Appropriate Use of Antitussives and Protussives
A Practical Review

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Contents

Summary
1. Antitussive Therapy
   1.1 Definitive Therapy
   1.2 Nonspecific Therapy
2. Protussive Therapy
   2.1 Cough Effectiveness
   2.2 Cough Frequency
3. Conclusions

Summary
As a symptom of an underlying condition, cough is one of the most common reasons patients see physicians. To the majority, a cough means that ‘something is wrong’ and it causes exhaustion and/or self-consciousness. Patients find these reasons as well as effects on lifestyle, fear of cancer and/or AIDS or tuberculosis to be the most troublesome concerns for which they seek medical attention.

The treatment of cough can be divided into two main categories: (a) therapy that controls, prevents or eliminates cough (i.e. antitussive); and (b) therapy that makes cough more effective (i.e. protussive).

Antitussive therapy can be either specific or nonspecific. Definitive or specific antitussive therapy depends on determining the aetiology or operant pathophysiological mechanism, and then initiating specific treatment. Since the cause of chronic cough can almost always be determined, it is possible to prescribe specific therapy that can be almost uniformly successful. Nonspecific antitussive therapy is directed at the symptom; it is indicated when definitive therapy cannot be given. Practically speaking, the efficacy of nonspecific therapy must be evaluated in double-blind, placebo-controlled, randomised studies of pathological cough in humans.

Such studies have demonstrated the efficacy of dextromethorphan, codeine and ipratropium bromide aerosol in patients with chronic bronchitis. While the preferred treatment for patients with cough due to angiotensin converting enzyme (ACE) inhibitor therapy is withdrawal of the offending drugs, it may be possible to ameliorate the cough by adding nifedipine, sulindac or indomethacin to the treatment regimen.

The efficacy of protussive therapy has not been well documented. Although hypertonic saline aerosol and erdosteine in patients with bronchitis, and amiloride aerosol in patients with cystic fibrosis have been shown to improve mucus clearance, their clinical utility has not been adequately studied.
The effects of clinically useful drugs on cough have been previously critically reviewed (Irwin et al. 1987; Irwin & Curley 1991). This review updates our current understanding of this subject.

Cough is one of the most common reasons people seek medical treatment (National Health Survey 1978). Although the act of coughing itself has previously been reported to cause a variety of complications in the musculoskeletal, pulmonary, cardiovascular and central nervous systems (Irwin et al. 1977), these are not the most common or troublesome reasons for which patients with chronic cough (i.e. >3 weeks' duration) seek medical treatment. Reasons cited by patients cover a wide spectrum, ranging from somewhat vague concerns such as 'something is wrong' to more specific concerns such as exhaustion, insomnia and fear of AIDS or tuberculosis (Irwin & Curley 1991).

Cough serves a number of functions, including acting as an indicator of an underlying illness and as an important defence mechanism. Therefore, the treatment of cough depends on which function the cough is serving. When cough indicates an underlying illness, treatment should attempt to control, prevent or eliminate cough by using antitussive therapy. If the cough is an important component of a defensive reaction, then therapy aims to make cough more effective through protussive therapy.

1. Antitussive Therapy

Antitussive therapy is recommended when cough performs no useful function (i.e. is non-productive), and its complications represent a real or potential hazard. Definitive or specific antitussive therapy eliminates cough by being directed in a specific manner at either the aetiology (e.g. smoking cessation in chronic bronchitis) or the presumed operant pathophysiological mechanism responsible for cough (e.g. eliminating postnasal drip in allergic rhinitis). Nonspecific antitussive therapy is directed at the symptom rather than the underlying aetiology or pathophysiology, and aims to control rather than to eliminate cough. Nonspecific therapy is indicated when definitive therapy cannot be given either because the aetiology of cough is unknown or because definitive therapy has not had a chance to work or will not work (e.g. inoperable lung cancer).

1.1 Definitive Therapy

Studies examining the cause of cough in patients with chronic cough have clearly demonstrated that although the ability of different physicians to effectively manage chronic cough will vary (Irwin et al. 1981), the optimal treatment approach is first to determine its cause, and then to direct therapy specifically at eliminating the aetiology or pathophysiological mechanism (Fuller & Jackson 1991; Holinger 1986; Holinger & Sanders 1991; Irwin et al. 1981, 1990; Poe et al. 1989).

Following utilisation of an anatomical diagnostic protocol, specific antitussive therapy for chronic cough has been reported to have a success rate of between 88% (Holinger 1986) and 98% (Irwin et al. 1990). The success rate depends upon the specific patient population seen by the physician, the diagnostic protocol used and the treatment regimen used for the various causes of cough. An anatomical diagnostic protocol has been described previously (Irwin & Curley 1989, 1991; Irwin et al. 1990) [table I].

The specific treatment approach depends on the cause of the cough. These are outlined in table II.

1.2 Nonspecific Therapy

Since the primary aim of this review is to evaluate the clinical efficacy of nonspecific antitussive therapy, we restrict our attention primarily to studies which have revealed a treatment that decreases cough frequency and/or intensity using objective means, counts or standardised questionnaires, in patients with pathological cough. Further, only studies designed in a double-blind, placebo-controlled fashion are considered. The rationale for these guidelines has been previously detailed (Irwin & Curley 1991). With few exceptions, only those drugs that have been adequately evaluated according to these guidelines will be mentioned in this review.