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Identification of Medication-Related Risks in Bariatric Surgery Patients by Performing Structured Medication Reviews

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Abstract

Purpose More medication-related issues are seen with the growing demand for bariatric surgery, because of possible altered pharmacokinetics after surgery. Collaboration with a pharmacist could improve the short- and long-term safety and efficacy of pharmacotherapy in patients undergoing bariatric surgery. The aim of this study was to evaluate the impact of a structured medication review to identify medication-related risks before bariatric surgery.

Materials and Methods The impact on pharmacy-led interventions of introducing a structured medication review was evaluated in a historically controlled study. In the retrospective part, we evaluated patient characteristics, medication use, and number of pre-surgery consultations with a pharmacist before the introduction of medication reviews. A flowchart was developed to detect the use of medicines with risks associated with bariatric surgery. In the prospective part, we evaluated pharmacy-led interventions after the introduction of structured medication reviews using the flowchart. Outcome effectiveness was measured through the number of pre-surgery pharmacy-led interventions.

Results Before using the flowchart for screening on risk medicines, 40 (2.6%) pharmacy-led interventions were identified in 1536 patients. In the prospective group, 195 patients were included and 88 (45%) interventions were identified ($p < 0.001$).

Conclusion A structured medication review before bariatric surgery significantly increased the number of pharmacy-led interventions in bariatric surgery patients. This procedure will shift interventions to pre-surgery instead of post-surgery, contributing to the optimization of pharmacotherapy at an early stage.

Keywords Pharmacotherapy · Bariatric surgery · Medication-related risks · Pharmacy-led interventions · Structured medication reviews

Key Points

- Bariatric surgery can alter pharmacokinetics.
- Influence of surgery on safety and efficacy of pharmacotherapy should be considered.
- Structured medication reviews can identify medication-related risks before surgery.

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Introduction

In the Netherlands, around 50% of the adults met the criteria for overweight and 14% for obesity in 2021 [1]. Bariatric surgery is currently the most effective treatment for obesity with bodyweight reductions maintained in the long-term [2–4]. The number of patients being admitted to bariatric centers increases rapidly [5].

Bariatric surgery substantially alters gastrointestinal anatomy and may influence drug absorption and bioavailability, depending on the chemical properties of the substance and the drug formulation. Changes in plasma concentrations of drugs can lead to adverse events and loss of efficacy with a high variability among individuals.

Medication use and type are currently only minimally considered in the decision to undergo bariatric surgery. Medication-related issues are often discovered after surgery

thus missing the opportunity to prevent suboptimal pharmacotherapy before surgery. Collaboration with a pharmacist before surgery has shown to improve short- and long-term safety and efficacy of pharmacotherapy in patients undergoing bariatric surgery [6–8]. The purpose of this study was to extend these promising results to our hospital. A pre-assessment study at the obesity center of our hospital showed that pharmacy-led interventions (PLIs) took place in only a minority of the patients. More PLIs were expected based on estimated rates of medication use [9]. This might be explained by the absence of a standard procedure for reviewing medication at the bariatric department and the pharmacy not being involved in the pre-surgery phase.

To identify medication-related risks, a structured flowchart with risk medicines (FLORIMED) was designed as a tool for screening for risk medicines. The aim of this study was to provide a proof-of-concept for the use of FLORIMED by comparing pre-surgery PLIs before and after the introduction of the structured medication review.

Methods

Study Design

This study was designed as a single-center historically controlled study and conducted at a tertiary teaching hospital (Catharina Ziekenhuis Eindhoven, The Netherlands). The study was judged not to be subject to the Medical Research Involving Human Subjects Act (WMO) by the medical research ethical committee MEC-U (Nieuwegein, the Netherlands). For personal data protection, all patient data were coded with a research number and processed anonymously in the research database (Research Manager).

Study Population and Intervention

A flowchart was created which included medicines with a risk on altered absorption after bariatric surgery and thus a risk on reduced efficacy and safety of the pharmacotherapy (FLORIMED). Examples of risk medicines included in the flowchart are as follows: diuretics, antidepressants, anti-epileptics, direct-acting anticoagulants, digoxin, immunosuppressant, and antiretroviral drugs.

The reference group (pre-FLORIMED group) comprised all bariatric surgery patients from January 2019 until September 2021. Patients who did not give permission for sharing their medication data through the National Exchange Point (LSP) were excluded. In the pre-FLORIMED group, review of medication used at home by a pharmacist was not part of standard care. In this group, a PLI was registered in the following cases: (1) when a pharmacist was consulted

by the obesity center and (2) when a pharmacist intervened due to pharmacovigilance.

