PTERYGOPALATINE BLOCK EFFECTIVENESS IN POSTOPERATIVE PERIOD AFTER DONOR CORNEA TRANSPLANTATION

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RESUME

Keratoplasty is a surgical procedure for corneal transplantation, in which a donor graft replaces the patient's damaged cornea. Despite its high efficacy, the procedure carries a risk of postoperative complications (high level of intraocular pressure (IOP) and inflammatory reaction), which contribute to the development of pain syndrome and increase the risk of graft rejection due to the disruption of immune privilege.

The aim. *To evaluate the efficacy of analgesia and the anti-inflammatory effect of pterygopalatine block (PPB) in the early postoperative period in patients after penetrating keratoplasty.*

Material and methods. *The study included 56 patients divided into two groups: Group 1 (n = 28) received PPB with 0.5 % levobupivacaine (4 ml) for 3 days, Group 2 (n = 28) received standard analgesia with NSAIDs (ketoprofen) and intraocular pressure-lowering medications (acetazolamide, timolol). Subjective pain sensations (NRS – numeric rating scale), the presence of discomfort and foreign body sensation in the eye, ocular hypertension, and the level of cytokines (IL-6, IL-8, IL-10) in the patients' tear fluid were assessed on days 1, 3, and 5 after surgery.*

Results. *In Group 1, the mean pain level on the NRS was 1.2 ± 0.6 points (7.14 % of patients), while in Group 2 it was 2.9 ± 1.2 points (21.4 %) ($p \leq 0.05$). On day 1 after surgery, in Group 1, the levels of IL-6 and IL-8 increased by 4.3 and 1.5 times, respectively ($p = 0.002$; $p = 0.001$), whereas in Group 2 they increased by 4.9 and 2.1 times ($p = 0.001$, $p = 0.002$). The concentration of IL-10 in Group 1 increased to 2.61 ± 2.3 ng/ml on day 1 and to 3.08 ± 2.6 ng/ml on day 3 ($p = 0.0011$; $p = 0.0015$), while no significant changes were observed in Group 2. The IL-6/IL-10 and IL-8/IL-10 ratios were significantly lower in Group 1 on day 3 (112.18 ± 78.55) compared to Group 2 (313.96 ± 109.87) ($p = 0.0000$). The correlation between IL-8 and IOP on day 3 was $r = 0.8$ ($p = 0.0000$) in Group 2 and $r = 0.6$ ($p = 0.0049$) in Group 1.*

Conclusion. *After donor cornea transplantation, pterygopalatine block modulates the cytokine profile with a pronounced anti-inflammatory effect, making it an effective component of comprehensive postoperative treatment. It contributes to reduced pain and improved IOP control in patients.*

Keywords: *pterygopalatine block, keratoplasty, interleukins, levobupivacaine*

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ЭФФЕКТИВНОСТЬ КРЫЛОНЁБНОЙ БЛОКАДЫ В ПОСЛЕОПЕРАЦИОННОМ ЛЕЧЕНИИ ПАЦИЕНТОВ ПОСЛЕ ТРАНСПЛАНТАЦИИ ДОНОРСКОЙ РОГОВИЦЫ

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РЕЗЮМЕ

Кератопластика является хирургической операцией по пересадке роговицы, при которой донорский трансплантат заменяет поврежденную роговицу пациента. Несмотря на высокую эффективность, процедура связана с риском послеоперационных осложнений, (высокое внутриглазное давление (ВГД) и воспалительная реакция), способствующих развитию болевого синдрома и повышению риска отторжения трансплантата из-за нарушения иммунных привилегий.

