Possible celecoxib-induced gastroduodenal ulceration

TO THE EDITOR: Nonsteroidal antiinflammatory drugs (NSAIDs) are among the most commonly prescribed drugs in North America. At least 10–20% of patients experience dyspepsia while taking NSAIDs; 13 of every 1000 patients with rheumatoid arthritis who take NSAIDs for one year develop a serious gastrointestinal (GI) complication.1 It has been estimated that 16 500 NSAID-related deaths occur in patients with rheumatoid arthritis or osteoarthritis every year in the US. This has led to the development of cyclooxygenase (COX)-2 inhibitors such as celecoxib and rofecoxib. This newer class of drugs is intended to have a better GI adverse effect profile than nonspecific COX inhibitors.24 It has been suggested that for every 100 patients treated with a COX-2 inhibitor instead of a nonspecific COX inhibitor, one symptomatic ulcer may be prevented during the first year of exposure. We report a case of possible celecoxib-induced gastric and duodenal ulcers.

Case Report. A 57-year-old African-American man reported abdominal pain, bloating, and dizziness and was transported to the hospital by emergency medical services. He described four melena stools and two watery stools with frank blood, and one episode of hematemesis within the preceding 24 hours. His past medical history included coronary artery disease with angioplasty five years previously, hypertension, cardiomyopathy with left ventricular dysfunction (ejection fraction 25%), gastroesophageal reflux disease, dyslipidemia, and chronic left shoulder pain.

The medications on admission included losartan 25 mg/d; carvedilol 12.5 mg twice daily; digoxin 0.25 mg/d; furosemide 40 mg/d; enteric-coated aspirin 325 mg/d, which he had been taking for three years; nitroglycerin patch 0.4 mg/h for 12 hours per day; atorvastatin 20 mg/d; and celecoxib 200 mg twice daily. His family physician had prescribed celecoxib 200 mg twice daily four months prior to this event for shoulder pain.

Physical examination revealed a 5’7” obese man (91 kg). On admission, his BP was 80/60 mm Hg; HR 100 beats/min, RR 30 breaths/min, and an oxygen saturation of 93% on 4 L/min of oxygen. He received a 200-ml bolus of NaCl 0.9%, which increased his BP to 102/68 mm Hg. His cardiopulmonary examination revealed a grade I–II/VI pansystolic murmur and good breath sounds with fine crackles to both bases. A musculoskeletal examination showed decreased strength bilaterally in the upper extremities. His abdominal and central nervous system examinations were unremarkable.

Laboratory parameters on admission included chloride 107 mEq/L (normal 98–111), carbon dioxide 28 mEq/L (21–31), potassium 4.1 mEq/L (3.5–5), sodium 142 mEq/L (135–145), creatinine 1.1 mg/dL (0.6–1.2), and BUN 33.1 mg/dL (9–25). Complete blood cell count revealed hemoglobin 12 g/dL (14–18), white blood cells 7.8 × 10^3/mm^3 (3.8–11), and platelets 170 × 10^3/mm^3 (150–400). The international normalized ratio was 1.0 (0.9–1.1). Liver function tests showed a bilirubin of 0.7 mg/dL (0.1–1), alkaline phosphatase 40 U/L (39–117), and alanine aminotransferase 40 U/L (1–60). Creatine kinase (CK) was elevated (303 IU/L, normal 40–200), with three normal CK-MB fractions.

An electrocardiogram showed sinus bradycardia, left ventricular hypertrophy with QRs widening, and T-wave inversion consistent with ischemia. The patient did not complain of chest pain. A serum digoxin concentration was 1.3 ng/mL (0.9–2.2). The patient was cross-match for four units of blood, but did not receive a transfusion.

Endoscopy revealed a 1.5-cm duodenal ulcer and multiple small gastric ulcers. The duodenal ulcer was injected with 9 mL of epinephrine 1:10 000 and cauterized. The patient received an intravenous bolus of pantoprazole 40 mg, followed by a continuous infusion of 8 mg/h for 48 hours. Helicobacter pylori status was not tested; he was empirically started on eradication therapy with amoxicillin 1 g twice daily and clarithromycin 500 mg twice daily for seven days. Pantoprazole was discontinued and oral omeprazole 40 mg twice daily was started after 48 hours. The omeprazole dose was to be decreased to 20 mg daily after seven days. The patient had one melena stool 24 hours after admission, and a small amount of frank blood in his stool on day 2.

