

Do β -Blockers Really Enhance the Risk of Anaphylaxis During Immunotherapy?

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Both β -blockers and allergen immunotherapy are frequently prescribed, and allergy/immunology physicians commonly encounter patients who are candidates for immunotherapy and are receiving β -blockers. The evidence in the medical literature indicates that although anaphylaxis does not appear to be more frequent, β -blocker exposure is associated with greater risk for severe anaphylaxis, and for anaphylaxis refractory to treatment. Use of β -blocker suspension merits consideration to reduce risk for untoward outcomes, while supplanting the β -blocker medication with an equally efficacious non- β -blocker alternative. For patients who require a β -blocker for an indication for which there is no equally effective substitute, a management decision by the physician prescribing allergen immunotherapy should be approached carefully from an individualized risk-benefit standpoint.

Introduction

In addressing this clinically relevant topic, I will begin with the title proposed for this article. We will consult Webster's Dictionary [1] for definitions to clearly describe what is implied by the following terms in the title: "really," "enhance," and "risk":

- Really: "in reality, actually; *to see things as they really are.*"
- Enhance: "to raise to a higher degree, intensify, magnify; *the candlelight enhanced her beauty.*"
- Risk: "exposure to the chance of injury or loss, a hazard or dangerous chance; *it's not worth the risk.*"

With these terms clarified, anaphylaxis during immunotherapy, β -blockers, and the pertinent evidence will be reviewed.

Anaphylaxis during Immunotherapy

Numerous studies during the past five decades have shown statistically and clinically significant dose-dependent benefit with administration of allergen immunotherapy in properly selected patients with asthma and/or allergic rhinitis [2]. Immunotherapy is associated with *risk* for anaphylaxis in all patients, but is this risk *really enhanced* in patients receiving β -blockers?

Quantifying the risk

Walker et al. [3] reported a study of allergen immunotherapy with timothy grass pollen in patients with allergic rhinitis and mild asthma. In analyzing the 37 of 44 subjects who completed this 3-year study, statistically significant benefit was observed in treated subjects, which included reduced symptoms and medication reliance, compared with placebo. It is appropriate to mention that the external validity of the selected study may be questioned for the majority of patients seen in the United States who are receiving multiple allergen immunotherapy. Nonetheless, we can utilize this study to attach some numbers to the *risk* for anaphylaxis from immunotherapy, which in previous reports was reported at a rate of approximately 3 to 5 per 1000 injections [4,5•].

Number needed to treat (NNT) and number needed to harm (NNH) calculations can be used to express the magnitude of a treatment or harmful effect [6]. In the case of NNH, this is the number of patients who would need to undergo treatment for one to experience an adverse event. Walker et al. [3], reported a low rate of systemic reactions in their study—comparable to rates reported in previous studies [4,5•], for which the calculated NNH is 417; this means that for every 417 injections, there is one systemic reaction.

This risk—one reaction for every 417 injection events—implies that allergen immunotherapy would be favorable from a risk/benefit standpoint for patients with allergic rhinitis and/or asthma for whom a regimen of avoidance measures combined with regular medication use is not feasible, not preferred, or not optimal for achieving goals of therapy. However, let's assume that for a particular patient, a factor exists that is associated with enhanced risk. How much would risk need to be enhanced in order for immunotherapy to not be favorable from a risk/benefit standpoint? If the risk were doubled, this would translate

