

Side effects of drugs in Sjögren's syndrome

16

Drugs play an important role in the treatment of diseases, but every drug has its advantages and disadvantages.

Use of a drug is only justified if the expected advantages are greater than the disadvantages. In order to be able to evaluate the advantage, it needs to be clear what the purpose of the treatment is and how the effect can be evaluated after a specific period of time.

The disadvantages of drugs may be subdivided into different categories including allergic reactions, general side effects, disease-dependent side effects and interactions with other drugs. Special situations may also arise if the kidney function and/or liver function are impaired.

Dryness

In the case of patients with Sjögren's syndrome, it is important to note that a possible side effect of many drugs is dryness of the mucous membranes. This is sometimes scarcely noticeable, but in Sjögren's patients the existing complaints of dryness may be greatly exacerbated as a result of using the drug. It is often possible to replace a drug with this side effect by another drug which does not have this side effect.

It is impossible to give a comprehensive summary here of the drugs that can cause dryness of the mucous membranes. Package inserts usually provide detailed information about this. Table 16.1 gives examples of the generic names (*i.e.* not the brand names) of a number of these drugs.

Constipation

A large number of drugs can cause constipation. These include all diuretics and prostaglandin synthetase inhibitors (these include most anti-inflammatories, with the exception of *e.g.* hydroxychloroquine, colchicine, dapsone and corticosteroids).

Pregnancy

A special warning applies to the use of drugs during pregnancy. A number of specific drugs are known to have a potential risk of causing deformities in the foetus developing in the uterus and should therefore

absolutely not be taken during pregnancy. In addition, many drugs are also secreted in breast milk. Since the effect of most drugs in pregnancy is as yet unknown, these too should be avoided as far as possible. See also chapter 11.

Sjögren's syndrome and myasthenia gravis

A small percentage of patients with Sjögren's syndrome

Table 16.1 Examples of drugs which can cause or exacerbate dryness of mucous membranes

anti-diarrhoea drugs loperamide	tranquillizers hydroxyzine lorazepam meprobamate oxazepam diazepam alprazolam
antihistamines loratadine promethazine hydroxyzine terfenadine cetirizine	anticonvulsants carbamazepine
anti-inflammatories piroxicam ibuprofen ketoprofen naproxen	antidepressants clomipramine amitriptyline imipramine desipramine
analgesics morphine	antihypertensives methyldopa captopril, lisinopril clonidine guanethidine reserpine
antiasthmatics salbutamol ipratropium	diuretics spironolactone chlorthiazide triamterene chlorthalidone furosemide
betablockers metoprolol pindolol metoprolol	antispasmodics hyoscymine atropine oxybutynin propantheline scopolamine
calcium channel blockers nicardipine	
sleeping tablets triazolam flurazepam temazepam	

Table 16.2 Drugs which can exacerbate myasthenia gravis or trigger symptoms in subclinical myasthenia gravis

antibiotics	quinolones
aminoglycosides	quinine
tobramycin	quinidine
gentamycin	chloroquines
neomycin	
kanamycin	various
ciprofloxacin	magnesium
norfloxacin	preparations
tetracyclines	anaesthetic agents
sulphonamides	
penicillins	
azithromycin	

Table 16.3 Drugs which could form a risk with myasthenia gravis

betablockers	anticonvulsants
propranolol	phenytoin
oxprenolol	barbiturates
timolol	ethosuximide
atenolol	carbamazepine
labetolol	gabapentin
metoprolol	
	drugs for eye disorders
psychotropics	timolol
lithium carbonate	betaxolol
phenothiazines	ecothiophate
amitriptyline	
imipramine	various
amphetamines	procainamide
haloperidol	riluzole
	drugs used for
calcium channel blockers	anaesthesia
verapamil	

also have myasthenia gravis (see chapters 2 and 7). It is also possible to have a mild form of myasthenia gravis (MG) which under normal circumstances produces no symptoms (subclinical MG).

Certain drugs can exacerbate existing MG and have a triggering effect in the case of subclinical MG. In both forms of MG, problems may occur with drugs used for anaesthesia. This means that if a Sjögren's patient knows that (s)he also has MG, this should always be discussed with the anaesthetist before an operation.

If a patient has a problem with double vision, drooping eyelids or muscular weakness due to the use of certain drugs, this could be a subclinical form of MG.

Double vision and muscular weakness as a side effect of drugs

Everyone, but especially patients with auto-immune diseases such as Sjögren's syndrome, who gets double vision and/or (exacerbation of) muscular weakness as a side effect of a drug may possibly have a mild form of myasthenia gravis. These side effects should be reported to your specialist.

This should be discussed with the patient's specialist so that tests can be carried out to find out if this is indeed the case. Please note that both hydroxychloroquine (Plaquenil®) and chloroquine (Nivaquine®) belong to the chloroquine group in this list.