He was discharged after three days with a hemoglobin of 11 g/dL and was instructed not to restart atorvastatin until after the completion of clarithromycin therapy due to the risk of rhabdomyolysis. The family physician was made aware that clarithromycin may increase digoxin concentrations.

Discussion. NSAIDs increase the risk of upper GI bleeding in new users and those already on therapy for several months in the first year of treatment.5 Established risk factors for the development of NSAID-associated gastroduodenal ulcers include advanced age, history of an ulcer, concomitant use of corticosteroids or anticoagulants, and higher doses of NSAIDs, including the use of more than one NSAID.6 Concomitant infection with H. pylori, cigarette smoking, and consumption of alcohol are other possible risk factors associated with upper GI ulcers.7

H. pylori is a common infection and is frequently associated with peptic ulcer disease. It is present in up to 40% of the general population in the developed world, and up to 80% in the developing world.8 H. pylori is a pathogen in all hosts; it initially causes chronic active gastritis, although only 10–20% of individuals develop a clinically relevant disease. The lifetime risk of peptic ulcer disease in an infected adult is approximately twice as great as in individuals without H. pylori. Approximately 80–90% of patients who develop duodenal ulcers not associated with the use of NSAIDs, and 70% of those who develop non-NSAID-associated gastric ulcers are infected with H. pylori. Due to the high prevalence of H. pylori infection, patients frequently are not tested for its presence and are empirically treated to eradicate the bacteria.

In clinical trials with celecoxib,9 approximately 11% of patients (440/4000) enrolled in four of five endoscopic studies were taking aspirin (≤325 mg/d). In the celecoxib groups, the endoscopic ulcer rate appeared to be higher in patients who used aspirin than in nonusers.

CLASS (Celecoxib Long-Term Arthritis Safety Study)9 was a randomized, double-blind trial evaluating the GI toxicity of celecoxib, ibuprofen, and diclofenac. GI ulcer complications were defined as gastric or duodenal perforation, gastric outlet obstruction, or upper GI bleeding. The relative risk of an upper GI complication was 4.5 with low-dose aspirin use (p = 0.01) in the celecoxib group. Low-dose aspirin use did not have a significant effect on the rate of upper GI ulcer complications in patients receiving nonselective NSAIDs (RR 1.7; p = 0.29). For patients taking aspirin, the annualized incidence rates of GI ulcer complications alone for celecoxib and nonselective NSAIDs were 2.0% and 2.12%, respectively (p = 0.92); for GI ulcer complications combined with symptomatic ulcers, the rates were 4.7% and 6.0%, respectively (p = 0.49). In contrast, for patients not taking aspirin, the annualized incidence of GI ulcer complications was significantly lower with celecoxib compared with ibuprofen and diclofenac (0.44% vs. 1.2%; p = 0.04). Similarly, the annualized incidence of ulcer complications combined with symptomatic ulcers in patients not taking aspirin was significantly lower with celecoxib than with ibuprofen and diclofenac (1.4% vs. 2.91%; p = 0.02).

In CLASS,10 there were twice the number of patients enrolled on low-dose aspirin compared with other clinical trials11 with celecoxib. A small ulcer risk reduction for celecoxib patients taking low-dose aspirin may exist, as only 20% of the CLASS population were receiving low-dose aspirin (<325 mg/d). This may increase the probability of a type II error.11 A celecoxib dose of 400 mg twice daily — double the amount recommended by the manufacturer — was used in CLASS. It has been suggested that there is no dose–response relationship in the development of GI ulceration during treatment with celecoxib at doses of up to 400 mg twice daily.12 In summary, CLASS suggests that celecoxib combined with low-dose aspirin may increase the risk for ulcer complications.

The Naranjo probability scale13 ranks our patient’s gastric and duodenal ulcers as a possible adverse reaction related to celecoxib. Age, the
use of aspirin with a COX-2 inhibitor, and possible infection with H. pylori are the risk factors present in our patient. He had been taking aspirin for the past three years, which suggests celecoxib as a possible contributing cause to the development of the ulcer. COX-2 inhibitors combined with aspirin have the potential to cause serious GI adverse effects and should be used with caution in patients at increased risk for GI complications.