Table 1. β -Blockers

Brand name	Generic
Betapace	sotalol
Blocadren	timolol
Cartrol	carteolol
Coreg	carvedilol
Corgard	nadolol
Corzide	nadolol/bendroflunetazide
Inderal	propranolol
Inderide	propranolol/hydrochlorthiazide
Kerlone	betaxolol
Levatol	penbutolol
Lopressor	metoprolol
Normodyne	labetalol
Sectral	acebutolol
Tenoretic	atenolol/hydrochlorthiazide
Tenormin	atenolol
Timolide	timolol/hydrochlorthiazide
Toprol	metoprolol
Trandate	labetalol
Visken	pindolol
Zebeta	bisoprolol
Ziac	bisoprolol/hydrochlorthiazide
Topical ophthalmic β-blockers	
Betagan	levobunolol
AK-Beta	levobunolol
Betoptic	betaxolol
Optipranolol	metipranolol
Ocupress	carteolol
Timoptic	timolol

to an NNH of 208. If the risk were quadrupled, the NNH would be 104. If the risk were increased eight times, the NNH would be 52. An individual in the latter groups, with enhanced risk, would merit a different approach when considering whether allergen immunotherapy is favorable from a risk/benefit standpoint.

Additional elements must be considered in assessing risk for anaphylaxis from immunotherapy. What is the risk of more serious anaphylaxis, even if the frequency of reactions is not increased? And what is the risk of withholding immunotherapy?

For a patient who requires venom immunotherapy, there is potentially greater risk from withholding immunotherapy and substantial benefit associated with treatment. In a study published almost 30 years ago, Hunt et al. [7] established the therapeutic utility of immunotherapy for stinging insect allergy using Hyme-

noptera venom in lieu of whole-body extracts. The following rates of systemic reaction to sting challenges, performed after 6 to 10 weeks of immunotherapy, were observed: 1/18 treated with venom, 7/11 treated with whole-body extracts, and 7/12 treated with placebo. Compared with placebo, immunotherapy with venom was associated with a 90% relative risk reduction (RRR), and a calculated NNT of 1.9. To put this dramatic effect into context, the reduction in mortality associated with β -blockers for secondary cardioprotection is approximately 23% in prospective trials and up to 40% in observational studies [8,9]. The NNT over 2 years to reduce one death with β -blockers after infarction is 42, and this compares quite favorably with antiplatelets (NNT = 153) and statins (NNT = 94) [10]. Based upon the magnitude of benefit associated with venom immunotherapy, and the serious risk associated with untreated anaphylactic potential to Hymenoptera venom, it is appropriate to regard venom and inhalant allergen immunotherapy differently when making management decisions from a risk/benefit standpoint.

Qualifying the risk

In considering whether evidence supports the contention that β -blockers really enhance risk in patients receiving allergen immunotherapy, we look at three elements of risk. In the setting of β -blocker exposure:

- Is anaphylaxis more frequent?
- Is severe anaphylaxis more frequent?
- Is response to treatment obtunded?

The β -Blockers

The β -blockers were introduced in the early 1960s, and currently rank among the most frequently prescribed classes of drugs in the world. The β -blockers currently approved for use in the United States are listed in Table 1. Two—metoprolol and atenolol—ranked among the 15 most commonly used medications by Americans in 2005 [11]. Although most prescriptions for β -blockers are written for hypertension, ischemic heart disease, and prophylaxis against myocardial reinfarction, β -blockers are also prescribed for noncardiac conditions, including migraine headache, thyrotoxicosis, skeletal muscle tremor, and stage fright [12].

The β -blockers are generally well tolerated. Both desired and untoward effects of these drugs occur via β -adrenergic receptor blockade. The potential for severe, life-threatening bronchospasm in asthmatics given β -blockers was first reported in 1964 [13], and now is widely recognized. The bronchospastic potential of β -blockers has also been observed with exposure to topical ophthalmic β -blockers [14], reflecting the exquisite sensitivity and predisposition for untoward reaction that exists among selected asthmatics. Although the potential for provocation or worsening of bronchospasm is well known, the

potential for hazard associated with anaphylaxis in the setting of β -blocker exposure is not as widely appreciated among health care providers.

Based on the frequency with which β -blockers are prescribed, and allergen immunotherapy is prescribed, allergy/immunology practitioners may commonly encounter patients who are candidates for allergen (inhalant or venom) immunotherapy who are also receiving β -blockers. For this reason, allergy/immunology physicians should be aware of the evidence for enhanced risk for anaphylaxis with β -blockers, which includes clinical observations and data from studies in animals and humans.

