

Pamphlet #13: Anti-inflammatory Reliever (AIR)

Over the last several years, a dramatic change has emerged in our thinking about the treatment of asthma. This pamphlet will discuss this new approach to acute relief of asthma symptoms, its rationale, and its benefits. It is called "Anti-inflammatory Reliever" and nicknamed AIR, and it has been shown to successfully reduce the frequency of asthma attacks, including severe attacks requiring oral steroids for treatment.

For many decades our approach to asthma treatment has involved "controller" medications, to be taken every day to prevent and minimize the symptoms of asthma, and "reliever" medication, a quick-acting bronchodilator to alleviate asthma symptoms, typically acting within just a few minutes. Some people with only occasional symptoms of asthma could be treated with only their "quick reliever," such as albuterol (brand names: ProAir®, Proventil®, Ventolin®) or levalbuterol (brand name: Xopenex®) taken as needed for relief of symptoms (or sometimes preventively, such as prior to exercise). Others with more troublesome asthma are prescribed one or more daily medication(s) for asthma control and in addition use their "quick reliever" whenever necessary. The quick reliever is a bronchodilator: it relaxes the muscles surrounding the breathing tubes, acting quickly to widen the air tubes and improve breathing. Its great appeal is its almost immediate action to quiet asthma symptoms. Its shortcoming is that it does nothing to lessen the frequency of those symptoms or, in some cases, to prevent their recurrence just a short while later.

You recall that underlying the tendency in asthma of the bronchial tube muscles to contract too much and too often is a persistent inflammation of those bronchial tubes (see <a href="Pamphlet #2:"What is Meant by 'Inflammation' in Asthma?" by the Mass General Brigham Asthma Center). The quick-relief bronchodilators do nothing to treat this inflammation. Hence the idea for this new approach to quick-relief medication. What if, with each puff of bronchodilator medication, an anti-inflammatory steroid was also administered? What if, at the time when asthma symptoms are flaring, one administered both a medication to relax the bronchial muscles and a medication to quiet the underlying inflammation? Enter the "anti-inflammatory reliever."

The Need for This New Approach

Nearly half of all persons with asthma will experience an exacerbation or "attack" of their asthma over the course of a year; and nearly 10% will have an attack of such severity that they need to seek care in an emergency department. While it is true that the more severe or poorly controlled one's asthma is, the more likely one is to suffer such an asthma attack, even persons

who have only intermittent or rare asthma symptoms can experience severe and potentially dangerous attacks of their asthma. Regardless of the severity of your asthma, it remains true that you have some degree of the characteristic asthmatic inflammation throughout your breathing tubes. Whenever you experience symptoms of asthma and need relief from your quick-acting bronchodilator, wouldn't it be good to try to dampen down that inflammation with a dose of anti-inflammatory medication (an inhaled corticosteroid) (see Pamphlet #4: "Asthma and Inhaled Steroids")? For those persons already taking daily inhaled steroids, this strategy would provide extra doses of the steroids when symptoms are acting up. The dose of inhaled steroid is in this way titrated to the severity of symptoms: the more often that you find yourself needing your quick-relief bronchodilator, the more often you are administering anti-inflammatory medication to quiet the underlying process driving those symptoms.

How Is It Done?

Currently there are 3 ways in which you can deliver anti-inflammatory reliever therapy.

- If you have both a quick-acting bronchodilator like albuterol or levalbuterol and a separate inhaled steroid like beclomethasone (*Qvar*®), budesonide (*Pulmicort*®), ciclesonide (*Alvesco*®), fluticasone propionate (*Armonair*®), or mometasone (*Asmanex*®), you can simply take 1-2 puffs of your steroid inhaler every time that you use your quick-acting bronchodilator for relief of symptoms (one puff of steroid for each puff of bronchodilator). Simply keep the 2 inhalers together at all times, in a pouch or bound together with rubber bands. This approach to AIR has been dubbed "PARTICS," for Patient-Activated, Reliever-Triggered Inhaled Corticosteroid. Using a separate steroid inhaler with your quick-acting bronchodilator works particularly well if you rely on *nebulized* bronchodilator for quick relief, in which case 5 puffs from your steroid inhaler are recommended with each nebulizer treatment of your quick reliever.
- In 2023 a new inhaler was released that combines an inhaled steroid and the quickacting bronchodilator albuterol in each puff. This combination budesonide-albuterol inhaler containing the usual amount of albuterol with each dose is called *Airsupra®* and is to be taken 2 puffs as needed for relief of symptoms. With this device, you automatically receive a dose of anti-inflammatory medication every time you address bronchial muscle spasm with a bronchodilator. Because it contains an inhaled steroid, it is a good idea to try to rinse your mouth with water after each use, to minimize any risk of yeast infection in the mouth or throat ("thrush"). It has been approved by the Food and Drug Administration for use by persons 18 years of age and older. The maximum recommended daily dose is 6 doses (12 puffs) over 24 hours.
- Another inhaler is available that combines an inhaled steroid and a quick-acting bronchodilator. It differs from the budesonide-albuterol combination mentioned above in that the bronchodilator in this combination inhaler, called formoterol, has a

