

Therapeutic applications of bronchoalveolar lavage

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The value of bronchoalveolar lavage (BAL) in the exploration and management of interstitial lung diseases is now well-established, and has recently been updated in reports of the European Task group on BAL [1, 2]. Its place in therapy is not so clearly demonstrated, although BAL had been used for therapeutic purposes prior to its use as a diagnostic procedure. As early as 1963, RAMIREZ *et al.* [3] reported on whole lung lavage (WLL) using a large volume of fluid in patients with pulmonary alveolar proteinosis. Since then, this technique has been proposed for removal of any alveolar filling material, in conditions such as alveolar proteinosis [4, 5], alveolar microlithiasis [6], acute silicosis [7], or accidental inhalation of radioactive particles [8, 9]. Its use has also been proposed in obstructive lung diseases [10], to remove the mucous secretions accumulated in the bronchial tree, as in asthma [11, 12], or cystic fibrosis [13, 14]. This lavage differs from the segmental BAL currently used for diagnostic or research purposes, in that it is performed under general anaesthesia, and uses a much larger volume of fluid. The actual procedure varies slightly from one centre to another and has not yet been standardized [4, 15]. WLL is a safe procedure, as shown by the absence of chronic side-effects over periods as long as 25 yrs in patients treated for alveolar proteinosis [16]. On the other hand, its efficacy is known to be dependent on the type of disorder in which it is performed.

We will briefly review the main pathological conditions in which WLL is currently performed and will show that alveolar proteinosis is the only disease which clearly profits from WLL. In all other conditions mentioned above, the value of WLL is doubtful, or not yet clearly established.

Alveolar proteinosis

The benefit of therapeutic WLL is now well demonstrated in this disease. First proposed by RAMIREZ *et al.* [3], the technique has been slightly modified over the years. When the diagnosis of primary alveolar proteinosis is established, the decision to perform a therapeutic bronchopulmonary lavage should be based upon the patient's tolerance to exercise and on his symptomatology, since a spontaneous remission is

always possible. When indicated, the performance of a WLL requires experienced staff and considerable back-up facilities [4]. Although the technique has not been standardized, the common principles can be outlined as follows [3-5, 10, 15, 17].

Therapeutic WLL is performed under general anaesthesia, using a double lumen endotracheal tube. Most groups lavage the dependent lung with the patient in the lateral decubitus position, others in the supine position [10, 15, 17]. Both lungs are ventilated with 100% oxygen for 10-15 min to wash out the nitrogen. One lung is then excluded from the ventilatory circuit and lavaged with isotonic saline at 37°C, coming out of a container usually suspended at 150 cm above the carina. The usual filling volume is 500-1,000 ml. The same volume is then allowed to drain by gravity, with the assistance of mechanical chest percussion. The first aliquots to be recovered have a milky aspect, which gradually clarifies during the lavage. The filling and draining procedures are then repeated until the effluent is completely clear, usually after 10-40 l. At the conclusion of the procedure, usually lasting from 3-4 h, an early extubation is generally the rule, after an appropriate ventilation facilitated by continuous ear oxymeter monitoring. Immediately after the procedure, a chest radiogram should be obtained to rule out a hydropneumothorax. Usually, the most affected lung is lavaged first. Symptomatic improvement generally takes place within 24-48 h. The other lung is lavaged 3-7 days after the first, using the same procedure. This therapeutic approach is safe, and its rare complications include hydropneumothorax, bronchospasm and pneumonia [3, 4, 15, 17-19].

Some authors have shown a significant improvement of alveolar macrophage (AM) function after therapeutic WLL, demonstrating that the defect in AM function in alveolar proteinosis is reversible. Furthermore, this treatment could also reduce the rate of secondary infections [4, 5]. Idiopathic forms of alveolar proteinosis are always improved by WLL. The periodicity of the need for therapeutic BAL varies widely from one patient to another, depending on the individual course of the disease. A minority of patients with alveolar proteinosis may exhibit a lavage-induced complete remission of the disease. Others may require occasional repeated WLL every 6-24 months.

If after a WLL the clinical symptoms do not dramatically improve, a clinical and pathological search

should be made for an associated condition. An open lung biopsy is then required to eliminate, for instance, acute silicosis, infections and/or malignancy [7, 20].

