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# The risk of bronchospasm in asthmatics undergoing general anaesthesia and/or intravascular administration of radiographic contrast media. Physiopatology and clinical/functional evaluation

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## KEY WORDS

*Asthma control test (ACT),  
Bronchial asthma, Bronchial  
hyperreactivity, Bronchospasm,  
General anaesthesia,  
Hypersensitivity, Radio contrast  
media.*

## SUMMARY

*It is well known that patients suffering from bronchial asthma undergoing to surgical procedures requiring general anaesthesia (GA) or the administration of water soluble radiographic contrast media (RCM) experience a risk of potentially severe bronchospasm. Nevertheless, little attention has been devoted on the possible preventive measures to reduce the occurrence of this potentially life-threatening event. It has been shown that the most important risk factor for bronchospasm during GA induction and/or the use of RCM is represented by a high degree of bronchial hyperreactivity with airway instability not adequately controlled by long-term anti-inflammatory treatment. The aim of this review is to underline the need for an accurate clinical and functional evaluation of asthmatics (especially those with a relevant degree of asthma severity) undergoing GA or administration of RCM. Guidelines shared by pulmonologists, allergologists, anesthesiologists and radiologists should be produced in the future for a better evaluation and management of these patients. General practitioner plays an important role in managing asthmatic patients in "Real Life". It is likely that "Real Life"- optimally controlled asthmatics could undergo GA/RCM with lower risks especially in emergency conditions when it is not possible to perform any preoperative evaluation.*

## Introduction

Bronchial asthma is a common clinical condition, and it is widely recognized that its impact is higher in industrialized countries characterized by the so-called "westernized lifestyle" (1-3). An increased airways reactivity sustained by chronic inflammation constitutes the pathophysiologi-

cal hallmark of asthma. Several specific, non-specific as well as occupational factors are able to increase the degree of airway hyperreactivity and consequently the risk of inducing asthma exacerbations (4-7).

Little scientific attention has been paid by pulmonologists and allergists to the risk of perioperative bronchospasm in asthmatics undergoing surgical procedures requiring gen-

## Abbreviations

GA (General Anaesthesia), RCM (Radio Contrast Media), ACT (Asthma Control Test), FEV1 (Forced Expiratory Volume in 1 second), FVC (Forced Vital Capacity), SABA (Short Acting Beta2 Agonists), OC (Oral Corticosteroids), BAL (Broncho Alveolar Lavage), NO (Nitric Oxide), ECP (Eosinophil Cationic Protein),

eral anaesthesia (GA). Moreover, only few attention has been reported on the prevention of this risk in the last International GINA Guidelines (8).

The topic is highly relevant, especially considering that asthma is a chronic condition which usually persists throughout the patient's life, during which the occurrence of a surgical and/or a diagnostic procedure under general anaesthesia may be considered common. Moreover, severe perioperative bronchospasm could induce near-fatal/fatal events as well as irreversible brain damage (9).

Although the management of a bronchospasm started during GA must be carried out by anaesthesiologists, pre-operative assessment of asthmatic and /or allergic patients should be performed by pulmonologists, or allergologists, or by physicians trained in respiratory diseases.

The lung is an important target organ of the effects of water soluble radiographic contrast media (RCM). Bronchospasm constitutes the most common adverse effects that may follow the intravascular injection of RCM (10). These diagnostic procedures may be performed either in inpatient and outpatient clinic and usually don't require a respiratory (clinical/functional) assessment. As a consequence of the poor awareness of the potential risk of bronchospasm, little attention has been devoted to the prevention of these events.

The aim of this review is to underline the need for an accurate clinical and functional evaluation of asthmatics undergoing surgical procedures requiring GA or radiological procedures requiring the administration of RCM in order to obtain information useful for an adequate preventive pharmacological approach.

### **Prevalence of bronchospasm in asthmatics undergoing GA or administration of RCM**

The occurrence of severe perioperative bronchospasm has been reported to be 0.17-4.2% of all general anaesthesiological procedures carried out in asthmatics (11-14). Other authors reported higher percentages (up to 20%) (15-18). These obstructive reactions increased in proportion to the proximity of the latest asthmatic attack to the operative date (16).

It has been suggested that intraoperative bronchospasm represents one of common symptoms of anaphylaxis (about 19% of cases) whereas it may be the only symptom in the 4.5% (19).