considerably longer duration of effect than albuterol, lasting approximately 12 hours. When used twice daily, it provides around-the-clock widening of the bronchial tubes ("bronchodilation"). As a result, it was first introduced in combination with an inhaled steroid (budesonide or mometasone) as a regular maintenance medication for persons with more than mild asthma, to be taken every day, twice daily, for control of symptoms. However, formoterol also works quickly, as quickly as albuterol, and so can be used for quick relief of symptoms. In Europe, other parts of the world, and more and more in the United States, a budesonide-formoterol combination inhaler (*Breyna*®, *Symbicort*®) is prescribed for mild and intermittent asthma. In some persons with mild asthma who had been prescribed daily inhaled steroid and as-needed albuterol, use of only a budesonide-formoterol inhaler taken as needed has proved an effective and desirable substitute.

Other persons with more severe asthma, who a take budesonide-formoterol combination inhaler twice daily, can also use their budesonide-formoterol inhaler for quick relief of symptoms, thereby implementing the anti-inflammatory reliever strategy using their one inhaler. This treatment approach, which utilizes the budesonide-formoterol inhaler for both daily maintenance and quick relief of symptoms and bypasses the need for a separate albuterol inhaler, has been referred to as Single-Inhaler for Maintenance and Reliever Therapy or SMART. As with the budesonide-albuterol inhaler, the maximum recommended daily dose of the budesonide-formoterol combination is 6 doses (12 puffs) over 24 hours.

What Are the Benefits?

Most importantly, use of anti-inflammatory reliever therapy reduces the likelihood of an asthma attack, including (and especially) severe asthma attacks that require emergency care and a course of prednisone or other oral steroid for treatment. This benefit has been demonstrated in multiple carefully done research trials among persons with all different severities of asthma. Many patients report improved satisfaction with their asthma control when using anti-inflammatory reliever therapy. Some appreciate the convenience of having a single inhaler that can be used for both daily maintenance therapy and quick relief of symptoms as needed. Others with relatively mild asthma are happy to substitute the requirement for daily inhaled steroid use with a medication that they can use only when needed, guided by their symptoms.

Other Considerations

Are there any potential downsides to implementation of anti-inflammatory reliever therapy? Yes. One might consider the cost of the particular inhalers; an increased risk of irritation in the

throat and/or thrush from use of an inhaled steroid; and lack of utility for the subset of persons with asthma who do not significantly benefit from the action of inhaled steroids.

Is anti-inflammatory reliever therapy safe in pregnancy and during nursing? Yes. The medicines are safe for mother and fetus; and as a medication strategy that reduces the risk of asthma attacks, it is not only safe but desirable.

Can anti-inflammatory rescue be used before exercise, as albuterol or levalbuterol is, to prevent exercise-induced asthma symptoms? Yes. Although an inhaled steroid is not necessary in that circumstance, the anti-inflammatory reliever provided in combination steroid-bronchodilator inhalers will be effective in blunting the effect that exercise might have on provoking asthma symptoms. If you exercise frequently (that is, several times per week or more often) and don't need bronchodilator medication other than for prevention of exercise-induced symptoms, you may want to discuss with your medical provider whether a bronchodilator inhaler without steroid would be more appropriate for use pre-exercise.

In an acute asthma attack, is it safe to take 4 puffs at a time of a combination antiinflammatory reliever, as one might of an albuterol inhaler? Yes. The extra puffs of steroid medication may be helpful in quieting the acute attack. Try to limit the total dose in one day to 12 puffs.

If I am taking my albuterol inhaler 4 times a day on a regular basis, can I substitute a combination anti-inflammatory reliever inhaler taken 4 times a day? No. One should not be taking albuterol or levalbuterol on a regular schedule. It is meant to be taken only as needed, for relief of symptoms or prior to exercise. There is no benefit from taking albuterol on a regular schedule. So, too, the anti-inflammatory reliever is to be taken only as needed, guided by symptoms.