Table 16.2 lists a number of drugs known to sometimes exacerbate an existing MG or trigger symptoms in the case of subclinical MG.

Table 16.3 lists a number of drugs which could form a risk to patients with MG for the same reason.

Patients with Lambert-Eaton Myasthenia Syndrome (LEMS) run the same risk (see also chapter on disorders of the nervous system).

Sjögren's syndrome and hypertension

Hypertension is a common disease with major risks for stroke and myocardial infarction. Pharmacological treatment of hypertension is aimed at reducing these risks by lowering the blood pressure. Several groups of drugs are used with different effects, side-effects and costs. Relatively old are the thiazide-type diuretics and β -receptor blockers. Newer antihypertensive agents are calcium-channel blockers, ACE inhibitors, angiotensin-II receptor antagonists and renin inhibitors.

Diuretics and to a lesser degree, betablockers may increase the dryness of eyes and mouth.

Calcium channel blockers may improve symptoms of Raynaud phenomenon whereas betablockers are contraindicated in Raynaud phenomenon.

Pharmacological treatment of hypertension

Diuretics and blockers have been used widely in the treatment of hypertension and were recommended as

Betablockers for hypertension

Betablockers should not remain first choice in the treatment of primary hypertension.

*Lindholm LH et al 2005¹
National Collaborating Centre
for Chronic Condition 2006²*

IMPORTANT

The comments on betablockers in this chapter, only apply if they are prescribed for hypertension and NOT IF PRESCRIBED FOR CARDIOLOGICAL INDICATIONS.

first-line drugs in hypertension guidelines.

Lindholm *et al* searched The Cochrane Library and PubMed for betablocker treatment in patients with primary hypertension.¹ Thirteen randomised controlled trials (n=105951) were included in a meta-analysis comparing treatment with betablockers with other antihypertensive drugs. Seven studies (n=27433) were included in a comparison of betablockers and placebo or no treatment.

The relative risk of stroke was 16% higher for betablockers than for other drugs. There was no difference for myocardial infarction. When the effect of betablockers was compared with that of placebo or no treatment, the relative risk of stroke was reduced by 19% for all betablockers, about half that expected from previous hypertension trials. There was no difference for myocardial infarction or mortality.

Lindholm *et al* conclude that in comparison with other antihypertensive drugs, the effect of betablockers is less than optimum, with a raised risk of stroke.¹ Hence, they believe that blockers should not remain first choice in the treatment of primary hypertension.

For the general population, the following recommendations² have been given by the National Collaborating Centre for Chronic Conditions:

1. In hypertensive patients aged 55 or over, or black^a patients of any age, the first choice for initial therapy should be either a calcium channel blocker or a thiazide-type diuretic.
2. In hypertensive patients younger than 55, the first choice for initial therapy should be an ACE inhibitor.^b
3. If initial therapy was with a calcium channel blocker or a thiazide-type diuretic and a second drug is required, add an ACE inhibitor.^b
If initial therapy was with an ACE inhibitor, add a calcium-channel blocker or a thiazide-type diuretic.

^a including both Black African and Black Caribbean patients, not Asian, Chinese, mixed-race, or other ethnic groups

^b or an angiotensin-II receptor antagonist if an ACE inhibitor is not tolerated

Diuretics may increase complaints of dryness in patients with Sjögren's syndrome and should therefore not be a first choice in the treatment of hypertension in Sjögren's syndrome.

The recommendations above can thus be modified for Sjögren's patients as follows:

1. In hypertensive Sjögren's patients aged 55 or over, or black^a patients of any age, the first choice for initial therapy should be a calcium channel blocker.
2. In hypertensive Sjögren's patients younger than 55, the first choice for initial therapy should be an ACE inhibitor.^b
3. If initial therapy was with a calcium channel blocker and a second drug is required, add an ACE inhibitor.^b
If initial therapy was with an ACE inhibitor, add a calcium channel blocker.

References

1. Lindholm LH, Carlberg B, Samuelsson. Should β blockers remain first choice in the treatment of primary hypertension? A meta-analysis. *Lancet* 2005;366:1545-53.
2. National Collaborating Centre for Chronic Conditions. Hypertension: management in adults in primary care: pharmacological update. London: Royal College of Physicians, 2006

Recommendations for treatment of hypertension patients with Sjögren's syndrome (see text)

1. In hypertensive Sjögren's patients aged 55 or over, or black patients of any age, the first choice for initial therapy should be a calcium channel blocker.
2. In hypertensive Sjögren's patients younger than 55, the first choice for initial therapy should be an ACE inhibitor (or an angiotensin-II receptor antagonist if an ACE inhibitor is not tolerated).
3. If initial therapy was with a calcium channel blocker and a second drug is required, add an ACE inhibitor (or an angiotensin-II receptor antagonist if an ACE inhibitor is not tolerated).
If initial therapy was with an ACE inhibitor, add a calcium channel blocker.