Clinical observations

In 1979, Madowitz and Schweiger [15] described an unusually severe anaphylactoid reaction during performance of coronary angiography in a 46-year-old man receiving 320 mg of propranolol daily for hypertension. Based upon a prior history of anaphylactoid reaction from contrast media, he had been pretreated with H_1 antihistamine and corticosteroid. Seven minutes after contrast infusion, the patient developed bronchospasm, cyanosis, chest pain, and pulmonary edema, which required administration of epinephrine, diphenhydramine, and corticosteroids, and endotracheal intubation. After administration of epinephrine, his blood pressure rose paradoxically to 280/110. He subsequently recovered and successfully underwent coronary artery bypass grafting. The authors of this paper observed that premedication does not eliminate the possibility of a life-threatening anaphylactoid reaction with readministration of contrast media, but did not comment upon the potential importance of propranolol exposure.

In 1981, three more cases of potentiated anaphylaxis were described in patients receiving propranolol. Jacobs et al. [16] described two severe nonfatal anaphylactic reactions that featured an inappropriately slow pulse during profound hypotension and a sluggish response to pharmacotherapy. Newman and Schultz [17] reported a similar case. Additional cases of unusually severe anaphylaxis in patients receiving β -blockers have also been described [18–31]. In 1986, two fatal anaphylactic reactions to penicillin were reported. These reactions were unusual because they were associated with oral administration of penicillin V, to which fatal anaphylaxis is quite rare [24]. In 2006, a case of refractory anaphylaxis was described in association with oral amoxicillin [31]. These patients—a 47-year-old woman [31], a 48-year-old man, and a 51-year-old woman [24]—were all receiving β -blockers for hypertension.

Pharmacodynamics

Evidence from both human and animal studies has supported the contention that anaphylaxis is influenced by the pharmacodynamics of β -blockade. The challenge of managing serious anaphylaxis in patients receiving β -blockers, “whose response to catecholamines is likely to be absent or poor,”

was raised in 1971 by Corbascio [32]. Shereff et al. [33] observed that wheal reaction to injected allergen increased with prior iontophoresis of propranolol into skin-test sites, a finding consistent with the hypothesis that release of anaphylactogenic mediators is augmented in the setting of β -blocker exposure. The clinical relevance of this finding may be more important for atopic and/or asthmatic patients, who possess “intrinsic” β -adrenergic hyporesponsiveness [34,35].

Nisam et al. [36] studied anaphylactoid reaction in mixed-breed dogs challenged with aerosolized 48/80, with and without propranolol pretreatment. Exaggerated anaphylactoid reactions were observed in the dogs who received propranolol; of four dogs challenged, two had a protracted course and two became severely hypotensive and died. Matsumura et al. [37] found that propranolol pretreatment made mice more susceptible to passive systemic anaphylaxis. Interestingly, prior administration of cyclic adenosine monophosphate (AMP) and related nucleotides protected against this increased susceptibility. Because the effects of β -blockers are largely mediated by adenylyl cyclase, which converts adenosine triphosphate into adenosine 3',5'-cyclic AMP [38], these findings have been interpreted as implying that patients receiving β -blockers may have an increased propensity for amplification of anaphylaxis via enhanced mediator release, and decreased cardiac contractility with perpetuation of hypotension and bradycardia [39]. The capacity of β -blockers to act upon cyclic nucleotides and to augment mast cell mediator release also suggests that β -blocker exposure can influence the threshold for overt anaphylaxis [39].

