

Bioavailability of Methadone After Sleeve Gastrectomy: A Planned Case Observation

Magnus Strømme, RN, MSc^{1,2}; Arne Helland, MD^{3,4}; Bård Kulseng, MD, PhD¹; and Olav Spigset, MD, PhD^{3,4}

¹Centre for Obesity Research, Clinic of Surgery, St. Olav University Hospital, Trondheim, Norway; ²Department of Neuroscience, NTNU, Norwegian University of Science and Technology, Trondheim, Norway; ³Department of Clinical Pharmacology, Clinic of Laboratory Medicine, St. Olav University Hospital, Trondheim, Norway; and ⁴Department of Laboratory Medicine, Children's and Women's Health, NTNU, Norwegian University of Science and Technology, Trondheim, Norway

ABSTRACT

Objective: Morbidly obese patients on opioid-replacement therapy may be at risk for treatment refusal with regard to bariatric surgery. However, patients on opioid replacement may have the personal skills to facilitate the lifestyle changes required for successful outcomes after bariatric surgery. This planned case observation assessed the effects of sleeve gastrectomy on the pharmacokinetic properties of methadone.

Methods: A white woman in her 40s on methadone maintenance therapy and with morbid obesity was referred for bariatric surgery. Serial blood samples for methadone concentration measurements were obtained before and at 5 days and 1, 7, and 11 months after surgery.

Findings: Serum methadone concentrations increased from before to 5 days after surgery and continued to increase for 7 months thereafter. The predose measurement at 11 months postoperatively suggests a further increase compared with the previous predose measurements.

Implications: Clinicians should beware the potential for altered effects of methadone after bariatric surgery. We recommend that serum concentrations be routinely measured pre- and postoperatively, and that the dose be adjusted according to these measurements and regular clinical assessments. (*Clin Ther.* 2016;■:■■■-■■■) © 2016 The Authors. Published by Elsevier HS Journals, Inc.

Key words: bariatric surgery, methadone, opioid replacement, pharmacokinetics.

INTRODUCTION

Although there are no absolute contraindications to bariatric surgery,¹ most bariatric surgeons consider that patients with ongoing illicit drug use should not undergo such procedures.² The lack of clear recommendations within this field makes morbidly obese patients on opioid-replacement therapy a subgroup at risk for treatment refusal.

There is little evidence to provide guidance on these matters. Of the few relevant studies that exist, one found patients with past substance abuse to be at higher risk for dropout during the assessment process before bariatric surgery.³ However, a study evaluating weight loss 2 years after gastric bypass found that patients who previously and successfully had participated in treatment for substance abuse (alcohol or drugs) achieved more weight loss compared with patients with no history of substance abuse.⁴ The authors hypothesized that patients with such a history can gain valuable insight into personal skills relevant for lifestyle change, as well as draw strength from their experience with abstinence support programs.

Both preclinical and clinical studies have reported that chronic exposure to opioid μ -receptor agonists leads to sweet taste preference.⁵ It is also known that patients entering methadone maintenance therapy gain weight: One study found that women 2 years

Accepted for publication April 19, 2016.

<http://dx.doi.org/10.1016/j.clinthera.2016.04.033>

0149-2918/\$ - see front matter

© 2016 The Authors. Published by Elsevier HS Journals, Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

into treatment had increased on average 17.5% in weight.⁶ Consequently, occasional referrals of patients on methadone maintenance are likely to occur in bariatric clinics.

Clinicians may be reluctant to provide bariatric surgery in patients on opioid-replacement therapy, for fear of adverse outcomes. Uncertainties concerning the effects of the procedure on pharmacokinetics may contribute to such hesitation. Several mechanisms of bariatric surgery may influence the bioavailability of pharmaceuticals, such as shifts in gastric pH, changes in gastrointestinal transit time, reduced absorptive surface area, and altered presystemic drug metabolism. The effects of bariatric surgery on pharmacokinetic properties are known for only a few medications.⁷ Neither methadone nor buprenorphine, the drugs most commonly used for opioid-replacement therapy, are among these.

This planned case observation is the first systematic evaluation of the possible effects of sleeve gastrectomy on methadone pharmacokinetics.

CASE DESCRIPTION

A white woman in her 40s on methadone maintenance therapy and with morbid obesity was referred for bariatric surgery at a Norwegian university hospital. She had a 27-year history of illicit drug abuse and had injected heroin for 10 years before she entered a rehabilitation program that included opioid-replacement therapy with methadone ~10 years before presentation. After starting methadone therapy, she had gained ~30 kg in weight. At referral to hospital, her height was 159 cm, her weight was 127.8 kg, and her body mass index (BMI) was 50.6 kg/m². She presented with multiple complications of morbid obesity, including type 2 diabetes mellitus, obstructive sleep apnea, and depression. She also had hyperparathyroidism and was hepatitis B and C positive. In addition to methadone 120 mg/d (a dose that had been stable for several years), her drug therapy consisted of metformin 1600 mg/d and sitagliptin 100 mg/d for diabetes, fesoterodine 16 mg/d for urinary incontinence, pregabalin 900 mg/d for neuralgia, and lactulose as needed for constipation.

The patient underwent a multidisciplinary review, including a psychiatric assessment, in the bariatric clinic. She was informed about the lack of scientific evidence concerning the effects on the pharmacokinetic properties of methadone, and provided written consent to undergo surgery, including being followed up for

15 years for the evaluation of long-term effects. The authors also received approval for performing the study from the regional ethics committee. After completing a mandatory patient-education program, the patient was scheduled for laparoscopic sleeve gastrectomy and followed a liquid very-low-calorie diet the 3 weeks before surgery.

The patient's preoperative weight and BMI were 117.0 kg and 46.3 kg/m². Surgery took place with the patient under general anesthesia, and the patient had an epidural catheter placed for postoperative pain relief. The need for epidural analgesia prolonged her hospitalization, extending the regular stay of 1 to 2 days to 8 days. She received her regular dose of 120 mg methadone both on the day of surgery and on the subsequent in-hospital days.

One year after surgery, her weight and BMI had decreased to 92.1 kg and 36.4 kg/m², respectively, representing a 46.3% loss of her excess weight (using the upper BMI limit for normal weight, i.e. 25 kg/m², as reference). Her physical functioning had improved and she had stopped taking antidiabetic medication. The methadone dose was kept unchanged at 120 mg/d throughout the first postoperative year.

Serial blood samples for methadone concentration measurements were obtained at 8 days preoperatively, as well as at 5 days, 1 month, and 7 months postoperatively. Sampling took place at 0, 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 6, 8, 12, and 24 hours after methadone ingestion. Moreover, a single sample was obtained 24 hours after methadone ingestion at 11 months postoperatively. Serum concentrations of total methadone as well as of its enantiomers *R*-methadone and *S*-methadone were measured with an LC/MS method developed at our laboratory.⁸ Key pharmacokinetic variables of methadone were calculated by means of the pharmacokinetic analysis software package Kinetica version 5.0 (Thermo Scientific, Waltham, Massachusetts). The patient was genotyped for the cytochrome P-450 (CYP) enzymes CYP2B6, CYP3A4, and CYP3A5, which are involved in the metabolism of methadone,⁹ by allele-specific polymerase chain reaction (PCR).^{10,11}

RESULTS

The time-concentration curve of methadone in this patient is presented in the [Figure](#). In general, the serum concentrations of methadone were increased from the sampling preoperatively to 5 days postoperatively,

Download English Version:

<https://daneshyari.com/en/article/5824470>

Download Persian Version:

<https://daneshyari.com/article/5824470>

[Daneshyari.com](https://daneshyari.com)