Short communication

Osmotic Activity of Drugs is an Important Factor of Their Local Action at the Injection Site: What We Don't Use to Prevent Post-Injection Abscesses

Abstract:

It is established that very few modern high-quality drugs in the dosage form "Solution for injection" have isoosmotic activity in the range of 280-300 mosmol/l of water. The main part of solutions for injection is hypotonic or hypertonic solutions, which can have osmotic activity in the range of 0 - 4000 mosmol/l of water. The reason for this was that the osmotic activity of drugs is not included in the list of controlled indicators of drugs quality, so it is not subject to control. It is shown that the osmotic activity of drug solutions increases with an increase in the total concentration of all dissolved ingredients present in the solution. It was found that an excessively high concentration of the drug in the solution gives it an excessively large hyperosmotic activity, which can cause a local irritant and cauterizing effect at the injection sites due to dehydration of the cells. Therefore, to exclude post-injection abscesses, it is proposed to dilute the hypertonic drug with water for injection until it is given isotonic activity.

Keywords: drugs; solutions; osmotic activity; acidic activity; concentration; quality; safety.

Introduction

Post-injection abscesses still remain an "abandoned" area of research in pharmacy and pharmacology. To date, there is scant literature devoted to the study of the causes of abscesses in places of subcutaneous, intramuscular and intravenous injections of drug solutions. Traditionally it was believed that there are many causes of post injection abscess like technique and site of injection apart. In addition, in some cases, local allergic inflammation was considered the cause of the abscess. But in any case, a post-injection abscess was considered a purulent disease, so patients with this local purulent disease were treated in the purulent department. However, careful observance of aseptic and antiseptic measures does not exclude the appearance of local inflammation, necrosis and abscess in the metas of injections of many drugs. The risk of these iatrogenic complications is especially high if drug solutions with a concentration of ingredients of more than 5% accidentally enter the cellular tissues. Therefore, one of the causes of post-injection abscesses may be hidden in the solution of the drug itself, namely, in its excessively high concentration.

The Sources of the Problem

In the medical environment, it is not customary to doubt the safety of medicines in the dosage form "Solution for injection". Therefore, for a long period of time, no one assumed that some drugs could be the culprits of post-injection abscesses that sometimes occur at injection sites. It was believed that post-injection abscesses occur only through the fault of nurses, who sometimes mistakenly violate the rules of asepsis and antiseptics during injections. At the same time, at the beginning of the XXI century, an analysis of the list of controlled indicators of the quality of solutions for injection and the content of pharmacopoeia articles that define this control was carried out. It turned out that the standard quality control of solutions for injection does not include an assessment of their osmotic activity and the presence of cauterizing action. [1]. It has been established that many drugs in the dosage form "Solution for injection" do not have an iso-osmotic activity in the range of 280 -300 mosmol/l of water and with physiological alkaline

activity in the range of pH 7.4. Moreover, some of the solutions for injection, which are considered high-quality today, have very much hypotonic or hypertonic and/or hyperacidic activity [2]. In addition, it was shown that an isotonic solution of 0.9% sodium chloride for injection can have different osmotic activity in different series and from different manufacturers [3,4]. These data allow us to explain why some solutions for injection, which are considered high-quality today, can be very acidic and/or very salty (osmotically active). In turn, it becomes clear that it is the excessively high osmotic and / or acidic reactivity of some solutions for injection that can give them a non-specific pharmacological activity in the form of local irritant and cauterizing effects [5-7].

The values of the concentration of dissolved ingredients, osmotic and acid activity in 40 high-quality solutions for injection from different pharmacological groups were studied. The results showed that modern "Solution for injection" have concentrations of dissolved ingredients in the range of 0-76% and osmotic activity in the range of 0-4000 mosmol/l of water. It is established that the osmotic activity of the drug solution is greater, the greater the concentration of the dissolved ingredients.

In experiments on awake piglets, it was found that drug solutions with a total concentration of ingredients of less than 1% have hypotonic activity and high safety during subcutaneous injections and instillations into the conjunctival cavity. Drug solutions with a concentration index in the range of 1-10% may have hypo -, iso - or hypertonic activity and may have a local irritant effect on subcutaneous fat and conjunctival mucosa. Solutions of drugs with a concentration index of more than 10% have hypertonic activity, have a tear effect when instilled into the eye and a cauterizing effect when injected subcutaneously.

It was found that solutions of different drugs with the same concentration of 10% have different hypertonic, local irritant and cauterizing activity. Solutions of sodium, potassium and calcium salts have the greatest hypertonic activity and local irritating and cauterizing effects [8-10].

It is concluded that post-injection necrosis and abscesses that occur at the injection sites with a solution of drugs with hypertonic activity cannot occur due to tissue infection during injection, since hypertonic solutions have antiseptic activity. Consequently, these drugs with excessively high hypertonic activity cause post-injection necrosis and abscesses not because of violations of the rules of asepsis and antiseptics during injections, but because of an overly pronounced dehydrating effect.

