the delivery may indicate a bleeding disorder.

A congenital midline fusion anomaly of the genital area is sometimes noted during routine physical examination of young girls. Documentation of such congenital abnormalities in the patient's chart at the time of the newborn examination can help to differentiate them later from other lesions such as those caused by sexual abuse.[5,6]

Perineal lesions usually do not require aggressive treatment. Pressure with a moist saline pack often can control small vulvar hematomas. Analgesics are sometimes required. Topical bacteriostatic and anesthetic ointments are rarely needed.

Ana Carceller
Claire Dansereau
Department of Pediatrics
Hervé Blanchard
Department of Surgery
Hôpital Sainte-Justine
Montreal, Que.

References

1. Zitelli BJ, Davis HW, editors. *Atlas of pediatric physical diagnosis*. 3rd ed. St Louis: Mosby–Wolfe; 1997.
2. Behrman RE, Kliegman RM, Jenson HB, editors. *Nelson textbook of pediatrics*. 16th ed. Philadelphia: WB Saunders; 2000.
3. Sahaffer AJ. *Diseases of the newborn*. 2nd ed. Philadelphia: WB Saunders; 1966.
4. Spitz L, Steiner GM, Zachary RB. *Color atlas of pediatric surgical diagnosis*. Chicago: Year Book Medical Publishers; 1981.
5. Heger A, Emans SJ, Muram D, et al, editors. *Evaluation of the sexually abused child. A medical textbook and photographic atlas*. 2nd ed. New York: Oxford University Press; 2000.
6. Emans SJH, Laufer MR, Goldstein DP, editors. *Pediatric and adolescent gynecology*. 4th ed. Philadelphia: Lippincott–Raven; 1998.

Obesity drug sibutramine (Meridia): hypertension and cardiac arrhythmias

Reason for posting: Sibutramine has been taken off the market in Italy after 50 adverse events (primarily tachycardia, hypertension and arrhythmias) and 2 deaths from cardiovascular causes were reported in that country.[1] The European Medicines Evaluation Agency has begun a comprehensive risk-benefit assessment of the drug, which remains on the market in several European countries, including the United Kingdom, where 215 reports of 411 adverse reactions (including 95 serious reactions and 2 deaths) have been reported (Ryan Baker, Health Canada: personal communication 2002), and in France, where 99 adverse events have been reported (including 10 serious adverse events but no deaths).[2] Between February 1998 and September 2001 the US Food and Drug Administration received reports of 397 adverse events, including 143 cardiac arrhythmias and 29 deaths (19 due to cardiovascular causes).[3] Nineteen of the deaths in the United States were from cardiovascular causes; 10 involved people under 50 years of age, and 3 involved women under 30.[3] In Canada reports of 28 adverse events (no deaths) in patients using sibutramine were received between December 2000 and February 2002.

Most of the reported adverse events appear to be known effects (e.g., hypertension, arrhythmias and tachycardia). In Canada, 1 case of chest pain, 1 of stroke and 2 of eye hemorrhage have also been reported. In 3 of the cases reported in Canada, the patient was also taking an antidepressant (a contraindication to sibutramine therapy); however, it is currently unknown whether other patients experiencing adverse events were prescribed sibutramine inappropriately.

The drug: Sibutramine enhances satiety, acting centrally as an inhibitor of both norepinephrine and serotonin reuptake. It is also hypothesized to act peripherally, increasing the metabolic rate, thermogenesis and energy expenditures by

activating the sympathetic nervous system through β_3-adrenergic receptors.[4] Sibutramine minimally inhibits the reuptake of dopamine but has no recognized effect on acetylcholinergic or histaminergic systems.[5]

Sibutramine is indicated as an adjunct to nonmedical interventions such as diet to promote weight loss[6,7] and weight maintenance[8] in patients with an initial body mass index (BMI) of 30 kg/m^2 or higher or in those with a BMI of 27 kg/m^2 or higher in the presence of other cardiovascular risk factors. Over 6 months of sibutramine therapy, most patients lose about 5%–8% of their preintervention weight, as compared with 1%–4% of initial weight among patients receiving a placebo.[9] Trials lasting up to 18 months have shown that much of the weight loss can be maintained as long as patients continue to take the drug.[8] Sibutramine may also improve other cardiovascular risk factors including hyperlipidemia and glycemic control in patients with type 2 diabetes.[10,11]

Increases in heart rate and blood pressure are known to occur with the use of sibutramine and result in the drug therapy being discontinued in about 5% of patients.[9] Infrequent but serious adverse events reported include seizures, gallstones (due to rapid weight loss), glaucoma and manic episodes in bipolar patients.[5] Common but less serious effects include dry mouth, headache, insomnia and constipation.[5] Sibutramine does not appear to cause cardiac valve disease,[12] possibly because, unlike agents such as fenfluramine and dexfenfluramine, it does not cause serotonin release. It is not yet known whether sibutramine may be associated with primary pulmonary hypertension.

