

LETTER TO THE EDITOR

Bronchospasm and iodinated contrast media (ICM): an accurate evaluation is mandatory

G. Liccardi¹, M. Martini^{2,3}, M.B. Bilò^{3,4}, M. Milanese⁵, M.V. Liccardi⁶, G. Pane⁷, R. Zeccolini⁸ and P. Rogliani^{1,7}

¹ Postgraduate School of Respiratory Medicine. Department of Experimental Medicine, University of Rome "Tor Vergata", Rome, Italy

² Allergy Unit, Ospedali Riuniti Marche Nord, Fano, Italy

³ Department of Clinical and Molecular Sciences, Marche Polytechnic University, Ancona, Italy

⁴ Allergy Unit, Department of Internal Medicine, University Hospital Ospedali Riuniti, Ancona, Italy

⁵ Division of Pulmonology, S. Corona Hospital, Pietra Ligure, Italy.

⁶ Psychologist, Naples, Italy

⁷ Department of Experimental Medicine, Unit of Respiratory Medicine. University of Rome "Tor Vergata", Rome, Italy

⁸ Postgraduate School of Radiodiagnostics, University "Luigi Vanvitelli" Naples, Italy

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Summary statement: An accurate clinical evaluation of asthmatics (especially those with a relevant degree of asthma severity) is recommended, before ICM administration.

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Corresponding author

Gennaro Liccardi, MD

-Postgraduate School of Respiratory Medicine. Department of Experimental Medicine, University of Rome "Tor Vergata", Rome, Italy

Phone : +39 081 5780554; E-mail: gennaro.liccardi51@gmail.com

To the Editor

We have greatly appreciated the editorial and three articles about the relevant topic of hypersensitivity reactions to iodinated contrast media (ICM), published on *European Annals of Allergy and Clinical Immunology* on March 2022.

With this letter we wish to stress (A) the importance of respiratory symptoms (with or without concomitant manifestations) as adverse events to ICM, and (B) the need for an accurate clinical evaluation of asthmatics undergoing radiological procedures with ICM, aiming at (C) deciding when and which preventive pharmacological approach should be recommended.

A) Bronchospasm as a respiratory adverse event to ICM

According to the Ring and Messmer scale commonly adopted for reaction severity, respiratory symptoms are included into II and III grade and are associated to other multiorgan clinical manifestations (1-4). However, bronchospasm can be the only or prevalent symptom in particular circumstances, particularly in non-controlled asthma (5). Moreover, asthma severity is a risk factor for acute adverse events to contrast agents (6), and this is true also within Step 1 of GINA classification. The apparently unexplainable higher risk in Step 1, reported by Kobayashi et al. (6), could be justified by the fact that their study enrolled much more GINA Step 1 asthmatics than patients belonging to the other Steps and, above all, none of them were taking inhaled corticosteroids. On the contrary, from a general point of view, there is a direct correlation between the degree of asthma severity and female sex, and the risk of developing anaphylactic reactions (7).

Lung is a key target for water soluble ICM, and this is reflected by bronchospasm, that constitutes the most common adverse event, among respiratory reactions, to ICM (8), with a reported occurrence of 23% and 5% cases of moderate and severe reactions, respectively (9). Although symptomatic / severe bronchospasm seems to be rare, sub-clinical bronchospasm assessed by a fall in FEV₁ values is quite common, particularly in patients with an history of allergy and /or asthma (10). Furthermore, a bronchospasm can develop both during systemic reactions (e.g., IgE / non IgE-mediated anaphylaxis) and as isolated events (10).

Although low osmolar ICM have been reported to induce a reduced frequency of bronchospasm, Wilson and Davies (11) found that both high osmolar and low osmolar non-ionic ICM produce a comparable fall in FEV₁ and FVC, the latter an expression of air trapping (theoretically more dangerous). Other studies have shown percentages of bronchospasm between 0.18 and 4% with non-ionic ICM for computer tomography and fluorescein angiography, and also with magnetic resonance contrast medium (RCM)-gadolinium chelates (12).