The intervention group (FLORIMED group) comprised all patients referred to our obesity center after the introduction of FLORIMED into the clinic between October 25, 2021, and January 3, 2022. Patients (BMI > 35 kg/m²) who came for their first bariatric screening visit were included. Data of this group were gathered prospectively.

In the FLORIMED group, medication used at home was reviewed on risk medicines by a pharmacist using the flowchart (FLORIMED). When more risk medicines were used, this was considered as one PLI. All PLIs were registered in the electronic medical record following a standard format in which the risk medicine was described in combination with the suggested intervention to be applied perioperative. All recommendations belonging to one PLI were categorized separately.

Outcome Measures

Primary Outcome

The primary endpoint was the proportion of patients with a pre-surgery PLI based on medication use in the period between the first screening visit and surgery. The objective of this study was to compare the proportion of pre-surgery PLIs in patients before and after the introduction of FLORIMED.

Secondary Outcome

The secondary objective of this study was categorization of the subsequent actions belonging to PLIs. The following categories were made: (1) changes in pharmacotherapy, (2) therapeutic drug monitoring, (3) discontinuation of pharmacotherapy, (4) additional monitoring, and (5) other. Furthermore, the secondary objectives included a group description of bariatric surgery-seeking patients based on their medication use. Frequency of use was collected of the following drugs: antidepressant/antipsychotic/anti-epileptic drugs, antihypertensive drugs, anticoagulants, non-steroidal anti-inflammatory drugs (NSAIDs), levothyroxine, and systemic contraception.

Data Collection

From the electronic medical record, age, sex, last measured BMI before surgery, comorbidities, and medication use were collected for all patients. PLIs in the retrospective group were collected from the electronic medical record in the hospital and only included interventions from patients who had surgery during the above-mentioned period. Drugs used at home from the pre-FLORIMED group were extracted from

the electronic medical record in the hospital. This extraction included medication used at home 10 days pre-surgery or medication that was stopped in this period due to surgery. The criterion ‘medication user’ was met when a patient used at least one oral drug formulation. Dermal and subcutaneous formulations, inhalers, vitamins, minerals, and paracetamol were excluded.

The list of drugs used at home from the FLORIMED group patients was collected from the National Exchange Point (LSP) where medical data are shared with permission from patients. All prospective PLIs were directly registered in the electronic medical record after the structured medication review.

Data Analysis

The hypothesis was that the number of PLIs will increase after the introduction of FLORIMED leading to optimization of pharmacotherapy. The expected difference between PLIs was set at 5.15%, based on 0.85% pre-surgery PLIs found from chart view and an estimated increase to 6%, which is considered a clinically relevant difference. Sample size was determined on the basis of statistical power calculations using ClinCalc® calculator. A power of 0.80 and alpha of 0.05 were used. A sample size of 195 patients per group was needed.

The proportion of patients with a pre-surgery PLI and patients without a pre-surgery PLI was assessed and compared between the two groups. Continuous normally distributed variables are presented as mean with standard deviation (SD) when normally distributed. Categorical variables are presented as counts with corresponding percentages.

A chi-squared test was used to compare the category variables: proportion of patients with a PLI, categories of PLIs, and proportion of medication users. Unpaired *t*-tests were performed for normally distributed continuous variables and the Wilcoxon rank-sum test for non-normally distributed continuous variables. Statistical significance was defined for *p*-values smaller than 0.05. Statistical analysis was performed using SPSS version 25 (IBM® SPSS® Software).

Results

Baseline Characteristics

In the pre-FLORIMED group, 1536 patients were included and in the FLORIMED group, 195 patients were included (Table 1). The groups were similar with regard to mean age (43.6 vs 43.7 years, *p* = 0.191), mean BMI (42.0 vs. 42.4 kg/m², *p* = 0.975), and sex (24% vs. 29% male,