Studies Assessing Whether Greater Risk for Anaphylactic or Anaphylactoid Reaction Exists in Association with β -Blockers

Foods, drugs, and insect stings are common causes of anaphylactic (immunoglobulin [Ig] E-mediated) reactions [40]. Radiocontrast media (RCM) infusion is the most common cause of anaphylactoid reaction (non-IgE-mediated anaphylaxis) in the modern medical era [40]. Intravenous infusion of conventional contrast agents can promote systemic histamine release [41], subclinical bronchospasm [42], and oxygen desaturation [43], even in nonreactors.

Anaphylactic and anaphylactoid reactions may occur suddenly and unexpectedly, and can be life-threatening. For persons with known anaphylactic potential (eg, to peanuts or Hymenoptera venom), exposure can be expected to provoke potentially serious reactions. For this reason, avoidance is recommended along with prophylactic measures such as carrying injectable epinephrine [40]. Suspension of β -blockers also merits consideration for patients with anaphylactic potential, including those receiving venom or inhalant allergen immunotherapy [2,40,44]. The evidence supporting this recommendation will be examined.

Examination of the evidence

The most desirable study from the standpoint of strength of evidence is a randomized controlled trial (RCT) [45]. There are two reasons why we are unable to identify RCTs that will help us determine whether *risk* for anaphylaxis is *enhanced* in patients on allergen immunotherapy who are receiving β -blockers:

- Based upon the evidence in the literature from observational studies, it would be unethical to randomize patients to an exposure such as β -blocker therapy that would be potentially harmful.
- Such an RCT would require an extremely large sample size, and would be challenging from a logistical standpoint.

For the above reasons, our critical assessment of published papers in the medical literature relies on observational studies. These are appropriate when a harmful outcome is infrequent or rare [45]. The limitation of observational studies, however, is that exposed and unexposed patients may begin with a different risk of the target outcome due to confounding variables.

Case series and cohort studies

Benitah et al. [20] reported a retrospective cohort study in which patients who were candidates for venom immunotherapy (based on a history of systemic reactions to bee stings), and who were receiving β -blockers at the time of Hymenoptera sting, had greater risk for severe anaphylactic reaction with hypotension. Of 249 patients, 14 were receiving β -blockers at the time of sting, primarily for hypertension. All had severe reactions with hypotension, compared with 107 of 235 (42%) who were not receiving β -blockers, and only nine of 16 (5%) “atheromatous patients” not receiving β -blockers.

Greenberger et al. [46•] evaluated risk for anaphylactoid reaction associated with β -blocker exposure in 952 patients undergoing coronary angiography. Patients were categorized into four groups according to medication exposures: one group (216 patients) received β -blockers; another group (147 patients) received calcium channel antagonists; a third group (447 patients) received neither; a fourth group (142 patients) received both. The reaction rates in the four groups were, respectively, 7.41%, 5.44%, 4.47%, and 4.93%. The rates of anaphylactoid reaction were not associated with the use of medications in any of the groups ($X^2 = 2.531$; $P = 0.47$); however, reactions in this study were mild in degree.

Hepner et al. [5•] performed a large prospective cohort study of patients receiving inhalant and venom immunotherapy, and found no increased risk for more frequent systemic reactions in patients taking β -blockers compared with those who were not. Over a 12-month period, 56,105 immunotherapy injections were administered to 3178 patients; 166 systemic reactions were recorded in 144 patients, a reaction rate of 3.0 per 1000 injections.

Only 1 of 68 patients receiving a β -blocker had a systemic reaction. However, 87% of reactions were categorized as “mild,” and only two (1%) were severe. No reactions with hypotension were observed.

Müller and Haeberli [47•] reported a retrospective cohort study of patients receiving venom immunotherapy. The authors studied 1389 patients who were candidates for venom immunotherapy, of whom 11.2% had cardiovascular disease and 44 (3.2%) were taking β -blockers, primarily for hypertension. Of these 44, in 31 cases, β -blockers were suspended prior to initiating immunotherapy; in 9 of these 31, β -blockers were resumed, and in 12 other cases, β -blockers were initiated after immunotherapy was underway. No greater rate of systemic reaction with immunotherapy or field stings was observed in association with β -blocker exposure.