Цель. *Оценить эффективность обезболивания и противовоспалительного действия крылонёбной блокады (КНБ) в раннем послеоперационном периоде у пациентов, перенесших сквозную кератопластику.*

Материал и методы. *В исследование включены 56 пациентов, разделённых на две группы: 1-я группа (n = 28) получала КНБ левобупивакаином 0,5 % (4 мл) в течение 3 дней, 2-я группа (n = 28) – стандартное обезболивание НПВС (кетопрофен) и препараты для снижения внутриглазного давления (ацетазоламид, тимолол). Оценивали субъективные болевые ощущения (цифровая рейтинговая шкала – ЦРШ), наличие дискомфорта и ощущения инородного тела в глазу, уровень ВГД и уровень цитокинов (ИЛ-6, ИЛ-8, ИЛ-10) в слезной жидкости пациентов на 1, 3 и 5 сутки после операции.*

Результаты. *В 1-й группе средняя степень боли по ЦРШ – 1,2 ± 0,6 балла (7,14 % пациентов), во 2-й группе – 2,9 ± 1,2 балла (21,4 %) ($p \leq 0,05$). В 1 сутки после операции в 1-й группе уровни ИЛ-6 и ИЛ-8 выросли в 4,3 и 1,5 раза соответственно ($p = 0,002$; $p = 0,001$), во 2-й группе в 4,9 и 2,1 раза ($p = 0,001$ и $p = 0,002$). Концентрация ИЛ-10 в 1-й группе возросла до 2,61 ± 2,3 нг/мл на 1 сутки и 3,08 ± 2,6 нг/мл на 3 сутки ($p = 0,0011$; $p = 0,0015$), в 2-й группе изменений отмечено не было. Соотношение ИЛ-6/ИЛ-10 и ИЛ-8/ИЛ-10 было значительно ниже в 1-й группе на 3 сутки – 112,18 ± 78,55, по сравнению с результатами во 2-ой группе – 313,96 ± 109,87 ($p = 0,0000$). Корреляция между ИЛ-8 и ВГД на 3 сутки: $r = 0,8$ ($p = 0,0000$) во 2-й группе и $r = 0,6$ ($p = 0,0049$) в 1-й группе.*

Заключение. *После операции по поводу трансплантации донорской роговицы, крылонёбная блокада модулирует цитокиновый профиль с выраженным противовоспалительным эффектом, благодаря чему является эффективным компонентом комплексного послеоперационного лечения пациентов, способствующим уменьшению болевого синдрома и контролю ВГД.*

Ключевые слова: *крылонебная блокада, кератопластика, интерлейкины, левобупивакаин*

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The pterygopalatine ganglion is an important neuroanatomical structure that plays a role in both the autonomic and sensory regulation of facial functions. It contains parasympathetic, nociceptive, and sympathetic fibers. Due to its complex structure, the pterygopalatine ganglion has the ability to affect various neural pathways through the use of a pterygopalatine block (PPB) [1]. Because of its accessibility and flexibility in approach, PPB has been widely used in interventional treatments for headaches and facial pain [2]. Regional anesthesia, including PPB, has a powerful anti-inflammatory effect, partly due to the blocking of sympathetic nerves, which reduces the production of pro-inflammatory mediators [3].

Local anesthetics also contribute to the anti-inflammatory effect by inhibiting the migration and activation of neutrophils, thereby reducing the inflammatory response [4]. Clinical data confirm that regional anesthesia reduces the intensity and duration of postoperative inflammation, decreases the need for opioid analgesics, and improves the recovery period [5]. Postoperative inflammation is accompanied by a complex regulation of pro- and anti-inflammatory mediators, including the key cytokines such as IL-6, IL-8, and IL-10. The levels of IL-6 change depending on the phase and nature of the immune response, reflecting the dynamics of the inflammatory process. IL-8 plays an important role in the initial stage of neutrophil activation and migration, which is responsible for early inflammation. However, its excess is associated with an increased risk of complications [6]. Increased levels of the anti-inflammatory cytokine IL-10 have an immunomodulatory effect, which helps to reduce inflammation and enhance graft survival by promoting the development of tolerogenic cells and inhibiting T-cell activation [7]. This mechanism is particularly significant in corneal transplantation, as the balance between pro-inflammatory and anti-inflammatory mediators significantly influences the surgical outcome [8]. An imbalance in inflammatory processes can result in adverse consequences such as immune-mediated graft rejection and delayed tissue regeneration.

