trations in such subjects raises the need for further studies and highlights a possible area of intervention.

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Effects of long term octreotide on gall stone formation and gall bladder function

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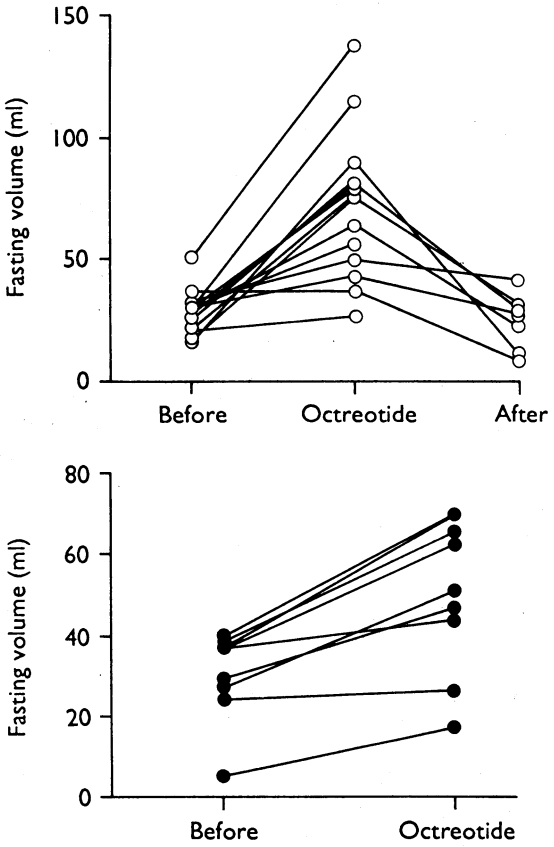
Gall stones seem to be a complication of prolonged treatment of acromegaly with the long acting somatostatin analogue octreotide (Sandostatin).[1-3] To get further information on the risk of cholelithiasis we conducted a study in patients with and without acromegaly having octreotide in a therapeutic trial. We also evaluated the effect on fasting gall bladder volume and the potential reversibility of gall stones on withdrawing octreotide.

Patients, methods, and results

We studied 15 subjects with active acromegaly (11 men, four women; mean age 50) and 10 non-acromegalic subjects with obstructive sleep apnoea (all men; mean age 51). All subjects gave written informed consent. The data in nine of the acromegalic subjects have been reported.[1] All 15 acromegalic subjects were treated for a median of 12 months (range 4-32 months) with variable doses of octreotide ranging from 100 to 500 μg thrice daily subcutaneously. All 10 subjects with sleep apnoea received 100 μg twice daily for two to three months. The results of the sleep study will be reported separately. All subjects had ultrasound examination before beginning octreotide. Seven subjects who formed new gall stones with octreotide were withdrawn from treatment and studied further. At all examinations fasting gall bladder volumes were estimated by the ellipsoid method,[4] studies during treatment being performed two hours after the morning injection of octreotide. The presence or absence of gall stones and the gall bladder volume were determined by one of us (GB-W) in a blinded manner. Data are presented as means and standard error of mean (SEM). Paired and unpaired *t* tests were performed as appropriate.

Gall stones formed in six of the 15 subjects with acromegaly and two of the 10 with sleep apnoea. The combined incidence was therefore 32% (eight of 25 subjects). There was no significant difference in incidence of gall stones between the two groups (χ^2 analysis). All gall stones were very small (1-2 mm) or small (2-5 mm) and varied in number from a few to the gall bladder being packed with calculi. In seven subjects with new gall stones who were studied up to eight months after withdrawal of octreotide gall stones completely resolved or substantially decreased in number in all but one. In five subjects who had studies available three months after withdrawal gall stone resolution had occurred in only two.

Fasting gall bladder volume was significantly increased during treatment with octreotide. In acromegalic subjects fasting volume increased nearly three-fold, from 27 (SEM 3) ml to 71 (8) ml (p=0·0002). (figure), and in sleep apnoea subjects there was also a significant increase, from 30 (4) ml to 50 (6) ml (p=0·0006) (figure). The baseline and treatment fasting gall bladder volumes were not significantly different between the two groups. There was no significant difference in mean fasting gall bladder volume between subjects who developed gall stones and those who did not. A subgroup of seven acromegalic subjects had studies performed before, during, and after withdrawal of treatment. Fasting gall bladder volume was similarly increased during treatment (27 (3) ml to 63 (7) ml) and reversed to normal after treatment withdrawal (25 (4) ml) (figure).