As noted above, observational studies do not control for bias as effectively as RCTs. Compared with the general population, patients taking β -blockers tend to be older and are more likely to have comorbid conditions—particularly cardiovascular disease. One may argue that such patients are at greater risk for more frequent and/or more severe reactions due to their baseline characteristics. On the other hand, in the context of an allergy/immunology patient population receiving allergen immunotherapy, the prevalence of asthma is quite high. Asthmatic patients are at significantly elevated risk for anaphylaxis from allergen immunotherapy [2], and such patients would be unlikely to be receiving β -blockers. These considerations would bias our estimates in opposite directions.

In the study reported by Müller and Haeberli [47•], baseline distribution of risk may have been unequal due to selective physician prescribing behavior. Physicians tend to avoid prescribing medication that they perceive may increase risk. For this reason, patients who continued to take β -blockers after initiation of immunotherapy may have been different from those whose β -blocker was suspended. A properly designed randomized, placebo-controlled, prospective study would address potential confounders; however, in a retrospective or prospective cohort study, it is difficult to adequately control for these influences.

The study by Hepner et al. [5•] provides the best evidence in the literature that addresses one of our questions concerning anaphylaxis risk: does β -blocker exposure influence the rate of anaphylaxis in patients receiving allergen immunotherapy? Based on their data, it appears that such *risk* is *not really* enhanced. However, these data do not allow one to make a determination about the additional two elements of risk, because few severe reactions were observed in this study.

Severe anaphylactoid reaction occurs at a rate of approximately 1 in 1000 patients receiving intravenous RCM infusions, and at a slightly lower rate with intra-arterial procedures. For this reason, a study of 952 RCM exposures in which statistically increased risk associated with β -blockers was not found [46•], although reassuring,

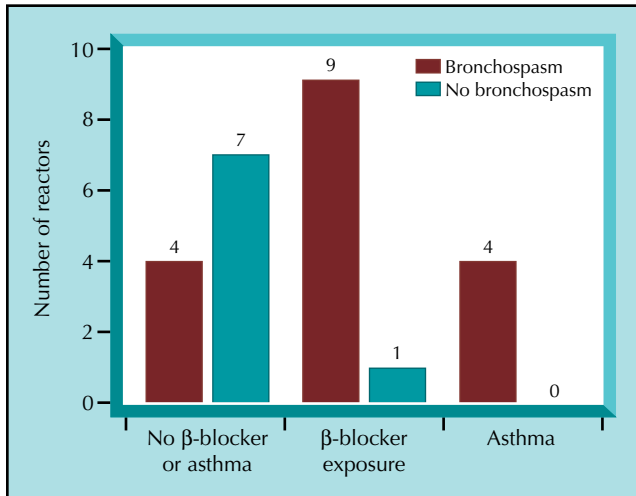


Figure 1. The frequency of bronchospasm among patients with cardiovascular conditions who had severe anaphylactoid reactions from infusion of radiographic contrast media, classified based on the presence of β -blocker use or asthma. Of 21 who were nonasthmatic, 10 were receiving β -blockers; 9 (90%) of these 10 experienced bronchospasm, compared to only 4 of 11 (36.4%) who were not receiving β -blockers (odds ratio = 15.75; $P = 0.023$, Fisher's exact test). In all four with asthma, bronchospasm occurred with severe anaphylactoid reaction ($P = 0.077$, Fisher's exact test). (From Lang et al. [49•]; with permission).

lacks sufficient power. It is important to note that studies in which a statistically significant difference is not found are to be judged on the basis of the study's power, not on the basis of a P -value. The type 2 error [45]—the probability that a statistically significant difference is present, but not detected due to the small size of the study—calculated by the authors and published in the abstract of this paper was 0.75 [46•].

