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Pseudoephedrine: ischaemic colitis

● **Do not use nasal decongestants.**

In early 2016, Health Canada issued a warning about the risk of ischaemic colitis associated with *pseudoephedrine*, a sympathomimetic vasoconstrictor used as a nasal decongestant (1,2). Health Canada's analysis, prompted by a case report published in 2014, identified 24 reports in the World Health Organization (WHO) pharmacovigilance database and 9 published cases.

The 2014 case report involved an otherwise healthy 49-year-old woman who was hospitalised 12 hours after developing abdominal pain and bloody diarrhoea (3). There was nothing in her history that could explain these symptoms, such as recent travel, antibiotic use, fever, eating unusual foods, similar symptoms in the past, similar cases in her family, colon disease, vigorous exercise, smoking, excessive alcohol consumption or use of illicit drugs. The symptoms persisted for 48 hours. Colonoscopy revealed erythematous, oedematous and irregular mucosa of the sigmoid and descending colon with a fibrinopurulent exudate, suggestive of colonic ischaemia. The only potential cause identified was the use of oral *pseudoephedrine* 120 mg twice daily for allergic rhinitis. The last dose was taken 12 hours before onset of her symptoms (3). The disorders resolved within a few days.

Sympathomimetic vasoconstrictors can provoke neurological and cardiovascular adverse effects, including hypertensive crisis, stroke and arrhythmia. A few cases of localised colonic ischaemia have been reported (2-4).

Pseudoephedrine and other sympathomimetic vasoconstrictors are authorised in France for oral or nasal administration, alone or in combination with other drugs, to treat symptoms of the common cold or allergic rhinitis: *ephedrine*, *naphazoline*, *oxymetazoline*, *phenylephrine* (*m-synephrine*) and *tuaminoheptane*. In France, the oral forms are available without a prescription and often heavily advertised to the general public, which trivialises their use.

In practice. There is no justification for using drugs capable of provoking ischaemic events, with potentially serious or even fatal consequences, simply to alleviate a few transient and complication-free symptoms of the common cold. These drugs should quite simply never be used.

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Selected references from Prescrire's literature search.

1- Health Canada "Summary safety review - Over-the-counter products containing pseudoephedrine - Assessing the potential risk of inflammation and injury of the large intestine due to insufficient blood supply (ischemic colitis)" 24 February 2016: 2 pages.

2- Prescrire Rédaction "16-1-2 Patients sous vasoconstricteur décongestionnant" *Rev Prescrire* 2016; **36** (386 suppl. Interactions médicamenteuses).

3- Sherid M et al. "Pseudoephedrine-induced ischemic colitis: case report and literature review" *J Digest Dis* 2014; **15**: 276-280.

4- Prescrire Editorial Staff "Ischaemic colitis on pseudoephedrine" *Prescrire Int* 2001; **10** (54): 117.

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Sofosbuvir: pulmonary arterial hypertension?

● **Adverse reactions to this drug should be reported.**

In early 2016, the French Health Products Agency (ANSM) reported that the serious adverse drug reactions reported in France with *sofosbuvir* for the treatment of hepatitis C include 7 cases of pulmonary arterial hypertension (PAH). The patients were also taking *daclatasvir* in 3 cases, *simeprevir* in 1 case, *ribavirin* in 1 case, *ledipasvir* in 1 case and several antivirals in 1 case (1).

A French article reported 2 cases of new-onset PAH and 1 of worsened pre-existing PAH in patients taking *sofosbuvir*. The patients had syncope, right heart failure and severe haemodynamic disorder (2). All 3 patients had other risk factors for PAH: portal hypertension or HIV infection.

Another French group identified 16 patients with PAH who had been exposed to direct-acting antivirals for the treatment of hepatitis C among all the patients monitored by the French referral centre for severe pulmonary arterial hypertension (3). In 13 cases, the patients had PAH before exposure to these antivirals, other risk factors and a disease course that did not suggest a causal role for these drugs. A causal role seemed likely however in the other 3 patients. They were all diagnosed with PAH after starting direct-acting antiviral therapy, and all were taking *sofosbuvir* in combination with other antivirals. The PAH of one patient, who did not have portal hypertension, resolved after cessation of antiviral therapy, without treatment for PAH, and still had normal pulmonary artery pressure 9 months later. The PAH of the other two patients improved with treatment after stopping antiviral therapy: pulmonary vascular resistance improved by 75% in one patient and returned to near-normal levels in the other.

In practice. Very little research was conducted on the adverse effects of *sofosbuvir* before its market introduction (4). Healthcare professionals must pay attention to events that occur during treatment and report them. As of 18 August 2016, the EU summaries of product characteristics (SPCs) of drugs containing *sofosbuvir* make no mention of this adverse effect (5,6). Healthcare professionals should be aware of it, so that they can arrange appropriate monitoring for patients taking *sofosbuvir*.

We shall continue to monitor this potential risk.

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Selected references from Prescrire's literature search.

1- ANSM "Réunion du comité technique de pharmacovigilance, compte rendu de la séance du 15 décembre 2015. Suivi national de pharmacovigilance des spécialités à base de sofosbuvir et daclatasvir Sovaldi Harvoni Daklinza" 9 January 2016: 18-21.

2- Renard S et al. "Severe pulmonary arterial hypertension in patients treated for hepatitis C with sofosbuvir" *Chest* 2016; **149** (3): 69-73.

3- Savale L et al. "Direct-acting antiviral medications for hepatitis C virus infection and pulmonary arterial hypertension" *Chest* 2016; **150** (1): 256-258.

4- Prescrire Rédaction "Notice Harvoni® (sofosbuvir + lédipasvir): quasi-absence d'information sur les effets indésirables" *Rev Prescrire* 2016; **36** (389): 223.

5- European Commission "SPC-Harvoni" 22 July 2016: 53 pages.

6- European Commission "SPC-Sovaldi" 28 January 2016: 44 pages.