Therefore, the regulation of postoperative inflammation through the use of regional anesthesia and the targeted control of cytokine levels is a promising approach for improving surgical outcomes and patient rehabilitation, as supported by the findings of recent research.

THE AIM OF THE STUDY

To evaluate the efficacy of analgesia and the anti-inflammatory effect of pterygopalatine block (PPB) in the early postoperative period in patients after penetrating keratoplasty.

MATERIALS AND METHODS

A longitudinal, randomized, blinded study was conducted in accordance with the approval of the local ethics committee of the Irkutsk Branch of S.N. Fyodorov Eye Microsurgery Federal State Institution (protocol No. 2, dated January 15, 2024).

The study involved 56 patients who underwent penetrating keratoplasty with donor cornea transplantation. Patients were randomized into two groups:

Group 1 ($n = 28$): postoperative pain relief and IOP control were achieved using a pterygopalatine block with 0.5 % levobupivacaine administered at a dose of 4.0 ml for a period of three days;

Group 2 ($n = 28$): pain relief was achieved using nonsteroidal anti-inflammatory medications (ketoprofen 2.0 mg intramuscularly for pain), and ocular hypertension was managed with acetazolamide 0.5 g once daily and timolol 0.5 % twice daily, according to the standard protocol.

Inclusion criteria: indications for corneal transplantation (penetrating keratoplasty) in cases of corneal opacity following trauma, infections, or severe keratoconus.

Exclusion criteria: history of allergy to local anesthetics, patient unwillingness to participate in the study.

Patients' subjective sensations were evaluated: the degree of pain was assessed using a 10-point numeric rating scale (NRS), with 0 indicating "no pain" and 10 representing the "greatest possible, unbearable, intolerable pain". Discomfort and the sensation of a foreign body in the eye were also recorded. Intraocular pressure (IOP) was measured using the Maklakov method. Cytokine concentrations (IL-6, IL-8, and IL-10) in lacrimal fluid were measured on days 1, 3, and 5 after surgery using an Immunochem-2100 multifunctional microplate photometer with an 8-channel optical reading system. The samples were analyzed using the ELISA method, employing the IL-6-ELISA, IL-8-ELISA, and IL-10-ELISA kits from Vector Best. The measurements were performed in 96-well microplates.

The study was conducted at the Irkutsk Branch of S.N. Fyodorov Eye Microsurgery Federal State Institution from January 16, 2024 to December 20, 2024.

Statistical analysis was conducted using the Statistica 6.0 software. The distribution of the data obtained was tested using the Shapiro – Wilk test. Due to the normal distribution, the data were presented as mean (M) and standard deviation (SD). As a measure of the representativeness of the mean values, the boundaries of the 95% confidence interval (95% CI) were indicated. Student's *t*-test was used to compare the mean values of two groups. For the comparison of three or more groups on a quantitative indicator, whose distribution in each group was normal, one-way analysis of variance was used. Pearson's correlation analysis was used to examine relationships. The critical significance level (p) for the testing of statistical hypotheses was set at 0.05.

RESULTS

The analysis of subjective symptoms is presented in Figure 1. It has been found that in Group 1, with moderate severity, the pain syndrome on the NRC was 1.2 ± 0.6 points in 7.14 % of patients ($n = 2$), while, in Group 2, it was significantly higher – 2.9 ± 1.2 points ($p \leq 0.05$) in 21.4 %

of patients (n = 6). Complaints of discomfort and the sensation of a foreign body in the eye were noted in equal proportions in 6 patients (21.4 %) in Group 1 and in 2 (7.1 %) and 14 (50 %) patients in Group 2, respectively.

The incidence of ocular hypertension on days 2 and 3 after surgery in Group 2 was approximately twice that of Group 1, amounting to 21.4 %, compared to 10.7 % ($p \leq 0.05$) in Group 1. This indicates better IOP control when using PPB.