Case-control study

A study with a case-control design found that β -blocker-related anaphylaxis is more likely to be severe and refractory to management.

In a case-control study, participants are selected on the basis of experiencing a target outcome, such that individuals who did or did not have an event are enrolled, in contrast to study designs based on having or not having an exposure or intervention. This design has utility for rare outcomes that can challenge the feasibility of an alternative study design [45]. The study enrolls cases who experienced the target outcome, and controls who did not suffer the outcome, and compares factors that may be more frequent in one group than another. This design permits simultaneous assessment of multiple factors that may be associated with the target outcome, and can provide similar distributions of baseline characteristics by including gender, age, and other factors as criteria for identifying “matched” controls.

A case-control study was designed to determine whether greater risk for anaphylactoid reaction from

RCM exists among patients receiving β -blockers or with asthma [48•]. Patients who experienced anaphylactoid reactions from RCM infusion were identified, along with controls who were matched based on age, gender, body mass index, date, and type of contrast study. The rate of moderate-severe anaphylactoid reaction in this study was 0.17%; 13/49 (27%) who had anaphylactoid reactions were receiving a β -blocker, compared with 10/83 (12%) matched controls. Greater prevalence of asthma and β -blocker exposure was found among reactors compared with matched controls (39% compared with 16%; odds ratio [OR] = 3.43, 95% CI = 1.45–8.15, $P = 0.005$), and exposure to β -blockers was found to be a statistically significant risk factor for anaphylactoid reaction (OR = 2.67, CI = 1.01–7.05; $P = 0.036$).

An expanded case-control study with both retrospective and concurrent subject selection [49•] was also carried out to determine whether risk associated with β -blocker exposure was independent of cardiovascular conditions for which these agents are usually prescribed. This study found that β -blocker exposure was associated with greater risk for severe anaphylactoid reaction with bronchospasm (OR = 3.73, 95% CI = 1.18–11.75; $P = 0.025$), and patients receiving β -blockers were also almost eight times (OR = 7.67, 95% CI = 1.79–32.85, $P = 0.029$) more likely to be hospitalized after anaphylactoid reaction. Although β -blocker exposure and presence of a cardiovascular disorder were highly associated ($X^2 = 49$, $P < 0.001$), greater risk for bronchospasm with severe reaction was observed, as shown in Figure 1, in nonasthmatic patients with cardiovascular disorders receiving β -blockers (OR = 15.75, $P = .023$).

The above study involved more than 34,000 intravenous RCM infusions, and had sufficient power to demonstrate statistically significant risk associated with β -blocker exposure independent from the underlying cardiovascular conditions for which these drugs are frequently prescribed, and adjusting for asthma, a condition for which β -blockers are unlikely to be prescribed. This study provides information that pertains to the additional two questions regarding β -blocker risk: are severe reactions more frequent, and are they more likely to be refractory to management? These data imply that patients receiving β -blockers are at elevated risk for both, and are consistent with previous reports of unusually severe anaphylaxis occurring in patients receiving β -blockers [15–31].

Cardioselective β -Blockers

It is well known that β -blockers that selectively block β_1 receptors, located primarily in the cardiovascular system, are less likely to promote bronchospasm compared with nonselective β -blockers, which inhibit both β_1 and β_2 adrenoceptor systems [12]. However, the relative advantage of “cardioselective” β -blockers with respect to enhanced risk for anaphylaxis is uncertain. The contention that greater risk for more serious anaphylaxis

extends to “cardioselective” β -blockers is supported by reports of unusually severe anaphylaxis in association with β_1 -selective antagonists [19,20,21,28] and in vitro histamine release demonstrated with either β_1 or β_2 antagonists [50,51]. Until more data are available, absence of increased risk for potentiated anaphylaxis with use of selective β -blockers cannot be assumed.