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Benzy1penicillin-induced prolonged cholestasis

TO THE EDITOR: Liver toxicity is a rare adverse reaction to antibacterial drugs; most reports implicate newer compounds such as amoxicillin/clavulanic acid. Older antimicrobial agents including flucloxacillin, clexacillin, erythromycin, and sulfonamides are associated with hepatic cholestasis.4 Despite the widespread use of natural penicillins since the middle of the 20th century, there are only a few reports4 of adverse hepatic reactions leading to severe hepatotoxicity. We describe a patient who experienced protracted cholestasis after a single dose of benzylpenicillin.

Case Report. A 28-year-old woman was admitted to the hospital in early April 1996 because of a two-day history of upper abdominal pain, asthma, and dark urine. Seven days before admission, streptococcal pharyngitis was suspected, and benzylpenicillin (in a single intramuscular injection of 2 million units) was administered. Blood monophenox 500 mg orally three times daily were started. There was no history of drug allergy, and she denied the use of alcohol, any other drugs, or herbal products. On admission, she was alert, febrile (37.8°C), and moderately jaundiced. There was no rash or lymphadenopathy. The tonsils were enlarged and erythematous, but exudates were not seen. Laboratory results were serum total bilirubin 7.6 mg/dL (normal <1.1), with direct bilirubin 0.5 mg/dL; serum albumin 28 g/L (>35); serum aspartate transaminase 261 U/L (>40); serum alanine transaminase 357 U/L (>40); serum alkaline phosphatase 844 U/L (>258); and γ-glutamyl transpeptidase 550 U/L (>35). The serum white blood cell count was 17.8 x 10^9/mm^3 (with 87% neutrophils and 1% eosinophils), and the platelet count was 445 x 10^9/mm^3. The rest of the complete blood count and the prothrombin activity were in normal range. Serology ruled out hepatitis A (immunoglobulin [Ig]M antibody negative), B (surface antigen and IgM core antibody absent), C (repeated testing for IgG antibody negative), and cytomegalovirus and Epstein–Barr virus (IgM negative for both). Screening for autoimmune liver disorders was negative. Abdominal ultrasonography showed normal liver and bile ducts. On day 5 (12 d after benzylpenicillin administration), a generalized scaling on the palms and soles was evident. Thereafter, jaundice resolved spontaneously, and the patient was discharged on day 20, although the liver dysfunction persisted up to 18 months (Figure 1). Repeated ultrasound examination of the biliary tract showed no abnormalities. No specific or symptomatic therapy was given. Assessment of this case with the Naranjo probability scale6 rated the likelihood of benzylpenicillin being the cause of cholestasis as probable.

Discussion. Toxic injury to the liver can cause any clinicopathologic variety of liver disease, including acute and chronic cholestasis. Hepatocellular cholestasis may be “pure,” without hepatocellular damage, and has been termed canalicular, bili, or steroid cholestasis. The other type of cholestasis is called hepatocanicular or cholangiolic, and is accompanied by portal inflammation and slight hepatocyte injury, usually associated with hypersensitivity features. A protracted course of drug-induced cholestasis can be defined as the persistence of jaundice for more than six months or the persistence of biochemical changes of anicteric cholestasis for more than one year after drug-induced acute cholestasis, despite withdrawal of the causative drug and in the absence of a history of chronic disease of the liver or the biliary tract. This protracted course is usually due to inflammation of small intrahepatic bile ducts, which sometimes results in vanishing bile duct syndrome.8

The lack of specific diagnostic tests for hepatic drug reactions highly complicates the diagnosis of drug-induced liver disease. In clinical practice, it is supported by the exclusion of other causes of hepatobiliary disease and compatible temporal relationships between drug ingestion and liver injury.

The prolonged cholestasis observed in our patient can be reasonably ascribed to benzylpenicillin since there was no history of biliary tract disease, the biliary tract was normal on ultrasonography, and other caus-

![Figure 1. Liver function test results after benzylpenicillin administration. ALT = alanine transaminase; AP = alkaline phosphatase; AST = aspartate transaminase; TB = total bilirubin.](image-url)
reviews of liver damage were excluded. The initial presentation mimicked that observed in a previously reported case, with jaundice occurring shortly after drug administration and little alteration in the patient’s general well-being.

In addition, the patient denied the use of drugs other than benzylpenicillin except for acenocumarol at therapeutic doses. Aenocumarol is a well-known intrinsic hepatotoxic agent, but the only report in the literature of idiosyncratic hepatotoxicity associated with this drug described a hepatocellular pattern of damage.10

Natural penicillins have been implicated as a cause of hepatotoxicity in three reports2-4 in the English literature during the last two decades, and in only one of these cases3 was the type of liver damage cholestatic. Furthermore, the prolonged course of cholestasis seen in our patient has not been previously reported with benzylpenicillin.