Thus, some solutions of medicines that are considered to be of high quality today may have excessively high hyper-tonic and/or hyper-acidic activity. Therefore, such drugs can have an excessively strong aggressive physical and chemical effect on the tissues at the injection sites, causing post-injection necrosis and abscesses. The results of the experiments showed that the most dangerous solutions are drugs with excessively high hypertonic activity. We believe that knowing the actual values of the osmotic and acidic activity of drugs produced in the dosage form "Solution for injection" can improve the safety of injections and avoid erroneous conclusions today. In this regard, to improve the safety of medicines, it is proposed to monitor their osmotic activity and label their osmotic activity on the labels of solutions.

Discussion

The appearance of an abscess at the injection site of the drug solution can be a serious problem in the treatment of any disease. The appearance of a local purulent-inflammatory process at the injection sites is the reason for diagnosing an additional disease in the patient, namely, purulent

disease. This often requires hospitalization and surgical treatment. It turned out that one of the reasons for post-injection abscesses may be the lack of control of osmotic activity of drug solutions, allowing the presence of drug solutions with a high concentration of dissolved ingredients that give them hypertonic activity. In this regard, an excessively high concentration of dissolved ingredients and an excessively high hypertonic activity of drugs can become one of the causes of local nonspecific aggressive action on tissues, which may be associated with cell dehydration. The fact is that the cells are surrounded by a semipermeable membrane. Excessive dehydration of cells can very quickly cause irreversible damage in them. After that, the dead cells can become a breeding ground for infection. So an abscess may occur at the injection site, even of an antiseptic and/or disinfectant.

Therefore, to increase the safety of drug injections, it is necessary to monitor their osmotic activity, label their osmotic activity on the labels of solutions, and it is necessary to stop the frivolous administration of drug solutions with excessively high hypertonic activity.

References

1. United States Pharmacopeia 36 and National Formulary 31. 2013. (3 Vol Set).
2. Urakova NA. Temperature, osmotic and acidic activity of infusion solutions as an integral part of their mechanism of action. *Reviews on Clinical Pharmacology and Drug Therapy*. 2021;19(2):175-182. doi: 10.17816/RCF192175-182.
3. Kasatkin A, Urakov A, Nigmatullina A, Kopytov M. Balanced Crystalloid versus 0.9% Sodium Chloride: What We Overlook in Our Research. *Anesthesiology*. 2021;134:353–354. https://doi.org/10.1097/ALN.0000000000003614.
4. Friedrich Mertzlufft, Franz Brettner, George J. Crystal, Markus W. Hollmann, Anton Kasatkin, Per-Arne Lonnqvist, Dominique Singer, Robert Su € ¨mpelmann, Volker Wenzel, Rolf Zander and Thomas Ziegenfuß. Intravenous fluids: issues warranting concern. *Eur. J. Anaesthesiol.* 2021; 38:1–3. DOI: 10.1097/EJA.0000000000001568.
5. Urakov AL. The change of physical-chemical factors of the local interaction with the human body as the basis for the creation of materials with new properties. *Epitőanyag – Journal of Silicate Based and Composite Materials*. 2015;67:2–6. http://dx.doi.org/10.14382/ epitoanyag-jsbcm.2015.1.
6. Urakov AL, Urakova NA, Lovtsova LV, Sorokina YuA, Zanozina OV. Osmotic activity and safety of injectable forms of nonsteroidal anti-inflammatory drugs. Experimental and clinical pharmacology. 2018;81(10):15-19.https://doi.org/10.30906/0869-2092-2018-81-10-15-19
7. Urakov A, Gurevich K, Alies M, Reshetnikov A, Kasatkin A, Urakova N. The tissue temperature during injection of drug solution into it as an integral indicator of rheology. Journal of Physics: Conference Series, 4th International Conference on Rheology and Modeling of Materials (ic-rmm4) 7-11 October 2019, Miskolc-Lillafured, Hungary. 2020;1527: 012003. doi:10.1088/1742-6596/1527/1/012003.
8. Anton Kasatkin, Aleksandr Urakov, Anna Nigmatullina, Mikhail Kopytov; Balanced Crystalloid versus 0.9% Sodium Chloride: What We Overlook in Our Research. Anesthesiology. February 2021; 134(2):353–354. https://doi.org/10.1097/ALN.0000000000003614.
9. Urakov AL, Urakova NA, Reshetnikov AP. Physical-Chemical Properties of Antibiotic Drugs: What We Miss in Our Research. Japanese Dental Science Review. 2021; 57: 158–159. https://doi.org/10.1016/j.jdsr.2021.08.005.
10. Bodduluri VP, Gurevich KG, Urakov AL. Physico-Chemical Properties of Antiseptics in Surgery: What is not Taken into Account in Treating Long-Term Non-Healing Wounds. Creative Surgery and Oncology. 2021;11(3):256–259. https://doi.org/10.24060/2076-3093-2021-11-3-256-259.