Top: Fasting gall bladder volume two hours after octreotide injection in 13 acromegalic subjects both before and during octreotide treatment and after withdrawal of treatment in seven subjects. Bottom: Fasting gall bladder volume in nine sleep apnoea subjects both before and during octreotide treatment

Comment

This study confirms our observation that long term octreotide increases the risk of cholelithiasis in acromegalic subjects[1] and shows that this risk extends to a non-acromegalic population, with an overall incidence of 32% (eight to 25 subjects), implying a generalised lithogenic risk with octreotide use. Our study design did not allow us to determine whether dose and duration of treatment were important determinants of gall stone formation.

Impaired gall bladder motility and subsequent bile

stasis are thought to be of primary importance predisposing to octreotide induced gall stones,[3] and this is supported by a report of impaired postprandial contractility[5] and our observation of a substantially increased fasting gall bladder volume.

In conclusion, our findings show recovery of gall bladder function and asymptomatic resolution of gall stones when octreotide is withdrawn.

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Oral and dental disease in terminally ill cancer patients

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Oral disease in patients with advanced malignancy has received scant attention despite its obvious relevance to palliative medicine. A recent pilot study of 20 hospice residents showed a wide range of oral problems.[1] We studied oral signs and symptoms in a large cohort of patients at the same hospice.

Patients, methods, and results

The 197 patients studied were consecutively admitted to the Holme Tower Marie Curie Centre. Personal details, diagnosis, and drug history were obtained from the medical records. A smoking history and details of oral and dental symptoms were collected by interview within two days of admission.

Mouths were examined under fibre optic illumination by a dental surgeon. The teeth and visible caries were charted. Xerostomia was rated clinically. Oral hygiene and gingival inflammation were assessed from the buccal surface of each tooth. Dentures were examined for quality of fit and cleanliness. Abnormalities of the oral mucosa and dorsum of the tongue were recorded.

The patients (112 men, 85 women) were aged from 34 to 91 (mean 69) years. Overall, 105 (53%) had never smoked and 46 (23%) still smoked. The drug regimens were complex and personalised. Only 21 (11%, 95% confidence interval 6% to 15%) of the patients were free of oral symptoms. The table shows the prevalences of the various oral problems.

Prevalence of oral symptoms among 197 patients terminally ill with cancer

Symptom	No of patients	Prevalence (%)
Xerostomia	152	77
Denture problems	70	45*
Taste disturbance	73	37
Swallowing difficulty	69	35
Oral soreness	64	33
Overall	176	89

*Based on 156 patients with dentures.

On examination xerostomia was mild in 95 (48%) patients, moderate in 27 (14%), and severe in nine (5%). Oral mucosal disease was present in 162 (82%) patients and was predominantly erythema in 64 (32%), plaques in 60 (30%), and ulceration in 24 (12%). Abnormalities of the dorsum of the tongue were detected in 167 patients, including papillary atrophy in 45 (23%) and erythema in 33 (17%).

Visible dental caries was present in 34 of the 97 (35%) dentate subjects. The mean plaque score was 1·1 (SD 0·6) and the mean gingivitis score 0·5 (0·4).

Of the 156 patients with dentures, 70 (45%) reported having denture problems. Only 27 (17%) dentures were clinically well fitting. Upper dentures were worn day and night by 76 (49%) of the denture wearers, and denture hygiene was poor in at least 42 (27%) of them.

Comment

Distressing oral dryness affected more than three quarters of the study group. The drug regimens of terminally ill patients may be at least partly responsible for xerostomia, although a search for other causes would be merited.

Many patients had oral mucosal disease, some of which may relate to reduced salivary flow. Oral candidosis (confirmed by culture in 85% of the patients) is a recognised complication of xerostomia, causing both mucosal plaques and erythema.[2] Mouth ulceration may be exacerbated by haematinic deficiencies,[3] which are likely to occur in terminally ill patients. However, other causes of ulceration should be considered, such as herpes simplex virus in patients with neutropenia.[4] Atrophy of the filiform papillae and erythema of the dorsum of the tongue are features of anaemia but may also result from chronic candidosis.

Oral hygiene was fair, with a low prevalence of gingivitis. The lack of clinically apparent gingival inflammation may also reflect immunosuppression in terminally ill patients.

Denture problems were common. Inadequate denture fit and stability are exaggerated by wasting of the facial musculature in terminal illness, but temporary relining of dentures can improve their function and aesthetics. For optimal mucosal health dentures should be removed at night, but in this study almost half of the denture wearers wore their prostheses continuously. The high rate of candidal carriage and candidosis in terminally ill patients[5] make it essential that dentures are soaked in a denture cleanser overnight, a simple measure that also improves denture hygiene.

Palliative medicine aims at making terminally ill patients as comfortable as possible during their last days of life. We found a high prevalence of oral problems in patients with advanced cancer. Devising and testing specific mouth care regimens for such seriously ill people should clearly be made a priority.

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