A comparative analysis of cytokine levels in lacrimal fluid is presented in Figure 2. Following surgery, patients in Group 1 demonstrated an increase in IL-6 and IL-8 levels on the first day (by 4.3- and 1.5-fold, respectively), which were statistically significant (p = 0.002 and p = 0.001, respectively) compared to baseline values. These levels then decreased by the third day (p = 0.003 and p = 0.001 for IL-6 and IL-8, respectively). Patients in Group 2 also demonstrated an initial increase in IL-6 (4.9-fold) and IL-8 (2.1-fold) on the first day, which was also statistically significant (both p = 0.001), but IL-6 levels remained elevated on the third day. Additionally, IL-8 concentrations continued to increase (p = 0.000) at this time.

The concentration of the anti-inflammatory cytokine IL-10 increased significantly in Group 1 on days 1 and 3 after surgery, to 2.61 ± 2.3 ng/ml and 3.08 ± 2.6 ng/ml, respectively (p = 0.0011; p = 0.0015). In contrast, no significant changes in IL-10 levels were observed in Group 2, with a mean value of 2.44 ± 1.7 ng/ml (p = 0.0002). A statistically significant intergroup difference in IL-10 levels was observed on day 3 (p = 0.0002).

An assessment of the IL-6/IL-10 and IL-8/IL-10 antagonist cytokine ratios, as a criterion for the pathophysiological mechanisms of postoperative inflammation and healing, revealed the following concentrations in patients of Group 1 who received pterygopalatine block in their

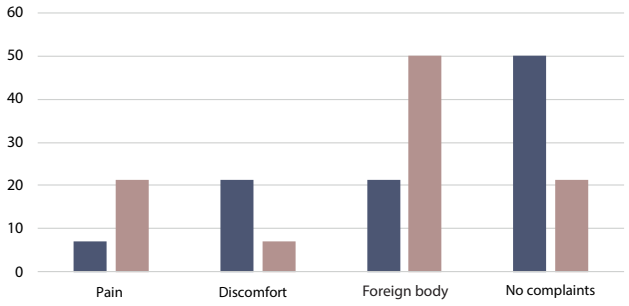


FIG. 1.
Characteristics of subjective sensations in the early postoperative period in groups (%)