The pathogenesis of ICM-induced bronchospasm is complex and not completely understood, but it is likely that this could be multifactorial (Figure 1): the chemical structure itself, the release of bronchoconstrictor mediators (such as histamine, endothelin, prostaglandins, thromboxane and bradykinin), and the cholinesterase inhibition may play a role (13). Some of these released mediators can also cause leakage of fluids from the lung microvasculature which further contributes to increase airways resistance (13). Recently, the role of stress as predisposing / triggering factor in asthma has been extensively studied. Individuals with stress due to psychological disorders or to the fear of ICM administration might experience vagal hypertone and, consequently, increased risk of bronchospasm (14).

B) An accurate evaluation of respiratory status is of essence

Despite this well-known relevance of respiratory adverse events to ICM, little attention has been paid by healthcare professionals to the risk of bronchospasm in allergic / asthmatic patients requiring ICM. In fact, no recent articles have been published on this topic to suggest diagnostic evaluations or pharmacological preventive treatments (e.g. β_2 agonists), with consequent poor awareness about this risk.

This is true either in inpatient care (and, consequently, in the controlled environment of the hospital setting) and in outpatient care (e.g. private radiology centres).

Bearing in mind the risk of potentially fatal respiratory adverse events, all patients suffering from persistent (moderate/severe) bronchial asthma should undergo an accurate evaluation, before ICM administration. This should include a thorough clinical assessment, ideally performed by pulmonologists/allergists or by internists trained in respiratory medicine, aimed at optimizing asthma control (15), as it is likely that an optimal control of asthma symptoms could be useful in reducing the risk of bronchospasm in asthmatic patients (8). Evaluation of Asthma Control Test (ACT) score could be very useful to detect uncontrolled patients potentially at higher risk of bronchospasm. In patients suffering from seasonal allergic asthma the examination with ICM could be postponed, if possible, outside the peak of the pollen season or after adequate pharmacologic treatment.

C) Approach to prevent ICM-induced bronchospasm

Patients at risk of respiratory adverse events should be treated with an optimal anti-inflammatory and reliever therapy to reduce bronchial hyperreactivity and consequently the risk of bronchospasm. It is likely that subclinical bronchospasm might determine greater obstructive effects in airways of asthmatics with uncontrolled asthma (11). Although uncontrolled asthma, does not represent a contraindication to perform ICM administration in emergency setting, it is quite likely that ICM administration would be safer in asthmatic patients that are usually well-controlled, during their daily life, when it is possible to perform a clinical evaluation and stepping up the therapy in case of poor control.

For this reason, general practitioners (GP) play an important preventive role, as they manage asthmatic patients in “Real Life”, leveraging on their long-term knowledge of patients’ medical history and their constant commitment in managing and following up their chronic conditions (16). This high level of knowledge of the specific patient cannot be reached by the radiologist, as he/she may have just one single contact with the patient (i.e. when the radiologic procedure is performed) (16). Figure 2 shows a possible flow-chart for the management of the risk of ICM – induced bronchospasm, for different healthcare professionals and settings (GPs, radiologists, and pulmonologists / internists, working in inpatient or outpatient care).

Conclusions

It is well known that asthmatic patients undergoing administration of water soluble ICM have an increased risk of potentially severe bronchospasm. It has been shown that the most important risk factor for bronchospasm is represented by a high degree of bronchial hyperreactivity with airway instability, not adequately controlled by long-term anti-inflammatory treatments. Therefore, an accurate clinical evaluation of asthmatics (especially those with a relevant degree of asthma severity) should be recommended, before ICM administration. Guidelines shared by pulmonologists, allergists and radiologists should be developed in the future for a better evaluation and management of these patients.