Table 1 Baseline characteristics

Variable	Pre-FLORIMED group (<i>n</i> = 1536)	FLORIMED group (<i>n</i> = 195)	<i>p</i> -value
Mean age, years (SD)	43.6 (11.8)	43.7 (12.8)	0.191
Age, years (SD)			-
17–29	232 (15.1)	34 (17.4)	
30–39	336 (21.9)	32 (16.4)	
40–49	420 (27.3)	55 (28.2)	
50–59	428 (27.9)	56 (28.7)	
60–69	118 (7.7)	18 (9.2)	
70–79	2 (0.13)	0 (0)	
Sex, <i>n</i> (%)			0.118
Male	363 (24)	56 (29)	
Female	1173 (76)	139 (71)	
Mean BMI in kg/m ² (SD)	42.0 (5.0)	42.4 (5.9)	0.975
Medication users, <i>n</i> (%)	1144 (74)	136 (70)	0.156
≥ 2 drugs in use, <i>n</i> (%)	813 (53)	89 (45)	0.055
Comorbidities, <i>n</i> (%)	1017 (66)	150 (77)	0.011
Hypertension	512 (33)	76 (39)	0.117
Diabetes	218 (14)	34 (17)	0.226
Dyslipidaemia	368 (24)	45 (23)	0.786
Sleep apnoea	272 (18)	40 (21)	0.337
Joint Pain	571 (37)	103 (53)	< 0.001

Data are represented as *n* (%) or mean (SD). *BMI* body mass index, *FLORIMED* flowchart with risk medicines, *SD* standard deviation

p = 0.118). There was no significant difference in type of comorbidities, except for joint pain. Possible higher use of NSAIDs in this group was considered and a sub-analysis performed, which is described below.

Outcome Measurements

Primary Outcome

In the pre-FLORIMED group, PLIs were registered for 40 patients (2.6%), of which 13 were before surgery. In the FLORIMED group, PLIs were registered for 88 patients. The difference in the proportion of pre-surgery PLIs in the pre-FLORIMED group (13 [0.85%]) and the FLORIMED group (88 [45%]) is statistically significant. The difference was 44% with a *p*-value < 0.001 (Table 2). It was assumed that all PLIs were registered in the electronic medical record while this criterion was possibly not met in clinical practice. Recommendations for switching NSAIDs and contraception were already given during the screening visit by the obesity center and handled independently of a pharmacist. These interventions were

Table 2 Primary and secondary outcome measurements to evaluate the impact of a structured medication review to identify medication-related risks before bariatric surgery

Outcome	Pre-FLORIMED group (n = 1536)	FLORIMED group (n = 195)	p-value
PLIs, n (%)			
Total	40 (2.6)	88 (45)	< 0.001
Pre-surgery	13 (0.85)	88 (45)	< 0.001
Post-surgery	27 (1.8)	NA ^a	NA
Number of patients with PLI and ≥ 2 drugs in use, n (%)	32 (80)	58 (66)	
Distribution of intervention types, sorted per category			
Total different advices within PLIs	51	137	
Change in therapy	22 (43%)	51 (37%)	
Oral contraception	3	22	
Oral anticoagulant	15	4	
Thiazide diuretic	1	11	
Other	3	14	
Therapeutic drug monitoring	17 (33%)	31 (23%)	
Antidepressants	10	18	
Antipsychotics	7	7	
Anti-epileptic	0	5	
Digoxin	0	1	
Discontinuation of therapy	6 (12%)	26 (19%)	
NSAIDS	5	20	
Lisdiuretics	0	6	
Other	1	0	
Additional monitoring	3 (5.9%)	25 (18%)	
Levothyroxin	2	16	
Controlled release formulation	1	9	
Other consults	3 (5.9%)	4 (2.9%)	
Oral antibiotics	2	2	
Immunosuppressants	1	2	

The pre-FLORIMED data were collected retrospectively with applied pharmacy-led intervention (PLIs), the FLORIMED group data were collected prospectively with theoretical PLIs

^aNA not applicable, no statistical analysis, FLORIMED flowchart with risk medication

not registered in the electronic medical record in the pre-FLORIMED group, but were registered as a valid PLI in the FLORIMED-group. For 25 patients in the FLORIMED group PLIs were solely interventions on use of an NSAID or oral contraception. A subgroup analysis excluding PLIs on the use of NSAIDs and oral contraception showed that the number of PLIs before and after surgery still increased significantly from 2.6% (40 PLIs in 1536 patients) in the pre FLORIMED group to 32% (63 PLIs in 195 patients) in the FLORIMED group ($p < 0.001$) (Table 3).

Secondary Outcomes

The categorization of the PLIs is presented in Table 2. The most common PLI in both groups was an advice to change

therapy (43% in the pre-FLORIMED group and 37% in the FLORIMED group), which often included switching to an alternative dosage form such as immediate-release tablets or

Table 3 Outcomes of the subgroup analysis excluding PLIs on the use of NSAIDs and oral contraception

Outcome	Pre-FLORIMED group (n = 1536)	FLORIMED group (n = 195)	p-value
PLIs, n (%)	40 (2.6)	63 (32)	< 0.001
Number of patients with a PLI and ≥ 2 drugs in use, n (%)	32 (80)	51 (81)	NA ^a

^aNA not applicable, no statistical analysis, FLORIMED flowchart with risk medication, PLI pharmacy-led intervention

a different class of anticoagulants. The second most common PLI was therapeutic drug monitoring, frequently for an antidepressant or antipsychotic drug.