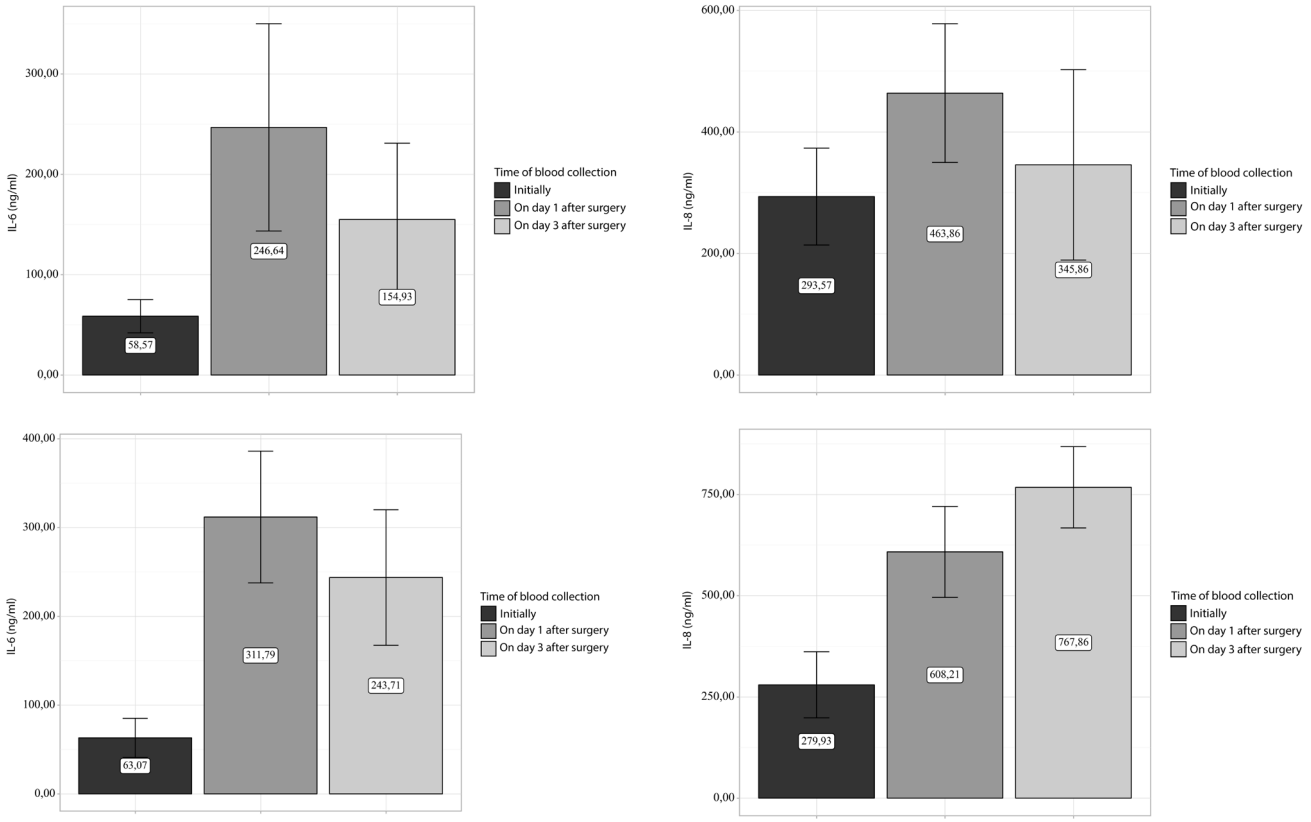


FIG. 2.
Dynamics of changes in IL-6 and IL-8 at the stages of the study in groups (1 – dynamics of changes in IL-6 in patients of the 1st group; 2 – dynamics of changes in IL-8 in patients of the 1st group; 3 – dynamics of changes in IL-6 in patients of the 2nd group; 4 – dynamics of changes in IL-8 in patients of the 2nd group)

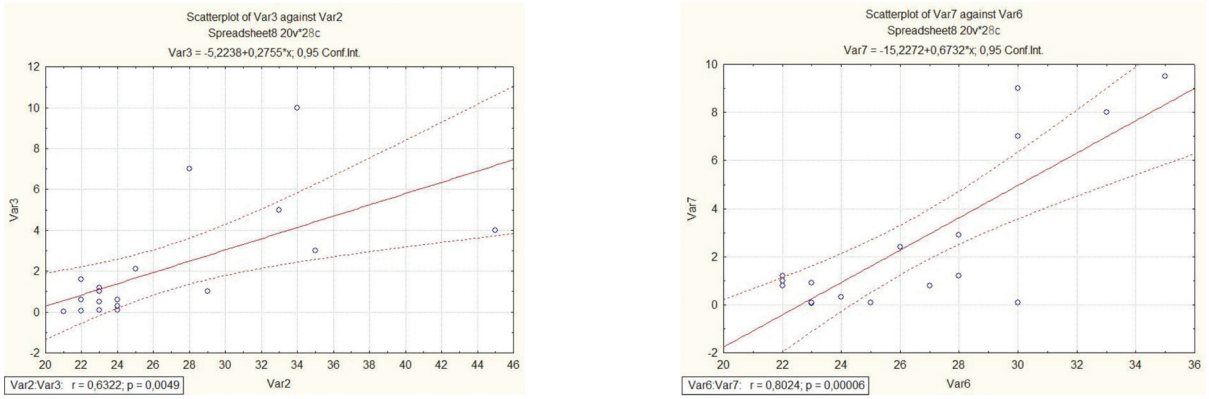
postoperative treatment regimen. On day 3 after surgery, the IL-6/IL-10 and IL-8/IL-10 ratios were significantly lower in Group 1 compared to the values obtained in patients of Group 2 (Table 1). These findings suggest a reduced inflammatory activity in patients of Group 1.

