Old Meets New: Desensitization for Drug Allergy

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True drug allergy is usually caused by immune mechanisms and presents as allergic-symptoms such as itching, urticaria, angioedema, coughing, wheezing, difficulty breathing, and hypotension. Once drug allergy develops, the memory to a particular drug can be sustained for a long time although it fades away by prolonged time of non-exposure. If re-exposed to a drug to which memory was already formed, allergic reaction may be enhanced. Therefore, subjects who had experienced severe drug allergy should be taught not to use the culprit again. However, there are occasions to use the culprit drug inevitably. Although mild hypersensitivity reactions can be treated with slowing down the rate of infusion and increasing the doses and/or varieties of premedications, desesnisitization is recommended for subjects who previously suffered moderate to severe reactions.

Desensitization or tolerance induction is a method, procedure, or approach used to induce the temporary state of tolerance to a compound responsible for an allergic hypersensitivity reaction. It covers respiratory, ocular, and cutaneous allergic conditions, venom, drug, and food allergies. Long term tolerance induction for treating chronic allergic disorders is usually defined as "immunotherapy", more specifically "allergen immunotherapy". In contrast, desensitization is a tolerance induction procedure, or approach used to attain temporary tolerance to a compound responsible for an allergic and/or hypersensitivity reaction, mainly for drug allergy.

While drug desensitization was used for subjects with type I penicillin allergy, it is being frequently used in the setting of allergy to a wide range of chemotherapeutic drugs. Many papers supports the clinical applicability of desensitization and its safety. Desensitization has clinical benefit by enabling patients to keep the first-line therapy.

Drug desensitization only induce temporary tolerance by tricking immune system not to turn on the alarm to activate to memory and effector cells which already exist in the body. To successfully do that, initial administration should be started with an extremely small amounts of drug (1/10,000 of the usual dose) and gradually increased over several hours (15 minutes to 1 hour for rapid desensitization) until the full dose is reached. In order to maintain a temporary non-allergic condition, the patient should continue to take medication regularly. Unless, the patient

returns to allergic condition a while after the drug is stopped.

Drug desensitization is commonly used for those with type I immediate hypersensitivity reactions which occur within hours of drug administration. A representative example is drug-induced anaphylaxis. However, drug desensitization can be applied for delayed drug reactions that occur several hours to days after drug administration. Not all drug desensitization succeed without complications, therefore, it should be considered if there is no substitutable, acceptable alternatives. For example, carboplatin is a primary chemotherapy drug for the treatment of ovarian cancer. If a patient are allergic to carboplatin desensitization with carboplatin would be better option for her than changing to a different class of chemotherapy which may be less effective.

Currently desensitization protocols have been widely performed by sequentially administering diluted solutions in multiple steps to attain tolerance. A typical example is the 3-bag, 12-step protocol suggested by Castells et al. With this protocol, all cases of desensitization were completed without severe side effects but BTRs occurred in 32.6% of cases.[1] Similarly, Lee et al. used a similar 3-bag, 12-step protocol[2] and Hesterberg et al. applied a protocol involving 2-3 dilutions and 8-10 steps, depending on the results of the skin test.[3] In addition, Madrigal-Burgaleta et al. and Wong et al. used protocols involving 1-3 dilutions with 8-13 steps.[4,5] Particularly, Nozawa et al. applied a desensitization protocol for colorectal cancer patients with oxaliplatin hypersensitivity in which they successfully administered a 1:10,000, 1:1,000, 1:100, and 1:10 dilutions to the patients for 1 hour each without changing infusion rate, followed by a 1:1 dilution for 4 hours.[6] Those previously reported protocols had a success rate of 95-100%; however, the incidence of BTRs was quite variable from 5% to 66.7% and the time spent for desensitization varied from 1.5 hours to 16 hours.[2-5,7-11] We recently evaluated the outcomes of a new simple 12-step desensitization protocol with an undiluted solution of platinum-based chemotherapeutic agents. All patients completed desensitization without any serious reactions in a shorter time compared to the multi-bag desensitization protocol. Hence, the dilution process is not essential for desensitization, and our recent study provides the efficacy and safety profiles of the one-bag desensitization.[12] Compared with previous protocols, our protocol has an advantage of the relatively short period required for desensitization and modest BTR rate. We compared the severity of BTRs between previous studies with 3-bag, 12-step protocol and our protocol, by using the same grading system for generalized hypersensitivity reaction.[13] Mild reactions occurred in 23 patients (13.1%) without chest pain, hypotension, dyspnea, hypoxia, and chest discomfort after desensitization. Meanwhile, severe reaction involving one or more of the above symptoms occurred in 6 patients (3.4%) including 1 patient with mild hypotension and 5 patients with chest discomfort. These findings were much lower than those noted in the study using the 3-bag, 12-step protocol, in which 6% had severe reactions.[1] Furthermore, the merits of our new protocol in desensitization are that there is reducing the labor requirement and the potential errors by simply controlling the flow of the infusion without changing bags. Therefore, our new protocol has the advantage of ease of use in clinical settings.

References

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