To Dive or Not To Dive with Bleomycin

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Introduction

Bleomycin is a chemotherapeutic agent used for the treatment of testicular and lymphomatous cancers. However, trials from the 1960s revealed its pulmonary toxicity, termed bleomycin-induced pneumonitis (BIP).

Pulmonary toxicity is predominantly fibrotic and the earliest detection of pulmonary fibrosis can be achieved with serial measurements of the carbon monoxide diffusion capacity (DLCO) which may indicate the presence of occult pulmonary changes. Exposure to a high FiO2 during the perioperative and postoperative period in a patient with prior exposure to bleomycin can produce occult pulmonary fibrosis.

Testicular cancer is the most common malignancy in men aged 20-34 years; their survival rate is over 90%. In this age group, many survivors practice outdoor sports such as scuba diving, using mainly compressed air (21% oxygen, FiO2 = 0.21 bar) for breathing. During a dive the partial pressure of oxygen increases as a function of increased water pressure. At a dive depth of 20 m where the pressure of air is 3 bar, the inspiratory fraction of oxygen (FiO2) will be 0.63 bar. Based on this calculation, after bleomycin treatment most clinicians would be reluctant to approve of scuba diving due to the risk of pulmonary toxicity caused by this high FiO2. However, in patients prior treated with bleomycin, one study showed that increased FiO2 (0.40-0.87) during the perioperative period made no significant contribution to complications of late-onset BIP or fibrosis and it was concluded that perioperative oxygen restriction was not necessary. Some physicians allow patients treated with bleomycin to continue scuba diving without any restriction; they refer to experiences of divers in their clinical population, who resumed scuba diving without complications of late-onset of BIP, fibrosis or pulmonary barotraumas.

We present here an algorithm, based on best evidence from the literature on oncology, anesthesiology and diving medicine, that can be used to evaluate patients treated with bleomycin who want to resume or start scuba diving. We have used the algorithm to examine the fitness of 16 sport divers (14 males, 2 females) treated with bleomycin for either testicular germ cell cancer or Hodgkin disease.

Methods

The algorithm (Fig.1) was divided into a two-part examination. The first part included a general medical history, a specific medical history in relation to cancer and bleomycin treatment, documentation of dives before and (if applicable) after cancer, and extensive pulmonary function tests, including spirometry, residual volume and singlebreath diffusion capacity. The pulmonary function tests should exclude any abnormalities which might cause the diver to be at risk for pulmonary barotrauma.

The second examination consisted of a maximum exercise bicycle test with direct VO2 max measurements, blood gas measurements and ECG monitoring. Since there is some evidence that chemotherapy increases the risk of developing cardiovascular diseases in patients with testicular cancer, our algorithm included an exercise bicycle test during which the level of aerobic fitness must be at least 80% of the predicted value. We also measured blood gases at the start of the exercise test and at maximum workload to assess diffusion abnormalities which are not necessarily evident in pulmonary diffusion tests at rest.

Finally, a high resolution (HR) CT scan of the lungs was made. Thoracic HR-CT scanning, which has greater sensitivity than standard chest radiography to detect lung parenchymal abnormalities, is included in this algorithm.

Pulmonary function tests were performed using V-max Encore apparatus. Spirometry, residual volumes, body box, single-breath diffusing capacity (DLCO) and transfer coefficient (DLCO/VA) were measured according the manufacturer's instruction. DLCO and DLCO/VA values were corrected for hemoglobin (Hb) values. The exercise test was performed during the continuous presence of a physician to read the exercise ECG and draw blood gas samples. Arterial blood gases were measured with a conventional analyser. According our algorithm, 10 of the 11 patients with testicular/germ cell cancer were fit to dive compared with 2 of the 5 patients with Hodgkin disease.

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Discussion

All patients were active sport divers before the disease; some continued scuba diving after treatment, others stopped on the advice of their physician. Based on our algorithm, 12 of the 16 patients would receive positive advice about resuming scuba diving. However, the difference in the number of (ex-)patients found fit to dive in the two groups (testicular/germ cell cancer versus Hodgkin) indicates that particular caution is needed with Hodgkin patients treated with combined bleomycin/radiation therapy because of the increased risk of radiation-induced pulmonary problems.

Our algorithm for divers is based on the risk of pulmonary barotrauma. Restrictive abnormalities (as shown on spirometric tests) reduce lung compliance and impair gas transfer: diving is therefore contraindicated. Clinical and subclinical pulmonary fibrosis will result in less distensible lungs placing the diver at risk for pneumothorax, pneumomediastinum and arterial gas embolism. Air trapping due to lung parenchyma

abnormalities, local fibrotic tissue and bulla formation is also a risk factor. Therefore, thoracic HRCT scanning, having greater sensitivity than standard chest radiography to detect lung parenchymal abnormalities, is a prerequisite in this algorithm.