Correlation analysis demonstrated a direct positive association between the levels of IL-8 and IOP on day 3, with r = 0.8 (p = 0.0000) in Group 2 and r = 0.6 (p = 0.0049) in Group 1 (Fig. 3).

DISCUSSION

The pterygopalatine ganglion is an important target for blockade as it is an extracranial structure that is accessible through minimally invasive techniques. The ganglion contains parasympathetic nerve fibers that synapse directly within the ganglion, as well as sensory and sympathetic fibers, which synapse within the ganglion, as well as sensory and sympathetic fibers, which pass through the ganglion without synapsing. This unique structure makes the pterygopalatine ganglion important in the modulation of autonomic and sensory innervation in the facial and ocular regions [9].

Our study demonstrated that the use of PPB in postoperative analgesia after penetrating donor cornea transplantation not only provides effective analgesia, but also has a significant anti-inflammatory effect. PPB reduces the levels of pro-inflammatory cytokines, such as IL-6 and IL-8, in lacrimal fluid while maintaining and increasing the levels of anti-inflammatory cytokine IL-10. This helps to improve the balance between pro- and anti-inflammatory cytokines. These findings are consistent with the previous research and clinical studies that have demonstrated the key roles of IL-6 and IL-8 in the early inflammatory response after surgery, as well as the immunoregulatory function of IL-10 in promoting graft survival [10, 11]. An increase in IL-10 has been shown to contribute to the suppression of pro-inflammatory cytokines and the improvement of postoperative immune balance [12]. In the group without PPB, a significant increase in cytokine imbalance was observed, with a predominance of pro-inflammatory IL-6 and IL-8, which are involved in inflammatory processes and may accompany alloantigen activation, increasing the risk of inflammatory complications. The IL-6/IL-10 ratio has been identified as an important prognostic marker in other medical fields, such as sepsis and cardiac surgery, where a decrease in this ratio is associated with better clinical outcomes [13]. The positive clinical effects of PPB in our study are likely due to the pathogenetic relationship between the levels of interleukins IL-6 and IL-8 and an increase in IOP and the degree of inflammatory response



Group 1 ***Group 2***

FIG. 3.
Correlation between IL-8 and post-op IOP level

TABLE 1

THE RATIO OF IL-6/IL-10 AND IL-8/IL-10 CONCENTRATIONS ON THE 3RD DAY AFTER PENETRATING KERATOPLASTY IN GROUPS

	IL-6/IL-10		IL-8/IL-10		*p*
	Initially	On day 3	Initially	On day 3	
Group 1	29.40 ± 11.44	50.25 ± 18.67	148.28 ± 107.11	112.18 ± 78.55	0.0000
Group 2	31.40 ± 13.67	99.64 ± 32.22	139.36 ± 111.44	313.96 ± 109.87	0.0000

Note. *p* – intergroup difference as determined by the Student's *t*-test.

to surgery. Our findings suggest that a reduction in the activity of the inflammatory response with the use of PPB in the postoperative period occurs through the suppression of its pathogenetic mechanisms due to drug-induced denervation.

Therefore, the results of our study support the potential use of PPB as a viable approach to modulating the postoperative inflammatory response in order to reduce the risk of potential complications, thereby enhancing patient quality of life and increasing the likelihood of successful graft survival.

CONCLUSION

After donor cornea transplantation, pterygopalatine block modulates the cytokine profile with a pronounced anti-inflammatory effect, making it an effective component of comprehensive postoperative treatment. It contributes to reduced pain and improved IOP control in patients.

Conflicts of interest

No potential conflict of interest relevant to this article reported.

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