Day surgery (DS) has significantly evolved and expanded in the last decades, with a great number of complex surgi-

cal procedures included and a great number of complicated patients scheduled into the outpatient setting (20). Given this evolution, it cannot be excluded that in coming years, DS perioperative morbidity (including bronchospasm) will increase (20).

Bronchospasm has been reported to be a contributory factor in 23% of moderate and 5% of severe RCM induced adverse reactions (21). Although symptomatic bronchospasm is very rare (occurring in 0.001% of all examined individuals), sub-clinical bronchospasm assessed by a fall in FEV1 values is common, particularly in patients with an history of allergy and/or asthma (22-25). It has been also recognized that a broncho-obstructive event may be induced either in the context of systemic (IgE/non IgE-mediated anaphylactic) reactions or as a single clinical manifestation following the use of RCM (10). It is generally accepted that RCM induced bronchospasm is less severe in comparison to that determined by the use of GA (26).

Although low osmolar RCM have been reported to induce with reduced frequency broncho-obstructive events, Wilson and Davies (27) found that both high osmolar and low osmolar non ionic RCM produce a comparable fall in FEV1 and FVC.

Recent studies have shown percentages of bronchospasm ranging between 0.18-4% when nonionic iodinated contrast medium for CT, fluorescein angiography and also magnetic resonance contrast medium- gadolinium chelates are used (28-31).

### **Mechanisms and factors increasing the risk of bronchospasm in asthmatics undergoing GA**

Several factors may induce different degrees of perioperative bronchospasm in asthmatics undergoing GA for surgery. Many pathophysiological conditions may increase the degree of airway resistance. Some of these, such as impairment of the ability to cough, impairment of the mucociliary function, reduction of the tone of palatal/pharyngeal muscles, alteration of diaphragmatic function and an increase of the layer of liquid on the airway wall, are common functional alterations under GA. Moreover, the direct mechanical stimulation of airway induced by endotracheal intubation itself is potentially able to determine bronchoconstriction reflexes through different mechanisms (parasympathetic nervous system or activation of peripheral terminations of C-fibers afferents and consequent release of substance P and neuropeptide Y) (32-35).

Finally, baseline uncontrolled clinical/functional conditions represent the most important risk factors for a severe increase of airway resistance during surgical procedures (9, 36). A high degree of bronchial hyperreactivity associated with inadequate control of asthma symptoms might determine a marked functional instability of airways caliber even in those individuals with apparently "normal" spirometric parameters (Fig. 1).

Other relevant risk factors for perioperative bronchospasm such as obesity, stress, intercurrent upper and lower airways infections, gastroesophageal reflux and aspiration of organic materials may be associated in asthmatic patients (37-41). Furthermore, smoking asthmatics who have poorer asthma control and increased acute care needs (42), might be at higher risk under GA.