Idiosyncratic hepatotoxicity can be allergic (immunologically mediated) or metabolic (due to the accumulation of aberrant metabolites).8 Immunological features are often associated with hypersensitivity features. In our patient, the short period of latency between benzylpenicillin administration and symptoms of liver injury, as well as the presence of mild pyrexia, leukocytosis (albeit within normal limits), and epidermolytic suggest an immunological-mediated toxicity. There is no specific therapy for this condition. The role of corticosteroids in drug-induced hepatic injury remains controversial. Their administration does not seem to be justified except for cases with evidence of vasculitis. Finally, there are scant data on the usefulness of ursodeoxycholic acid in cases of chronic cholestasis evolving to vanishing bile duct syndrome.11

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Neuroleptic malignant syndrome with antidepressant/antipsychotic drug combination

TO THE EDITOR: We report a case of neuroleptic malignant syndrome (NMS) associated with concomitant use of clozapine and haloperidol.

Case Report. A 68-year-old white man with a history of chronic paranoid schizophrenia beginning in the early 1950s had resided independently in the community for many years. He was receiving clozapine 600 mg/d (prescription initiated in August 1998) for alleviation of fixed paranoid delusions. The patient was also receiving venlafaxine 75 mg twice daily for alleviation of depressive target symptoms (e.g., suicidal ideations, dysphoric mood, poor appetite, lorazepam 0.5 mg four times daily for alleviation of anxiety, vitamin E 400 units/d, one aspirin 325-mg enteric-coated tablet daily, and a multivitamin with minerals daily.

On January 27, 1999, he was admitted to the hospital with diagnoses of right lower lobe pneumonia and sinusitis, for which he received ceftriaxone 1 g intravenously every eight hours. This was subsequently changed to intravenous ampicillin/sulbactam 1.5 g every six hours for better coverage of sinusitis. Due to concerns of noncompliance, the patient’s intolerance to higher doses of clozapine (sirolorhea, dizziness), as well as his persistent paranoid delusions and auditory hallucinations, treatment with haloperidol concentrate was initiated on January 30 concomitantly with clozapine and venlafaxine. When mental and respiratory status improved, ampicillin/sulbactam was discontinued and oral trimethoprim/sulfamethoxazole (TMP/SMX) every 12 hours for 14 days was prescribed. Following several days of concomitant treatment with antidepressive medications and venlafaxine, the fixed paranoid delusions and auditory hallucinations improved.

Since the patient was compliant with the treatment regimen, haloperidol concentrate was switched to tablet form. He was discharged on February 8 to an assisted living facility with the following medications: oral haloperidol 4 mg/d, clozapine 600 mg/d, enteric-coated aspirin 325 mg daily, multivitamin with minerals daily, TMP/SMX double-strength every 12 hours (9-d supply given to complete 14-d course), oral trihexyphenidyl 4 mg/d (for alleviation of drooling associated with clozapine), venlafaxine 75 mg by mouth twice daily, and vitamin E 400 units daily.

Two weeks after discharge (27 d after initiation of haloperidol), the patient was found slumped over a tray table; his skin was clammy and he was lethargic and difficult to arouse. There were no witnesses to any seizure activity, and no vital signs were taken at that time. He was subsequently brought to the emergency department, where it was noted that he had a fever (38.3 °C), autonomic instability (HR 112 beats/min, BP 100/73 mm Hg, diaphoresis), and appeared pale (hemoglobin 12.9 g/L, hematocrit 38.3%). He was admitted, and further examination revealed that he had mental status changes (dilirium, oriented on 1 instance, speech unintelligible, unable to answer simple yes/no questions).

