



Drugs and gingival bleeding

Ivan Darby, Senior Lecturer and Head of Periodontics, School of Dental Science, University of Melbourne

Summary

Gingival bleeding is an uncommon adverse effect, but some drugs may directly or indirectly cause bleeding gums. The gums may bleed spontaneously or following oral hygiene procedures or eating. Bleeding may result from anticoagulants and drug interactions which increase the bleeding time. Adverse effects such as gingival enlargement, oral ulceration, xerostomia and immune suppression are known to increase the likelihood of bleeding gums.

Key words: anticoagulants, gingival enlargement, periodontitis.

(*Aust Prescr* 2006;29:154–5)

Introduction

Bleeding gums are usually the result of plaque-induced gingival inflammation and swelling. The tissues bleed when traumatised by cleaning or eating. Occasionally bleeding may result from direct trauma, viral, fungal or bacterial infection, dermatoses, or as a manifestation of a systemic condition such as erythema multiforme or lupus erythematosus. Although it is a relatively uncommon reaction, a number of drugs have adverse effects that may directly or indirectly cause gingival bleeding. They may affect the oral mucosa, teeth, periodontium (supporting structures of the teeth) or salivary glands and impair or change taste. The adverse effects on the periodontal tissues may result in gingival bleeding.

Anticoagulant therapy

Patients taking anticoagulants such as warfarin or heparin may develop gingival bleeding. Those taking a combination of anticoagulants and antiplatelet drugs, for example warfarin and clopidogrel after cardiac surgery, have an increased risk of spontaneous and prolonged gingival bleeding. Patients on warfarin should have their INR checked.

The bleeding usually results from toothbrushing, interdental cleaning such as flossing, or eating, but it can also occur spontaneously, such as at night onto the pillow. This bleeding is usually easy to control.

Gingival enlargement

One of the most common adverse effects of drugs on the periodontium is overgrowth of the gingival tissues.¹ The

three main groups of drugs that cause gingival enlargement are the calcium channel blockers, anticonvulsants and immunosuppressants. The effect varies between patients and is influenced by age, gender, concomitant medication and genetic factors. It is somewhat dependent on the level of oral hygiene and the length of time the patient has been taking the drug.

The three most frequently implicated drugs are phenytoin, cyclosporin and nifedipine.² Phenytoin may cause overgrowth in 50% of dentate patients, cyclosporin in 30% and calcium channel blockers in 10%.² The three major drugs are usually prescribed with other medications, and expression of overgrowth may be affected by these other drugs. For example, nifedipine may be prescribed in transplant patients taking cyclosporin.²

Children and teenagers are more susceptible to phenytoin and cyclosporin-induced overgrowth than adults, suggesting that hormones, especially androgens, are important contributing factors. Males taking nifedipine are three times more likely to develop overgrowth than females, and men are also more prone to overgrowth when taking cyclosporin.

Other drugs may cause overgrowth, but only rarely. Tacrolimus seems to cause overgrowth in roughly 5% of kidney transplant patients, but in fewer liver transplant patients. Oral contraceptives have also been associated with some gingival overgrowth and bleeding mimicking the effects of pregnancy. This is probably a secondary reaction to irritation from plaque rather than a direct effect.

Clinical features

The overgrowth generally starts as painless enlargement of the papilla and proceeds to include the gingival margin, eventually developing to cover a substantial portion of the crown of the tooth. Histologically, the features of a drug-induced overgrowth are a fibrotic or expanded connective tissue and an enlarged gingival epithelium. It is thought that fibroblasts are primarily responsible. The gingival enlargement can be localised around one tooth, but is more commonly generalised throughout the whole mouth. It tends to affect the anterior teeth more severely.

While the overgrowth itself does not bleed, it is easily traumatised by the patient and will prevent adequate oral hygiene thus allowing the build-up of plaque. This accumulation will result in an inflammatory reaction with consequent bleeding. In addition, when the overgrowth reaches a large enough size it can be traumatised by biting.

Treatment

The treatment of overgrowth is initially by professional cleaning, but may require surgery to remove the overgrown tissue and restore normal architecture. If the patient remains on the causative drug then the problem will recur, possibly requiring re-treatment a couple of years later. The adverse effect may have to be accepted if the drug cannot be changed (Fig. 1).

Suppression of the natural flora

The use of antibiotics (both systemically and topically as a mouthwash), oral steroids and other drugs which allow the overgrowth of organisms such as *Candida albicans*, may occasionally cause an erythematous reaction which can result in gingival bleeding. This may be exaggerated by the presence of an upper denture, as some patients get a candidal infection underneath the plate.

Xerostomia

Many drugs cause a dry mouth or reduce the salivary flow, especially in elderly patients whose salivary flow is already diminished by age. These include antidepressants, antihypertensives, amphetamines, antihistamines, anticholinergics and drugs for Parkinson's disease. The effect of a dry mouth will increase both dental caries and periodontal disease due to decreased flushing of the mouth by the saliva and a reduced buffering capacity. The gingival inflammation from the periodontal disease may result in bleeding gums.

Immunosuppression

Drugs that suppress the immune response, such as methotrexate, can cause aplastic anaemia, agranulocytosis and thrombocytopenia. These conditions can result in a much more rapid destruction of periodontal tissues, excessive bleeding, a prolonged gingival bleeding time, oral ulceration, swollen gingiva or opportunistic infections. The patient may notice gingival bleeding spontaneously or following oral hygiene procedures and eating. Patients who develop gingival bleeding while taking these drugs need a full blood count.

Drug interactions

Drug interactions are especially common in elderly patients who may require treatment for several medical conditions. For example, patients taking non-steroidal anti-inflammatory drugs with anticoagulants such as warfarin, could have excessive and prolonged gingival bleeding because of the interaction. The interactions of warfarin and antiplatelet drugs are particularly problematic.³ The role of complementary medicines in increasing bleeding time is uncertain. However, a number of herbal preparations may interact with warfarin to increase its anticoagulant effect, including garlic and those containing coumarins such as arnica.⁴

Fig. 1

Gingival overgrowth as an adverse effect of nifedipine

Although this tissue is healthy, the patient complained that he was biting on the lower anterior gingival enlargement (not shown). The patient's doctor and periodontist changed his antihypertensive medication four times, but nifedipine was found to be the best for controlling his blood pressure. The patient accepted that he would continue to have gingival enlargement while on nifedipine. The tissue was surgically resected, but this procedure may need to be repeated in a few years.



Conclusion

Considering the large number of drugs prescribed, bleeding from the gums is an infrequent adverse effect. However, a number of medications can directly or indirectly result in bleeding from the gingival tissues. Patients presenting with excessive or prolonged gingival bleeding need to be thoroughly examined, and have a complete medical and medication history taken. Referral to a dentist or periodontist should be considered.

References

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Conflict of interest: none declared

Self-test questions

The following statements are either true or false (answers on page 171)

3. Up to 50% of patients taking phenytoin may develop gingival enlargement.
4. Nifedipine is responsible for most of the gingival enlargement associated with calcium channel blockers.