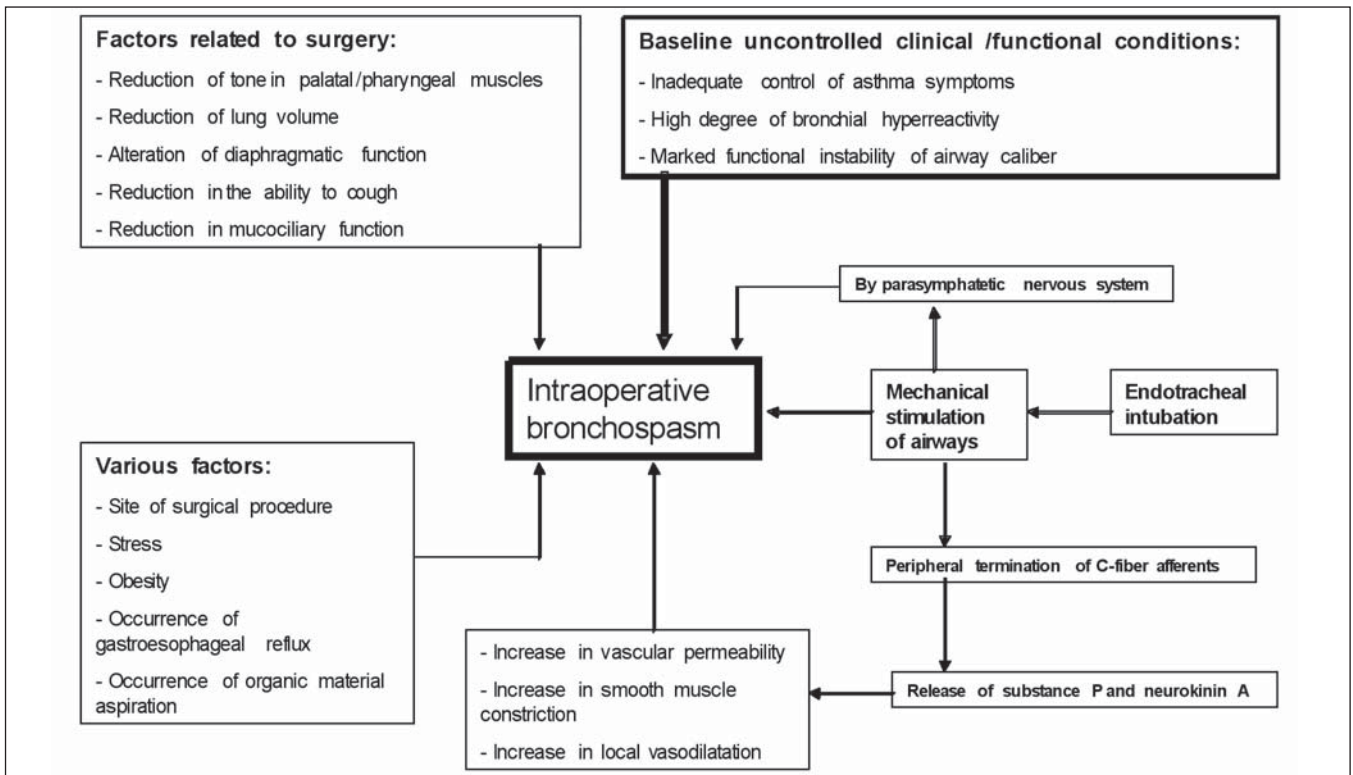
**Assessment of asthmatic patients before surgery**

Recent studies have shown that elective non-thoracic surgery is able to induce pro-inflammatory cytokines and cells production in serum and BAL fluids also in healthy individuals

and that these variations in human lungs should play a defensive role (43). It is likely that cells and cytokines production could be higher in asthmatic patients and, consequently, play a role in possible adverse events. The necessity to perform adequate preoperative functional evaluation is justified by prolonged hospitalizations, higher costs and increased morbidity and mortality determined by respiratory complications including bronchospasm (44, 45). From a general point of view, the site of surgical procedure constitutes a risk factor for adverse events in asthmatics (46). It has been shown that the risk of respiratory complications is inversely associated with the site of surgery and diaphragm and directly associated with duration of endotracheal intubation (37). On the contrary, with the exception of a single case report (47), epidural or spinal anesthesia are characterized by a lower risk of complications (48, 49).

In non emergency conditions, asthmatic patients should undergo clinical assessment at least one week before surgery in order to obtain optimal control of asthma symptoms (50-53). However, considering the wide diversity of asthma phenotypes in clinical practice, each requiring different diagnostic/therapeutic approaches, and that

**Figure 1** - Factors and mechanisms increasing the risk of perioperative bronchospasm in asthmatics [Adapted by permission from Informa Healthcare: Current Medical Research and Opinion (Ref. 53), copyright 2009].



asthma control is not associated with asthma severity classification, it is evident the necessity of a careful clinic-functional evaluation (54, 55).

Some simple preoperative information given by the patients such as increased use of SABA, recent asthma exacerbation requiring or not hospitalization, recent airway infections, use of OC etc., may be sufficient to identify individuals with uncontrolled or poor controlled asthmatic conditions (51, 56). Spirometric evaluation is essential in individuals suffering from severe bronchospasm as well as in those patients with uncertain anamnestic data/or limited perception of their respiratory symptoms (57). In asthmatic patients a reduction of Forced Expiratory Value in one second (FEV1) or Forced Vitality Capacity (FVC) less than 70% as well as FEV1/ FVC ratio under 65% of predicted values is usually considered a risk factor for perioperative obstructive complications (58). In patients with FEV1 values < 80% of predicted, it is useful to evaluate the degree of reversibility of bronchospasm after a standard dosage of a short acting  $\beta_2$  agonist (e.g. albuterol). A reversibility of bronchospasm > 15% means an instable, although reversible, airway caliber. In non emergency condition, long acting  $\beta_2$  agonists (LABA), if used, should be discontinued at least 12 hours before the test of bronchospasm reversibility. Warner et al. (59) demonstrated that asthmatics with reversible airway obstruction are at higher risk of perioperative and/or postoperative obstructive complications.