An examination performed on February 27 (hospital day 1) showed reeling BP 145/90 mm Hg with HR 100 beats/min and standing BP 110/70 mm Hg with HR 100 beats/min. Mental status examination demonstrated the patient to be initially lethargic, but within one hour he was awake and cooperative, and oriented to person, place, and time. He had difficulty with serial counting by sevens and was able to spell the word “world” forward, but not backward. There was no finger agnosia and no evidence of aphasia. Cranial nerves II through XII were intact. The
Weber’s test in the midline was normal. The discs were flat without evidence of papilledema. Motor examination determined mild to moderate generalized wasting with increased tone in all four extremities. There was no focal weakness with any drift or clonus. Deep tendon reflexes demonstrated biceps 3+ bilaterally, triceps 3+ bilaterally, knee 2–3+ bilaterally, and ankle 1+ bilaterally. There were dif-
fuse fuses including positive snout, suck, and right palmar reflex. With re-
gard to sensory stimulation, the patient responded appropriately to pain (pin on the face and in the extremities). Other responses could not be adequately tested. Cere-
bellum examination demonstrated no nystagmus. He had a short-stepped gait with decreased arm swing. Hematologic testing showed elevated serum creatine kinase (CK 826 U/L) and leukocytes (11.9 × 10^9/mm^3).

All neuroleptics were withheld February 27, as NMS was suspected. The pa-
tient was treated with an antipyrine and was hydrated. Vital signs and CK concent-
trations were checked periodically (day 1, 7,686 U/L; day 2, 4,398 U/L; day 3, 4,055 U/L; day 4, 14,141 U/L; day 6, 720 U/L). A computed tomography scan of the head, chest X-ray, urinalysis, complete blood count, and blood chemistry were per-
fomed to rule out other etiologies; all results were unremarkable. An electroen-
cephalogram and lumbar puncture were not performed. Psychiatry and neurology services were consulted, and a clinical diagnosis of NMS was established.

Subsequently, the symptoms of NMS resolved, and on hospital day 7, the pa-
tient was rechallenged with monotherapy clozapine. He tolerated the reintroduc-
tion of clozapine, and was discharged on March 12 with clozapine 100 mg at bed-
time, venlafaxine 75 mg twice daily, trihexyphenidyl 4 mg/d, enteric-coated aspirin 325 mg/d, and multivitamin with minerals daily.

Seventeen months after discharge, the patient is receiving oral clozapine 350 mg each night and oral venlafaxine 75 mg twice daily without symptoms of NMS. He is living independently in the community and has not been hospitalized since being discharged. The patient has not been rechallenged with the combination of clozapine, venlafaxine, and haloperidol. He continues to experience fixed paranoid delusions. 

Discussion. The cause of NMS is considered to be “the massive reduc-
tion of dopaminergic activity which is attributed to neuroleptic dopamine blockade,” particularly of the D2-receptors. Clozapine has a higher affini-
ty for D2-receptors, whereas typical antipsychotic agents, such as haloperidol, have a higher affinity for D2-receptors. Venlafaxine, which inhibits the reuptake of serotonin, norepinephrine, and dopamine in a dose-dependent manner, most likely did not contribute to the manifesta-
tion of NMS in this patient. Selective serotonin-reuptake inhibitors (SS-
RIs) have been reported to cause extrapyramidal side effects such as dys-
tonic reactions and akathisia within the first month of treatment. The mechanism is thought to be related to serotonin-induced reductions in dopamine concentrations; however, review of the literature did not reveal any reports of SSRI-associated NMS; nor of NMS or parkinsonian adverse effects associated with venlafaxine monotherapy. There have been numerous reports of NMS in patients receiving haloperidol mono-
therapy, and clozapine monotherapy.

To our knowledge, this is the first case report of NMS associated with the concomitant use of clozapine and haloperidol. Since the patient had never experienced NMS with clozapine and venlafaxine, and based on the pathophysiology of NMS as well as the pharmacologic mechanisms of antipsychotic agents and antidepressants (i.e., venlafaxine), the probable cause of NMS was the addition of haloperidol to an already-existing drug regimen of clozapine, as determined by the Naranjo probability scale.

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Letters

Comment: fluorouracil-induced aphasia: neurotoxicity versus cerebral ischemia

TO THE EDITOR: We read the interesting letter by Bofill et al. (2000;34:
955) describing a case of sudden aphasia as the initial symptom of fluo-
uracil neurotoxicity. Magnetic resonance imaging in this patient was
normal, and the neurologic symptomatology resolved within four weeks. The authors proposed several etiologic hypotheses, all related to possible fluorouracil neurotoxicity, including inhibition of the Krebs cycle or of the dihydroxyiminidate dehydrogenase.

