Myeloma and other cancers

For most patients with multiple myeloma treatment is palliative and comprises combined melphalan and prednisolone. Despite several clinical trials the evidence on more intensive combinations is conflicting. Nevertheless, in younger patients the results of trials of high dose chemotherapy with bone marrow transplantation seem promising.

Cytotoxic drugs have no established role in the palliative treatment of cancers of the thyroid, kidney, and prostate. The lipid soluble nitrosoureas have been used for treating gliomas, but evidence that they improve quality of life or survival is unconvincing.

Conclusions

Systemic cytotoxic treatment has been remarkably successful in curing a few uncommon disseminated tumours, notably testicular cancer, acute lymphoblastic leukaemia, and Hodgkin's disease. This has encouraged the widespread use of chemotherapy for other more common cancers, but progress has been slow despite the enormous clinical research effort worldwide. We have therefore cautioned against the uncritical use of chemotherapy and stressed the importance of giving it selectively and only with adequate supportive care. The guidelines suggested in this paper should encourage the more effective use of chemotherapy in the palliation of advanced cancer and be useful as predetermined standards for medical audit; commissioners of health care may also find them useful when deciding how best to deploy available resources. They should be considered as complementary to innovative clinical research directed towards finding more active and less toxic treatments for disseminated cancer.

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Lesson of the Week

Acute angle closure glaucoma associated with nebulised ipratropium bromide and salbutamol

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Coadministration of nebulised ipratropium bromide and salbutamol may cause acute angle closure glaucoma in susceptible patients

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Nebulised ipratropium bromide and salbutamol have become standard drugs for managing acute exacerbation of chronic obstructive airways disease. We report five cases of patients who presented with acute angle closure glaucoma provoked by the combined administration of these drugs.

Case reports

All five patients had been admitted by general physicians with a diagnosis of acute exacerbation of chronic obstructive airway disease and had been started on combined nebulised ipratropium and salbutamol six times a day. Each patient was referred to the ophthalmic department after a sudden reduction in visual acuity and severe ocular pain and periorbital headache on the affected side(s). Three patients also had nausea and vomiting. All patients had congested conjunctivae, hazy corneas, shallow anterior chambers, and fixed mid-dilated pupils in the affected eyes. Angle closure glaucoma was bilateral in three patients (table). The patient in case 3 gave a history suggestive of abortive attacks of acute angle closure glaucoma over the three months preceding admission. In case 4 the patient had had symptoms of abortive angle closure during his admission (before the development of acute angle closure glaucoma) that were related to the administration of nebulised drugs. The table shows the time between starting nebulised therapy and the onset of symptoms. The drugs received by all patients were reviewed to identify any other drugs that could contribute to angle closure. All patients were initially treated with intensive pilocarpine (4%) topically, intravenous acetazolamide (500 mg), and analgesia. After initial control of intraocular pressure, all patients had bilateral peripheral iridotomies with a neodymium-YAG (yttrium aluminium garnet) laser.

Discussion

We have observed five patients who developed acute angle closure glaucoma (bilateral in three cases) after receiving nebulised salbutamol and ipratropium bromide. There have been two previous case reports of this condition associated with these drugs: in one case after using nebulised salbutamol and ipratropium bromide[1] and in the other case after using only nebulised ipratropium bromide.[2]

Ipratropium is an anticholinergic drug and is known to cause pupil dilatation. Salbutamol is a β_2 adrenoreceptor agonist and increases production of aqueous humour. Eyes which are anatomically predisposed to acute angle closure glaucoma have shallow anterior chambers, narrow anterior chamber drainage angles, and are often hypermetropic. By semidilating the pupil, ipratropium will partially block the flow of aqueous humour from the posterior to the anterior chamber, which will result in the peripheral iris bowing anteriorly and obstructing the drainage angle. Salbutamol will compound this problem by increasing production of aqueous humour. Acting together these two drugs will increase intraocular pressure and precipitate acute angle closure glaucoma. The concomitant administration of other drugs with anti-