A relevant but "stable" reduction in FEV1 values with a low degree of reversibility of airway obstruction, doesn't imply an absolute contraindication to surgical procedures including those involving endotracheal intubation (60). It has been observed that the most important risk factor for perioperative bronchospasm is high degree of bronchial hyperreactivity not adequately controlled by long-term anti-inflammatory treatment and consequently the airway instability (36). In other words many patients, especially younger subjects, may have high level of bronchial hyperreactivity with spirometric parameters within normal range implying potential risk underestimation.

Groeben et al. (61) have demonstrated that asymptomatic but highly reactive individuals may develop a 50% or more reduction in FEV1 values after fiberoptic intubation under local anaesthesia. The importance of evaluation of the relationship between asthma severity and asthma control is essential also in children undergoing surgical procedure. As a matter of fact, inadequate control may lead to misinterpretation of either slight (even if symptomatic) either severe (even if well controlled) asthma (62). The

evaluation of ACT score could be very useful in order to detect uncontrolled individuals potentially at higher risk to develop bronchospasm.

Individuals suffering from symptoms of a suspected asthmatic etiology (e.g. persistent cough) and not requiring surgery in emergency situation, should undergo a non-specific bronchial provocation test to evaluate the presence and to quantify the degree of bronchial hyperreactivity. This information is essential for quantifying the risk of bronchospasm and optimizing preoperative therapy.

Even a slight hypoxia, induced by a recent asthma exacerbation, represents a potential risk factor for intraoperative bronchospasm. However, a comprehensive evaluation of risk factors in the single patient is needed before to consider a slight hypoxia as an absolute contraindication for non thoracic surgery (63).

If available, other diagnostic procedures might be useful to evaluate respiratory conditions of asthmatics undergoing GA. For example, recently it has been shown that the concentrations of exhaled NO correlate with the risk of perioperative bronchospasm either in established asthmatics or in individuals without an history of asthma (64). The levels of ECP in BAL fluids of children undergoing GA show a significant correlation with the degree of airway instability and, consequently, the risk of perioperative bronchospasm (65).

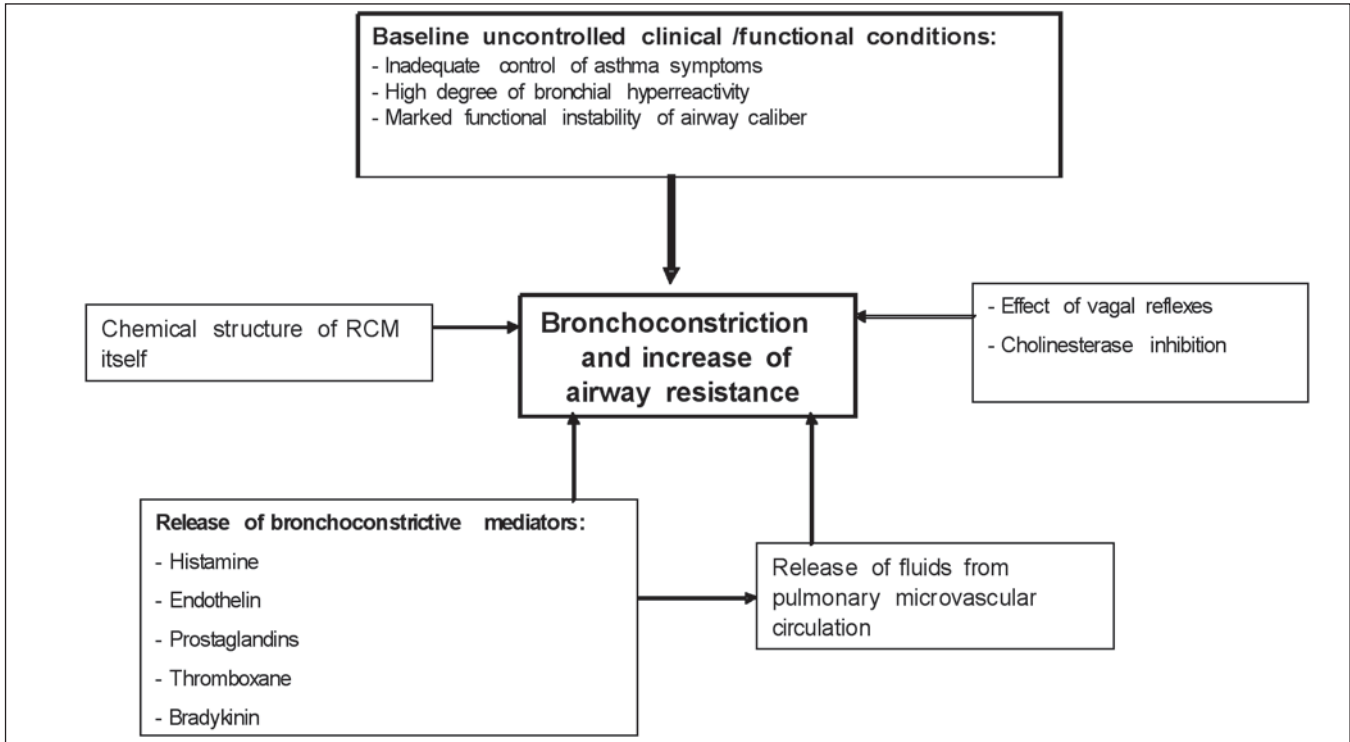
It is also essential an accurate evaluation of atopy-related -risk factors such as respiratory allergy, drug allergy as it has been shown that induction-related bronchospasm during AG is more severe if associated to IgE-mediated anaphylaxis in comparison to those induced by non-IgE mediated aetiology (66-69).

