely rare CD56-positive cellular elements, which are visually manifested by a significant weakening of staining and single positive cells in the field of view (Fig. 4) [14].

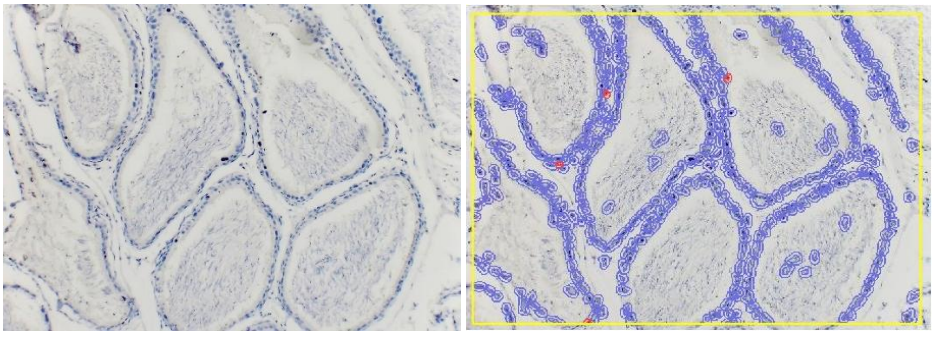

Figure 4. Expression of CD56 after intratesticular administration of novocaine. DAB, ×400.

Total number of identified cells	405
Positive cells	4
Negative cells	401
Positive expression	0.98%
Total area	321432 px^2

Of the 405 identified cells, only 4 were CD56-positive, representing 0.98%, or more than half the control level (2.1%). Thus, intratesticular novocaine administration exhibits the most unfavorable profile for CD56 and can be considered a method associated with decreased tissue regenerative potential.

Conduction anesthesia with lidocaine is characterized by a more favorable immunomorphological profile and is accompanied by increased CD56 expression, which may reflect enhanced reparative processes in the epididymal tissue. A significant increase in the number of CD56-positive cells compared to the control (DAB, ×400) is detected, primarily in the interstitial areas and around the tubular structures (Fig. 5) [15].

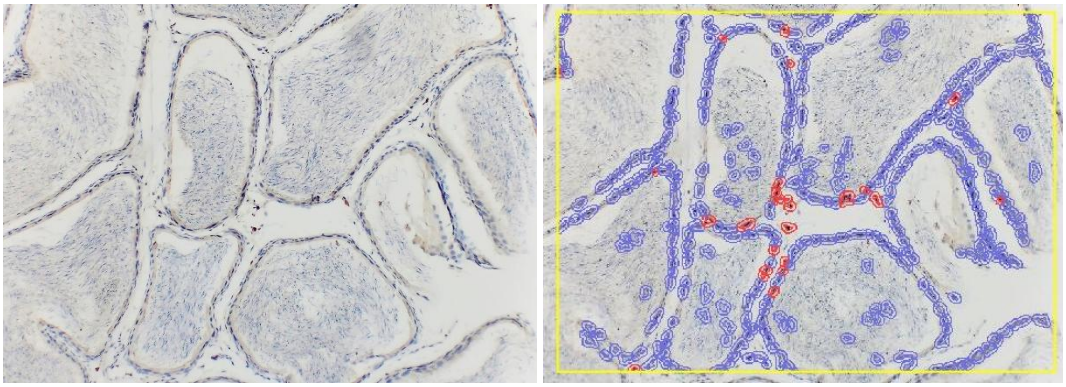

Figure 5. CD56 expression after conduction injection of lidocaine. DAB, ×400.

Total number of identified cells	365
Positive cells	27
Negative cells	338
Positive expression	7.39%
Total area	354200 px^2

Of the 365 identified cells, 27 were CD56-positive, representing 7.39% (versus 2.1% in the control). Consequently, conductive lidocaine administration is associated with greater regenerative potential and less tissue damage compared to intratesticular techniques.

Conclusion

1. Intratesticular administration of lidocaine causes a pronounced inflammatory reaction in the tissue of the epididymis, which is confirmed by a sharp increase in CD45-positive cells to 19.34% compared to the control (1.84%).
2. Intratesticular administration of novocaine reduces the regenerative potential of tissue, which is manifested by a decrease in CD56 expression to 0.98% versus 2.1% in the control group.

3. Conduction anesthesia with lidocaine is the most gentle technique, as it is accompanied by an increase in CD56 expression to 7.39%, which indicates more favorable conditions for reparation compared to intratesticular methods.

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