Management Recommendations

The evidence in the literature indicates that although anaphylaxis does not appear to be more frequent in association with β -blockers, use of these agents is associated with greater risk for severe anaphylaxis with bronchospasm, and for anaphylaxis refractory to treatment. A disclaimer merits mention: the case-control study that generated the data concerning risk for more serious anaphylaxis associated with β -blocker exposure involved a stimulus associated with non-IgE-mediated anaphylaxis; however, there are no similar studies involving patients receiving allergen immunotherapy. In considering data from a study examining RCM reactions in the context of a critical assessment of risk for more serious anaphylaxis in patients receiving allergen immunotherapy, we make the assumption that the anaphylactogenic stimulus of RCM infusion is generalizable to the stimulus of allergen immunotherapy extract injection.

Management decisions concerning β -blockers and allergen immunotherapy are much easier when patients require β -blockers for uncomplicated hypertension, and can receive an equally efficacious alternative antihypertensive agent, while receiving allergen immunotherapy. Since the introduction of β -blockers in the 1960s, several other classes of drugs—angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and calcium channel antagonists—have been introduced that can serve as equally efficacious alternative antihypertensive drugs in properly selected patients.

Management decisions become more complicated when risk is associated with suspension of β -blocker treatment, such as when a patient requires a β -blocker for myocardial re-infarction prophylaxis or for management of glaucoma. In such situations, there may be no equivalent substitute. An evidence-based management decision can be approached from the perspective of balancing risk associated with continuing β -blocker treatment with the potential untoward effects resulting from β -blocker suspension.

The risk-benefit assessment differs for patients receiving inhalant and venom allergen immunotherapy, because venom immunotherapy is associated with substantial benefit in preventing subsequent sting anaphylaxis in patients at risk [7]. Venom immunotherapy is viewed as being indicated regardless of age or the presence of other medical conditions [2]. For persons with anaphylactic potential to Hymenoptera venom, consideration of prophylactic β -blocker suspension is appropriate not only because of the enhanced risk for

anaphylaxis with “natural” exposure, but also from administration of venom immunotherapy injections. However, for cases when no equally efficacious non- β -blocker alternative is available, the physician is faced with a decision that must be made from an individualized risk/benefit standpoint. Due to the serious consequences of untreated anaphylactic potential to Hymenoptera venom, which would be amplified in a person receiving a β -blocker, administration of venom immunotherapy may be warranted in selected cases in patients who continue to receive β -blockers.

In patients for whom immunotherapy is judged to be risk-beneficial, glucagon should be maintained in the immediate vicinity in which immunotherapy extracts are administered. Glucagon raises cyclic adenosine monophosphate levels via noncatecholamine mechanisms and can exert potent chronotropic and inotropic effects [2]. Sherman et al. [52] have also reported a bronchodilator effect of glucagon in selected patients with asthma. Zaloga et al. [28] described dramatic improvement of refractory hypotension during anaphylactoid reaction from RCM following administration of intravenous glucagon, in a 75-year-old man receiving both atenolol and ophthalmic timolol.

Conclusions

This review highlights the importance of recognizing the potential hazards of β -blocker-associated anaphylaxis. Although anaphylaxis from allergen immunotherapy in patients taking β -blockers does not appear to be more frequent, it may be more serious. It is essential for physicians who prescribe allergen immunotherapy and who administer allergen immunotherapy injections to be aware that β -blockers *really enhance the risk* for more severe anaphylaxis, and that potential complications in anaphylaxis management exist in patients receiving β -blockers.

Prevention is the most important aspect of anaphylaxis management. When feasible, it is prudent to consider β -blocker suspension to reduce the risk for untoward outcomes in patients receiving allergen immunotherapy, while supplanting a β -blocker with an equally efficacious non- β -blocker alternative, as feasible. For patients who require a β -blocker for an indication for which there is no equally effective substitute available, a management decision by the physician prescribing allergen immunotherapy should be approached carefully from an individualized risk-benefit standpoint.

Disclosure

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