### **Assessment of asthmatics undergoing intravascular administration of radiographic contrast media (RCM)**

The pathogenesis of RCM-induced bronchospasm is complex and not completely understood, but it is likely that this could be multifactorial (Fig. 2). For example, Laude et al. (70) have shown that the onset of bronchospasm after administration of a low osmolar agent (ioxaglate) cannot be attributed to an osmotoxic effect but it is probably due to the chemical structure itself.

Other mechanisms may include release of bronchoconstrictor mediators (such as histamine, endothelin, prostaglandins, thromboxane and bradykinin), the cholinesterase inhibition and vagal reflexes (10, 68, 71-73). Some of these released mediators can also cause leakage

**Figure 2** - Factors and mechanisms increasing the risk of RCM induced bronchospasm in asthmatics [Adapted by permission from Informa Healthcare: Current Medical Research and Opinion (Ref. 53), copyright 2009].



of fluids from the lung microvasculature which further contributes to increase airways resistance (70).

The major problem of RCM administrations is that these diagnostic procedures may be performed either in patients admitted to hospital (and, consequently, in controlled conditions) or in outpatients referring to other settings such as private radiology centres. Since any specialistic (clinical/functional) preventive assessment is formally required, a poor awareness of potential risk of bronchospasm is commonly observed and, consequently, little attention has been devoted to the prevention of these events. Before RCM administration all patients suffering from persistent (moderate/severe) bronchial asthma should undergo an accurate clinical assessment (ideally performed by a pulmonologist or by an internist trained in respiratory medicine) as well as a spirometric evaluation.

It is likely that an optimal control of asthma symptoms could be useful in reducing the risk of bronchospasm in these asthmatics (10). Evaluation of ACT score could be very useful to detect uncontrolled individuals potentially at higher risk to develop bronchospasm. These patients should be treated with an optimal anti-inflammatory and

reliever therapy to reduce degree of bronchial hyperreactivity and consequently the risk of bronchospasm. It is likely that subclinical bronchospasm might determine greater obstructive effects in airways of asthmatics suffering from uncontrolled asthma (25).

## Conclusions

It is well known that patients suffering from bronchial asthma undergoing to surgical procedures requiring general anaesthesia (GA) or administration of water soluble radiographic contrast media (RCM) have an increased risk of potentially severe bronchospasm. Nevertheless, little attention has been devoted on the possible preventive measures to reduce the occurrence of this potentially life threatening event. It has been shown that the most important risk factor for bronchospasm during GA induction and/or the use of RCM is represented by a high degree of bronchial hyperreactivity with airway instability not adequately controlled by long-term anti-inflammatory treatment.

In this review we underline the need for an accurate clini-

cal and functional evaluation of asthmatics (especially those with a relevant degree of asthma severity) undergoing GA or administration of RCM. Guidelines shared by pulmonologists, allergologists, anesthesiologists and radiologists should be produced in the future for a better evaluation and managements of these patients. General practitioner plays an important role in managing asthmatic patients in "Real Life". It is likely that "Real Life"- optimally controlled asthmatics could undergo GA/RCM with lower risks especially in emergency conditions when it is not possible to perform any preoperative evaluation.

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