We recently reported a 42-year-old man who developed aphasia while being treated with a similar combination of chemotherapy (cis-
platin 100 mg/m², fluorouracil 1000 mg/m²). Four days after the second round of treatment, the patient suddenly exhibited aphasia, drowsiness, and right hemiplegia. The initial neuroimaging studies were normal, but the evolutive controls showed a severe brain infarction in the right med-
ceral cerebral artery. After ruling out other causes and considering pub-
lished data describing the in vitro and in vivo vasospastic properties of fluorouracil and cisplatin,1,2 we suggested the possibility of segmental cerebral artery vasospasm as a pathogenic contributor mechanism in this patient.

We agree with Bofill et al. because their patient did not present a clini-
cal picture suggesting specific arterial ischemia. Nevertheless, we think that multifocal toxic cerebral artery vasospasm may also explain the symptomatology in this patient.

In any case, we believe that vascular ischemia should be considered as the cause of sudden development of focal neurologic dysfunction in a patient receiving fluorouracil and cisplatin. To rule out the possibility of

Comments on articles previously published are submitted to the authors of those arti-
cles. When no reply is published, either the author chose not to respond or did not do so in a timely fashion. Comments and replies are not peer reviewed.—ED.
segmental or multisegmental cerebral vasospasm, neuroimaging studies, including transcranial Doppler or cerebral arteriography, should be repeated several days after the symptoms appear.

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AUTHOR’S REPLY: We do not agree with Serrano-Castro and Aguilar-Castillo, because the most characteristic feature of fluorouracil-induced neurotoxicity is a normal neuroimaging result.1,2 Our patient had a normal brain scan when the aphasia developed. We agree that neuroimaging studies must be repeated 48 hours after the symptoms develop, and magnetic resonance imaging was performed 48 hours later in our patient.

The patient described by Serrano-Castro and Aguilar-Castillo experienced a severe brain infarction, leading them to conclusions of vascular toxicity rather than neurotoxicity. This is very different from the fact that fluorouracil provokes vascular ischemia. It is possible that fluorouracil-induced vascular ischemia played a partial role in their patient, similar to fluorouracil-induced cardiotoxicity.3,4 However, according to the Naranjo probability scale,4 the brain infarction in the patient whom Serrano-Castro and Aguilar-Castillo describe was not caused by fluorouracil.

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Des modifications erronées ayant été apportées par les éditeurs à la traduction en français par Mr LE DUFF du résumé de l’article, nous en republieons ici la version correcte. Nous prions le traducteur et nos lecteurs francophones d’accepter nos excuses pour cette transformation malencontreuse.

RÉSUMÉ

RESUME: L’Information-Produit sur le Sildénafil est-elle adaptée à la prise de décisions thérapeutiques éclairées?

RAPPEL: L’optimisation thérapeutique et la prévention des effets indésirables des médicaments commencent par l’information la plus complète possible. Lors de la commercialisation d’une nouvelle spécialité, l’information-produit des laboratoires est la principale, et, souvent, la seule source d’information immédiatement disponible, et c’est pourquoi elle influence beaucoup les stratégies thérapeutiques. De ce fait, il est fondamental que les informations contenues dans la notice soient non seulement complètes, mais également aussi pertinentes que possible pour la grande diversité des patients que rencontrent les médecins.

OBJECTIF: Évaluer l’information-produit du sildénafil en matière d’exhaustivité et de précision, en considérant si elle est suffisante pour faciliter l’optimisation thérapeutique et prévenir les effets indésirables évitables pour la grande diversité des patients atteints de troubles de l’érection vus en pratique clinique.


SYNTÈSE DE DONNEES: Des insuffisances et des inexactitudes persistant dans l’information-produit du sildénafil en matière: d’effets du sildénafil sur la pression artérielle; d’interactions médicamenteuses potentielles avec la cinétidine, les inhibiteurs de protéase, certains antihypertenseurs, l’alcool et des médicaments qui peuvent inhiber compétitivement les voies métaboliques dépendant du cytochrome P450; de doses de sildénafil recommandées chez les patients âgés.

CONCLUSIONS: Pour conduire une thérapeutique de façon optimale, les médecins ont besoin d’une information sur les médicaments qui soit correcte et pertinente d’un point de vue clinique. Plusieurs modifications et compléments succincts dans l’information-produit sur le sildénafil aideraient les médecins dans leurs décisions thérapeutiques, pour ce qui concerne l’utilisation du sildénafil par une population de patients très diversifiée et la prévention d’effets indésirables.

Michel Le Duff