Use of sibutramine is contraindicated in patients with a history of coronary artery disease, heart failure, arrhythmias or cerebrovascular disease, those with inadequately controlled hypertension (blood pressure 145/90 mm Hg or higher), those with anorexia or bulimia nervosa, patients taking monoamine oxidase inhibitors (including St. John's wort), selective serotonin reuptake inhibitors or certain migraine drugs (the triptans) because of concerns about serotonin syndrome, and patients with narrow angle glaucoma. Safety in pregnant or lactating women, people with renal or hepatic impairment and people over 65 years of age has not been established.

In Canada and the United States sibutramine is marketed as Meridia. In Europe it is also sold as Reductil, Reduxade and Ectiva.

What to do: The benefits (reduced risks of obesity and improvements in glycemic control and hyperlipidemia) and the risks (especially cardiovascular adverse effects) of sibutramine treatment need to be discussed with patients along with alternative and complementary measures such as diet, exercise and lifestyle modification. Although sibutramine is not to be prescribed to patients with known cardiovascular disease, it is difficult to identify all patients at risk since many obese patients may have occult cardiac disease. No routine laboratory tests are recommended during treatment, but pulse and blood pressure should be checked before treatment and every 2 weeks in the first 3 months, and thereafter every 1 to 3 months.[5] Treatment should be stopped in patients who experience an increase in heart rate of 10 beats/min or an increase in either systolic or diastolic blood pressure of more than 10 mm Hg in 2 consecutive visits.[5]

Eric Wooltorton
Editorial Fellow, *CMAJ*

References

1. *Advisory: Health Canada investigates safety of Meridia (sibutramine)*. Ottawa: Health Canada; 2002 Mar 27. Available: www.hc-sc.gc.ca/english/protection/warnings/2002/2002_21e.htm (accessed 2002 Apr 17).
2. Woodman R. Abbott says no link between deaths, obesity drug. Reuters 2002 Mar 15; story ID 707119.
3. Wolfe SM, Sasich LD, Barbenhenn E. Petition to FDA to ban the diet drug sibutramine (Meridia) [HRG publ no 1613]. Washington: US Food and Drug Administration; 2002 Mar 19. Available (pdf format): www.fda.gov/ohrms/dockets/dailys/02/Mar02/032202/02p-0120_cp00001_vol1.pdf (accessed 2002 Apr 17).
4. Astrup A, Hansen DL, Lundsgaard C, Toubro S. Sibutramine and energy balance. Int J Obes Relat Metab Disord 1998 Aug;22 Suppl 1:S30-5
5. Meridia (sibutramine HCl monohydrate, anorexiant-antiobesity). In: *Compendium of Pharmaceuticals and Specialties*. Ottawa: Canadian Pharmacists Association; 2002. p. 980-4.
6. Fanghanel G, Cortinas L, Sanchez-Reyes L, Berber A. A clinical trial of the use of sibutramine for the treatment of patients suffering essential obesity. *Int J Obes Relat Metab Disord* 2000;24:144-50.
7. Wirth A, Krause J. Long-term weight loss with sibutramine: a randomized controlled trial. *JAMA* 2001;286:1331-9.
8. James WP, Astrup A, Finer N, Hilsted J, Kopelman P, Rossner S, et al. Effect of sibutramine on weight maintenance after weight loss: a randomised trial. *Lancet* 2000;356:2119-25.
9. Yanovski SZ, Yanovski JA. Drug therapy: obesity. *N Engl J Med* 2002;346(8):591-602.
10. Fujioka K, Seaton TB, Rowe E, Jelinek CA, Raskin P, Lebovitz HE, et al. Weight loss with sibutramine improves glycaemic control and other metabolic parameters in obese patients with type 2 diabetes mellitus. *Diabetes Obes Metab* 2000;2:175-87.
11. McMahon FG, Fujioka K, Singh BN, Mendel CM, Rowe E, Rolston K, et al. Efficacy and safety of sibutramine in obese white and African American patients with hypertension: a 1-year, double-blind, placebo-controlled, multicenter trial. *Arch Intern Med* 2000;160(14):2185-91.
12. Bach DS, Rissanen AM, Mendel CM, Shepherd G, Weinstein SP, Kelly F, et al. Absence of cardiac valve dysfunction in obese patients treated with sibutramine. *Obes Res* 1999;7:363-9.