Bleomycin and scuba diving: where is the harm?

Testicular cancer is the most frequent malignant disease in men aged 15–40 years. Due to its sensitivity to chemotherapeutic drugs, most patients, including those with widespread metastatic disease, can now be cured. Bleomycin is an essential component of the most effective chemotherapy regimen for testicular cancer—ie, bleomycin, etoposide, and cisplatin [BEP]. However, bleomycin is feared for its induction of bleomycin-induced pneumonitis (BIP), which is sometimes fatal. After reports in the 1980s of perioperative complications that were ascribed to bleomycin, high inspired-oxygen fractions during anaesthesia were avoided, as were high inspired-oxygen fractions under hyperbaric circumstances, such as scuba diving. Such restrictions are no longer necessary, but dive medics and diving organisations still maintain this conservative approach. Because recreational scuba diving is increasingly popular, this issue has had an effect on thousands of young men who are faced with conflicting opinions, with many choosing the safest option of not resuming diving after treatment.

The risk of BIP during, or shortly, after treatment is correlated with age above 40 years, smoking, renal-function impairment, and the cumulative dose of bleomycin—a total dose less than 300 mg rarely causes BIP, whereas the risk increases when the cumulative dose exceeds 400 mg. After establishment of BEP as the most effective regimen for testicular cancer in the 1980s, for more than a decade most patients received a total of four cycles of BEP, to achieve a cumulative dose of 360 mg of bleomycin. Recently, however, randomised controlled clinical trials have shown that for most patients with metastatic testicular cancer, three cycles of BEP (270 mg bleomycin) is sufficient, resulting in a cure rate of over 90%. In these patients, the frequency of bleomycin-related death has become as rare as 0.2%. The full regimen of four cycles of BEP has remained standard treatment for intermediate and poor-prognosis testicular cancer. However, findings from three randomised controlled studies in the 1990s, involving 354 patients treated with four cycles of BEP, showed that bleomycin-related death occurred in less than 1% of patients, even with a 360 mg total dose. Additionally, although tests of pulmonary function during or shortly after the completion of four BEP cycles have shown abnormalities in about 25% of patients, clinical sequelae are infrequent and these changes are mostly reversible within 1–2 years, especially in non-smokers.

Because bleomycin is assumed to induce toxic effects partly by the induction of free radicals, giving high inspired-oxygen fractions to patients treated with bleomycin might be considered hazardous. In animal studies, a relation between an increased risk of BIP or fibrosis and concomitant oxygen supplementation has been shown during actual bleomycin exposure. By contrast, for humans treated with bleomycin, no evidence for such a relation exists. In the 1980s, anecdotal findings of perioperative pulmonary complications were attributed to BIP, elicited by high inspired-oxygen fractions during surgery. On the basis of these case reports, the use of oxygen supplementation was discouraged after any bleomycin treatment. Nowadays, such pulmonary symptoms are categorised as adult respiratory distress syndrome (ARDS), and the paradigm of avoiding high inspired-oxygen fractions after previous bleomycin has been largely abandoned. Intravenous fluid management, including transfusion, is recognised as a crucial factor that affects postoperative pulmonary morbidity, including the development of ARDS. In a study of 77 patients with advanced testicular cancer who had a total of 97 operations to resect residual tumours a mean of 6.4 months after bleomycin-containing chemotherapy (mean cumulative dose as high as 437 mg), the importance of preoperative pulmonary status, anaesthesia time, fraction of inspired oxygen, fluid balance, bleomycin dose, oxygen saturation problems, and pulmonary symptoms was examined. The length of surgery and time under anaesthesia, amount of blood transfused, estimated blood loss, fluid balance, and type of fluids given were significant predictors of postoperative oxygen-saturation problems in a univariate analysis (p<0.0001), as was preoperative forced vital capacity (p=0.012). In a multivariate analysis only the amount of blood transfused, preoperative forced vital capacity, and surgical procedure time remained significant. Increased intraoperative fractional inspired-oxygen was not significant in either analysis, prompting the authors to conclude that perioperative oxygen restriction in patients treated with bleomycin is not necessary.

Although a detrimental effect of high inspired-oxygen fractions within days or weeks after bleomycin exposure cannot be excluded, the findings of the above study, and
the knowledge that most bleomycin is eliminated from the body within 24 hours after administration, provides little reason to withhold optimum anaesthesia from a patient. Therefore, patients can receive appropriate inspired-oxygen fractions several months after, and especially more than 6 months after their last exposure to bleomycin.2,9

Scuba diving with pressurised normal air (FiO2: 21%), or enriched air (FiO2: 21–40%) is increasingly popular in young men. After publication in the 1980s of the anecdotal findings of pulmonary complications being attributed to high inspired-oxygen fractions, physicians experienced in hyperbaric medicine and diving medical organisations advised patients against scuba diving after bleomycin treatment. Even if pressurised normal air is used, the increased underwater pressure increases the inspired-oxygen fraction, because the partial inspiratory oxygen pressure is a function of the fractional concentration of inspired oxygen, the ambient pressure, and the partial pressure of water vapour in humidified gas.10 Therefore, the partial pressure of oxygen in the inspired (compressed) air is a direct function of the depth of the dive. For example, at a dive depth of 20 metres (about 3 atmospheres total pressure), the partial pressure of inspired oxygen in a scuba diver who is breathing compressed air is 0·63 atmospheres, which is equivalent to breathing 63% oxygen on the surface. Although these computations are mathematically correct, and the conservative approach to refrain from further scuba diving might have been appropriate in the 1980s and 1990s, recent clinical data and current anaesthesiology practices warrant revision of this dogma. During the past 20 years, we have been the lead investigators in Europe for the study of patients with metastatic testicular cancer, through the frameworks of the European Organisation for Research and Treatment of Cancer (EORTC) Genitourinary Tract Cancer Cooperative Group. We have been involved in the treatment of several thousands of patients with metastatic testicular cancer, many of whom, especially during the past decade, were recreational scuba divers. On the basis of our recommendations, many of our previous patients have resumed scuba diving without complications. Several of these people, whom we have followed-up for 5 to 10 years, are men who dive almost daily (eg, diving instructors), use enriched air, or who dive at the maximum depth of 40 metres for recreational diving. We have never seen or heard of any late-onset BIP or fibrosis, or of barotrauma in these people. Although internet searches (including PubMed and Google) for complications associated with diving (using the keywords “scuba diving” with “medical conditions”, “pulmonary diseases”, or “barotrauma”) produced over 6000 results, none were even remotely ascribed to previous bleomycin exposure.

We strongly believe that resuming scuba diving 6–12 months after an uncomplicated series of three or four cycles of BEP is completely acceptable. Caution should only remain for patients who develop clinical signs of pulmonary-function impairment during or shortly after bleomycin treatment. We deem the conservative opinions of many physicians and diving organisations about recreational diving after bleomycin treatment as unnecessary—opinions that we hope to change. Young men affected by testicular cancer should be able to undertake their normal daily life as fully as possibly after treatment with bleomycin.

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