Scuba diving is a strenuous activity. A diver must be able to meet the physical requirements of the specific environment underwater, e.g. a strong current, the (possible) need to rescue a dive buddy, etc. Medical examiners must be sure that the candidate is fit enough with respect to aerobic fitness. More specifically, most young cancer patients need at least 6 months to 1 year before they are fit enough to undertake sports and diving. Thus, our algorithm consists of an exercise test.

The controversy about scuba diving after bleomycin treatment continues. The conservative approach is based on clinical and animal studies which strongly support the relationship between bleomycin toxicity and oxygen therapy. Most of these studies date from the 1980s and report anecdotal clinical findings of pulmonary complications being attributed to high inspired-oxygen fractions. Animal studies have yielded conflicting results: some examining the various factors affecting pulmonary morbidity associated with bleomycin exposure concluded that it has no significant impact on pulmonary toxicity. The majority of other animal studies have supported the data with regard to oxygen toxicity.

The more liberal approach in advice related to scuba diving refers to studies from anesthesiology which found no increased percentage of pulmonary problems (6.8%) in 835 patients treated with bleomycin. Another group studied 77 patients with a mean FiO2 of 0.87 for 56 min and an intraoperative FiO2 of 0.4 for 8 h; the authors concluded that in the multivariate analysis the FiO2 was not a significant factor contributing to the complications.

In the rare situation that a patient treated with bleomycin resumes scuba diving and develops DCS, s/he will need immediate hyperbaric treatment. The standard treatment tables have an FiO2 of 2.0-2.8 bar for 4-8 h, which might possibly induce pulmonary damage, fibrosis and BIP, so divers should be informed about the risks. However, in a report on 11 bleomycin patients undergoing hyperbaric oxygen therapy for radiation therapy, the number of hyperbaric treatments ranged from 8 to 44 with an FiO2 of 2.0 bar for 2 h during each treatment. Only one patient had significant chest discomfort and an objective decline (50%) of the diffusion capacity, which resolved with a break in the treatment cycle. The general advice given by the international hyperbaric community is that a one-year period is probably safe for hyperbaric oxygen therapy after bleomycin administration.

Our study has some limitations. First, a selection bias about the study population. Only patients who are physically fit after bleomycin treatment will continue with sports, particularly scuba diving, and participate in the study. Also, the (diving) magazines in which our announcements were published have contributed to selection bias.

Second, the study consists of a small group of patients with testicular/germ cell cancer or Hodgkin disease, who may differ in both the type and extent/stage of their disease. Three of the 16 patients (considered unfit to dive according our protocol) had radiation on the thorax as part of the treatment for Hodgkin; the fibrotic lesions in their lungs might be attributed to radiation and not to bleomycin therapy. The lungs are particularly sensitive to radiation, and abnormal radiographic findings or restrictive changes on pulmonary function testing is reported in more than 30% of patients receiving radiation directly or indirectly to the lung.

Third, the advice to dive to a depth of 25 m (FiO2 0.7 bar) without the use of nitrox is still not evidence-based and the opinions of the present authors will be seen as moderately conservative by the more experienced diver or instructor. In conclusion, there is a need for an algorithm to assist the international

diving medical community in the examination of scuba divers treated with bleomycin. Among millions of recreational divers in the world, a substantial percentage of young people will be cured with bleomycin. Many opinions exist regarding bleomycin and scuba diving and, although the information is not yet evidence-based, we believe that our algorithm will make a valuable contribution to this dispute. We think it reasonable to allow carefully selected patients to resume scuba diving after bleomycin therapy, but with some important limitations.

Results

Of the 16 patients in our study, 11 were treated with bleomycin for testicular or germ cell cancer, and 5 for Hodgkin disease. All patients except one were non-smokers.

Spirometry

The spirometric values (including flow-volume curves) were normal, with the exception of one patient (Hodgkin group) who had low values for VC and FEV1 predicted percentage. In this latter patient the distribution of residual volume/total lung capacity (RV/TLC) was approximately 75% of the predicted value, suggesting restrictive abnormalities. Therefore, he was unfit for diving already after the spirometry in the algorithm.

Diffusion capacity

Most patients had low values for diffusion and diffusion capacity at rest, but these were within the range of reference values.

Exercise test/arterial bloodgasses

During the exercise test, all patients had normal blood gases indicating a normal ventilation and diffusion, and a normal ECG and blood pressure. In 9 patients, PaO2 values increased during maximum exercise, 6 patients had a non-significant (<10%) decrease but normal exercise tolerance, and for 1 patient blood gas values were not available due to technical problems.

High resolution CT scan

Of the 16 patients, 4 had abnormal CT scans with fibrotic lesions and/or air trapping: patient 9 in the Testicular group (smoker), and 3 of these 4 patients were treated for Hodgkin disease with bleomycin and additional radiation on the thorax and lungs.