Discussion

The results of this study show that a structured medication review using a flowchart with risk medication (FLORIMED) increased the proportion of pre-surgery pharmacy-led interventions in bariatric surgery patients from 0.85 to 45%. In the pre-FLORIMED group, 32% of the PLIs occurred before surgery. In the FLORIMED group, all PLIs occurred before surgery, which is inherent to the method and purpose of the study to identify possible risks with medication before surgery. The type of PLI remained the same after the introduction of FLORIMED. Due to multidisciplinary collaboration, a protocol for structured medication review could be developed that matched clinical practice as much as possible. Although there remains the need to upgrade the flowchart when new information comes available, this study confirmed that performing medication reviews before surgery is feasible and resulted in recommendations to improve pharmacotherapy for bariatric surgery patients.

This study is one of the first to assess the impact of a pharmacist consultation before bariatric surgery to optimize pharmacotherapy. While other studies primarily aimed at post-surgery pharmacist consultation, this study focused on pre-surgery consultation, thus allowing more time to implement recommendations before surgery [7, 8]. In addition, the structured medication review might also support the decision for the type of bariatric surgery. Nearly half of the bariatric surgery candidates had two or more drugs in use at the moment of screening, which advocates for additional focus on medication.

A substantial increase in PLIs was seen with the use of FLORIMED. The total percentage of patients with PLIs before and after surgery increased from 2.6% in the pre-FLORIMED group to 45% in the FLORIMED group. This increase can be explained by the use of a predetermined list of risk medicines and a trained pharmacy staff member performing the structured review. Staff members of the pharmacy are by profession more focused on medication in contrast to staff members of the obesity center who have to include the medication review in the general screening visit where many topics have to be reviewed. Next to this, in the pre-FLORIMED group, most patients were not identified as bariatric patients in the electronic medical record during their hospital admission. Only when the pharmacy was involved in these patients due to other pharmacovigilance issues, bariatric surgery was included as contraindication in the electronic medical record allowing pharmacovigilance.

Additionally, the rate of 100% pre-surgery PLIs in the FLORIMED group can change since surgery was not yet performed. It is possible that post-surgery PLIs will be made despite the pre-surgery medication reviews and/or general screening at the obesity center.

While implementation of the structured medication review was successful, some limitations remain. First, the content of FLORIMED was mainly based on the recommendations of the Royal Dutch Association of Pharmacists (KNMP), for which only limited literature is available. Some of which are of low quality, such as case reports or pharmacokinetic studies, i.e. for therapeutic drug monitoring of antidepressants [10]. Furthermore, some of the PLIs may turn out to be unnecessary, for example when patients stop medication after surgery due to improvements of their blood pressure and glucose levels. The amount of medication was reduced from 3.7 to 3.3 on average per patient 12 months post-bariatric surgery [11]. Also, the type of surgery is not established at the time of medication review. Some of the pharmacist's recommendations may require adjustment depending on whether the patient receives a gastric sleeve or Roux-en-Y gastric bypass (RYGB) procedure, since the impact of a gastric sleeve on the absorption of medication is less than a RYGB. Second, the KNMP workgroup 'Therapy and dosing choice for obesity and bariatric patients' started giving recommendations over a year ago, but recommendations for some medications are not yet complete. Based on the results of this study, we recommend prioritizing the assessment of psychotropic drugs since these are commonly used by bariatric surgery patients, and there is much debate about the relevance of additional monitoring. Thirdly, the time to conduct this research was limited to 20 weeks, and therefore, not all relevant aspects could be studied. The average time between the screening visit and surgery was 124 days. Reviewing the medication on the day of screening and carrying out the suggested intervention at the time of surgery were infeasible within the time frame.

In conclusion, the implementation of a structured medication review using FLORIMED before surgery can be of clinical importance. On average one intervention was made per two to three bariatric-surgery seeking patients. The studied procedure can shift interventions from post-surgery to pre-surgery, which contributes to optimization of pharmacotherapy at an early stage. In this way, more time is available for necessary changes in therapy or extra support and monitoring of the patient.

We think that collaboration of a pharmacist with the obesity center to perform and training to perform structured medication reviews of bariatric surgery-seeking patients will ensure safe and effective short- and long-term pharmacotherapy.

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Declarations

Informed Consent Informed Consent does not apply.

Conflict of Interest The authors declare no competing interests.

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