Details of patients on referral to ophthalmologist

Case No	Age (years)	Time from start of nebulisers to onset of ocular symptoms	Visual acuity on referral*		Intraocular pressure on referral (mm Hg (kPa))	Delay to referral (hours)	Final visual acuity*	
			Right eye	Left eye			Right eye	Left eye
1	68	24 h	6/24†	Count fingers†	60 (8·0) 52 (6·9)	24	6/9	6/9
2	67	1 h	Count fingers†	6/9	64 (8·5) 22 (2·9)	72	6/36	6/9
3	69	36 h	6/60†	6/6	45 (6·0) 29 (3·9)	72	6/36	6/6
4	70	24 h	Hand movement†	Hand movement†	55 (7·3) 48 (6·4)	24	Hand movement	6/24
5	78	9 days	6/36†	6/36†	60 (8·0) 48 (6·4)	None	6/12	6/9

*Measured by Snellen's test. † Eye with acute angle closure glaucoma.

cholinergic activity (for example, amitriptyline in case 3) may aggravate the problem.

No cases of acute angle closure glaucoma have been reported with inhaled ipratropium or salbutamol. The higher doses achieved by nebulised administration and the fact that the drugs may escape around the mask and enter the eye probably account for their ability to cause acute angle closure glaucoma when administered with a nebuliser. A study on patients with chronic bronchitis showed that when ipratropium bromide and salbutamol were administered simultaneously with a nebuliser intraocular pressure increased in all patients with narrow drainage angles.[3] Transient angle closure occurred in half of these patients, although none required ophthalmic intervention. The use of goggles prevented the rise in intraocular pressure during nebulised administration of these drugs.

We suggest the following precautions to try to avoid acute angle closure glaucoma. Patients anatomically predisposed to the condition should be identified (those with shallow anterior chambers by the flashlight test,[4] or with severe hypermetropia). It is also important to exclude a history of abortive angle closure glaucoma with symptoms of blurred vision and haloes around lights associated with ocular or periorbital pain. Abortive acute angle closure glaucoma may be precipitated in a darkened room or when in a prone or semiprone position (for example, when reading) and may be aborted by going to sleep. When administering drugs the mask must be correctly placed to avoid aerosols and droplets spreading from around the mask into the patient's eyes. If possible try to avoid simultaneous administration of nebulised ipratropium and salbutamol. Any topical antiglaucoma treatment should be continued during the patient's admission to hospital. If acute angle closure glaucoma is suspected the patient must be referred to an ophthalmologist immediately.

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Medicine in Europe

This is the fifth in a series of articles looking at medical issues in Europe.

Medical education

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One of the principal objectives of the Treaty of Rome was the establishment of free migration within the European Economic Community (now the European Communities (EC)). Free migration implies a right to live and to work in any member state. For this to be practical for professional people a mechanism had to be found to recognise professional qualifications granted in one country in all the others. The first group for whom such a mechanism was set up was doctors, but it took 18 years from the signing of the treaty to agree the medical directives, which provide the essential framework.[1]

This delay was indicative of the diversity in medical training and qualifications which existed and still exists to a considerable extent in western Europe. Early negotiations on the directives sought to define precisely, in terms of duration and content, the training which doctors had to undergo if their qualifications were to be recognised throughout the community. An agreement of this nature proved impossible. It was the president of the European Commission, Ralf Dahrendorf, who cut the Gordian knot by declaring that, whatever their educational background, doctors throughout the community had similar skills and attributes and that, as the final product was the same, a qualification awarded by one member state should be regarded as satisfactory by all the others.

As a result the requirements of the directives, in terms of education leading to a basic medical qualification, are minimal (box). The directives have made free migration for doctors a reality but as a means of setting educational standards they have been a failure.

Mutual recognition of qualifications is a prerequisite for free migration because the titles attesting medical qualifications are legally protected in all EC states. Migrating doctors can practise only if their qualifications are recognised as giving them a right to that title. In many states the title medical specialist is also legally protected. This is a consequence of the reimbursement arrangements of social security systems, which differ for specialists and generalists. In order to enable specialists to migrate it was necessary for the directives to include provisions for the mutual recognition of specialist qualifications.

These provisions are almost as weak as those governing basic medical qualifications (box). In those countries where protected specialist titles exist the period of postgraduate training leading to them is normally between three and six years. This is reflected