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COMPARATIVE STUDIES OF THE EFFECT OF LORATADINE AND DESLORATADINE ON NOVOCAINE HYDROLYSIS

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A local anesthetic is a drug used to temporarily numb a small part of the body before surgery. The target of local anesthetics is blockade of sodium channels, which transmit nerve impulses. Novocaine, a derivative of para-aminobenzoic acid, belongs to the ester group. Although novocaine is not a highly effective drug by modern standards, it is safe and readily available. Novocaine, are less likely to cause toxic reactions because they are rapidly destroyed in the body by butyrylcholinesterase. Butyrylcholinesterase is synthesized in the liver and is present in high concentrations in the blood plasma. Therefore, when a local anesthetic is injected into the tissue, it is rapidly hydrolyzed and inactivated, which stops the blockade of sodium channels.

Due to the short-term effect of novocaine, it is important to search for butyrylcholinesterase inhibitors that ensure the long-term effect of the drug. For this study, we selected loratadine and desloratadine, second- and third-generation antihistamine active pharmaceutical ingredients (APIs). The administration of local anesthetics often activates histamine receptors, so the additional use of antihistamine APIs can reduce side effects. Loratadine and desloratadine are safe to use and have several advantages. They do not cause sedation or affect attention levels. This is due to the fact that these compounds do not penetrate the blood-brain barrier.

It was found that the first-order rate constant of hydrolysis of novocaine in the system with human serum with the addition of 100 μM loratadine significantly decreases from $K_{H(0)}^1=0,85\pm0,07\times10^{-3} \text{ s}^{-1}$ to $K_{H(100)}^1=0,09\pm0,01\times10^{-3} \text{ s}^{-1}$, while the decomposition of novocaine decreases by 9.4 times. At concentrations of loratadine in the system of 25 μM and 50 μM , the rate constant significantly decreases by 2.9 and 5.6 times, respectively ($K_{H(25)}^1=0,29\pm0,02\times10^{-3} \text{ s}^{-1}$, $K_{H(50)}^1=0,15\pm0,01\times10^{-3} \text{ s}^{-1}$) ($p\leq 0,05$).

The studies also revealed that the third-generation antihistamine API, desloratadine, exhibits more potent inhibitory properties against butyrylcholinesterase. A decrease in the first-order rate constant is observed when 75 μM desloratadine is added to the system by 12.1 times from $K_{H(0)}^1=0,85\pm0,07\times10^{-3} \text{ s}^{-1}$ to $K_{H(75)}^1=0,07\pm0,01\times10^{-3} \text{ s}^{-1}$. At concentrations of 25 μM and 50 μM , the rate constant significantly decreases by 3.9 and 7.7 times, respectively ($K_{H(25)}^1=0,22\pm0,01\times10^{-3} \text{ s}^{-1}$ and $K_{H(50)}^1=0,11\pm0,02\times10^{-3} \text{ s}^{-1}$) ($p\leq 0,05$).

Therefore, it can be concluded that both loratadine and desloratadine possess inhibitory properties against the decomposition process of novocaine by human serum butyrylcholinesterase. New drugs for local anesthesia with prolonged effects may be developed by combining loratadine or desloratadine with novocaine in a single dosage form.