Asthma

Mucus plugs are known to contribute to the severe hypoxaemia in patients with status asthmaticus. These plugs can be removed by suction through a bronchoscope, after the instillation of saline with or without acetylcysteine [11, 12]. However, this procedure was thought to have a high risk/benefit ratio, especially when performed with a flexible bronchoscope under local anaesthesia [10, 21]. Some investigators have markedly improved the benefit of this technique by limiting the indications to patients with severe intractable asthma and through technical modifications [11, 12, 22, 23].

A recent study used general anaesthesia and a rigid bronchoscope to perform segmental bronchial lavages with warmed saline, using 50–150 ml per lavaged segment [12]. A clinical benefit is likely if tenacious mucus plugging or tracheobronchial casts are present. Nevertheless, despite this study, it seems that therapeutic lavage in patients with severe asthma is recommended only in selected patients showing clinical criteria suggestive of mucus plugging, such as a decrease of mucus production within the last 48 h, diminished lung sounds in the lower lobes ("silent chest"), together with an absolute failure of applied therapeutic means [12]. Such therapeutic lavages should be performed only by well-trained physicians with an extensive experience in this field, in the context of an intensive care unit.

The volume of fluid used here is much smaller than that used for a WLL in alveolar proteinosis. Strictly taken, the therapeutic lavage in asthma is a bronchial lavage rather than a true BAL. Successful bronchial lavages have also been reported in intubated and ventilated patients with a severe asthmatic state, leading to the removal of mucus plugs and improvement of hypercapnia [24].

Pneumoconiosis

It is now well-known that inhaled inorganic dust damages the lung by inducing an inflammatory reaction that progressively leads to fibrosis. WLL has been proposed in order to remove the irritating dust before this irreversible damage occurs, especially in the acute form of silicosis [7, 25]. The aspect of the lavage fluid is usually striking, with its black or brown colour and numerous alveolar macrophages containing dust particles. It seems that the procedure results in rapid symptomatic improvement but without modification of the pulmonary function or the prognosis [25].

Inhalation of radioactive particles

The benefit of WLL in human contamination is not yet clearly defined [8, 9]. Experimental studies on

dogs and baboons have been carried out over the last 20 yrs to determine the efficacy of WLL in the removal of such particles. It seems that, although the longer the radioactive material is present in the lung and the greater is the dose delivered, WLL should not be performed in the early stages of contamination since it can prevent the physiological clearance of inhaled particles from the upper respiratory tract. WLL seems to be indicated in levels of contamination inducing acute effects, while its value in patients with lower levels of exposure is not clearly established.

Other therapeutic applications of BAL

WLL has been proposed for theoretical purposes to be of value in the treatment of some other pulmonary disorders, such as alveolar microlithiasis or exogenous lipoidosis [6].

Alveolar microlithiasis is a rare disease, characterized by the alveolar accumulation of slowly growing calcified microliths, ranging in size from 0.1–2.5 mm. There is only one case report on WLL, in a 15 yr old entirely asymptomatic girl with this disease [6]. In this patient, WLL with 11 l failed to demonstrate any radiological improvement. Unfortunately, functional studies after WLL were not reported. Interestingly, the number of microliths lavaged by the procedure did not exceed 500. All of the lavaged microliths measured less than 1 mm. The authors concluded that probably most microliths are larger than the terminal bronchioles, and this may be the reason why WLL was unsuccessful. In this issue of the Journal, RATJEN *et al.* [26] report on a 10 yr old girl with alveolar microlithiasis associated with a lymphocytic interstitial pneumonitis. A good response to corticosteroid treatment was seen. Obviously such unusual presentation of alveolar microlithiasis would benefit more from anti-inflammatory treatment of the lymphocytic infiltrates than from WLL.

In cystic fibrosis, the benefit of WLL is also difficult to evaluate. It was expected that periodically repeated WLL could, if not arrest, at least slow down the progressive deterioration of lung function caused by the accumulation of bronchial secretions [13, 14]. Some authors have proposed WLL using anti-fungal drugs as a local treatment of aspergillosis, a frequent complication of this disease. This requires further investigation.

Conclusions

The therapeutic value of BAL is now well-established in alveolar proteinosis, which remains the only definite indication of this procedure. In other lung disorders, the risk/benefit ratio of this therapeutic approach does not always argue for its use in routine clinical practice. Its indication should be discussed in each individual patient. When agreed upon, it should be performed by experienced staff in the context of an intensive care unit.

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