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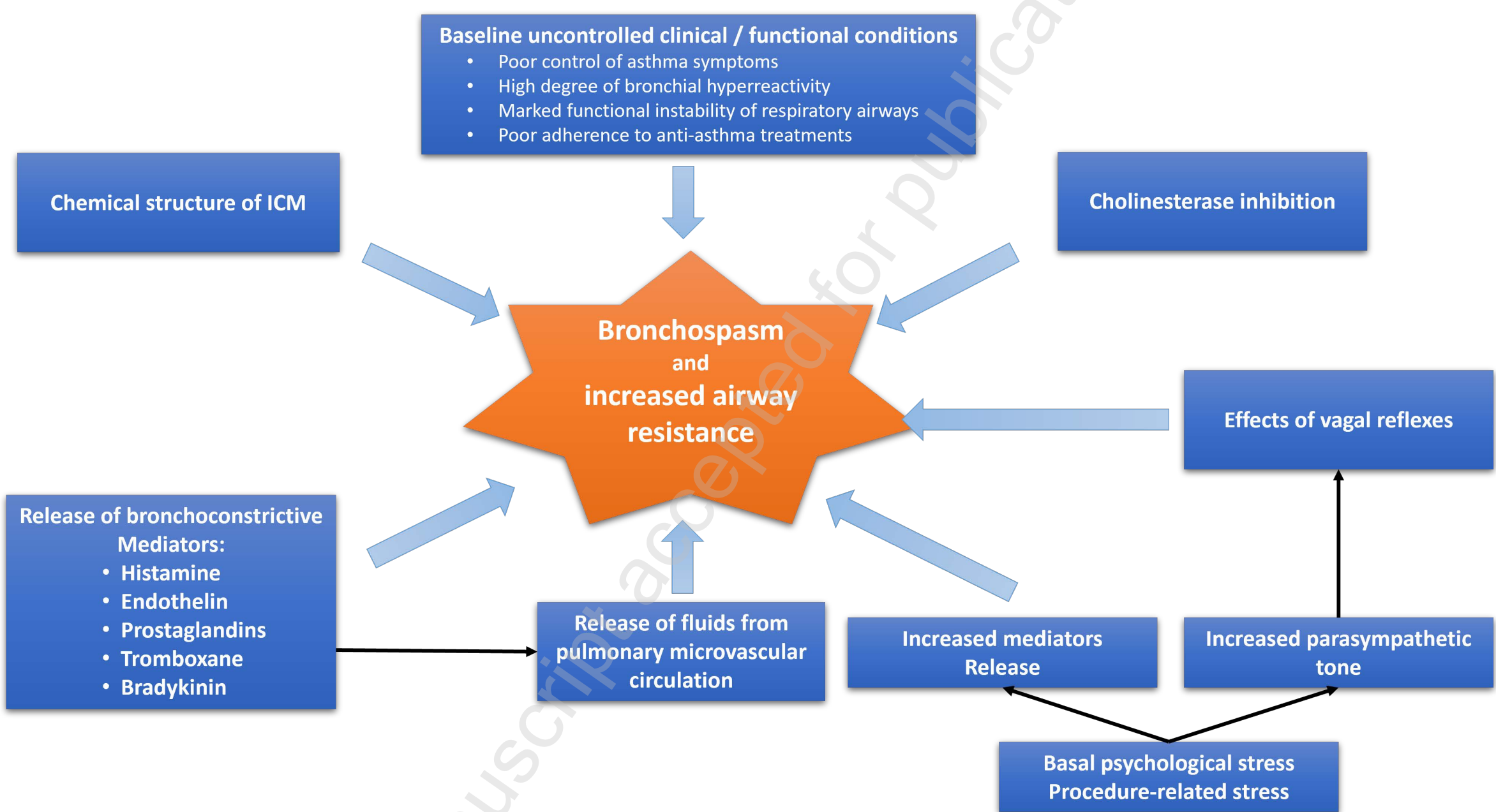
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Legend

Figure 1. Factors and mechanisms increasing the risk of ICM induced bronchospasm in asthmatics.

[Modified from Liccardi G. et al. The risk of bronchospasm in asthmatics undergoing general anaesthesia and/or intravascular administration of radiographic contrast media. physiopatology and clinical/functional evaluation. *Eur Ann Allergy Clin Immunol.* 2010; 42:167-73. (15)]

Figure 2. Suggested flow-chart (from GP to radiologist / internist) in managing asthmatic patient before ICM administration.



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GP CARE

MEDICAL / RADIOLOGICAL CARE

Primary Medical Center

Outpatient or inpatient facilities

Uncontrolled asthma
ACT < 20

- Clinical examination
- ACT test
- Specialist referral (if needed)
- Therapy revision

Non emergency
conditions

Start or continue controller
therapy + oral steroids in
the last 2-3 days

Uncontrolled pz.

Emergency
conditions

«Short» premedication
with i.v. steroids + short
acting β_2 agonists

Well-controlled pz.

Well controlled asthma
ACT ≥ 20

Continue controller therapy

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