Preoperative carbohydrate drink in fast-track primary total knee arthroplasty: a randomized controlled trial of 168 patients

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A key component in fast-track total knee arthroplasty (TKA) is early mobilization. Preoperative fasting might cause orthostatic hypotension and -intolerance which both can interfere with early mobilization. It was hypothesized that consuming a carbohydrate drink 2-3 hours prior to surgery is a viable option to reduce orthostatic hypotension, and as a result, improve rehabilitation. In this randomized controlled trial, all consecutive unilateral primary TKA patients were reviewed for eligibility. Exclusion criteria were American Society of Anesthesiologists (ASA) class above 3, older than 80 years of age, Diabetes Mellitus, and an insufficient comment of Dutch language. Patients were distributed in two groups. The control group was allowed to eat till 6 hours and drink clear fluids till 2 hours before surgery (standard treatment). The intervention group consumed, additionally to the standard treatment, a carbohydrate drink 2-3 hours before surgery. Blood pressure was measured both lying and standing as a measure for orthostatic hypotension during first time postoperative mobilization on day of surgery. A total of 168 patients were included. Prevalence of orthostatic hypotension in the control- and intervention group was 24 patients (34%) and 14 patients (19%) respectively, (p=0.05). Prevalence of orthostatic intolerance was 13 patients (19%) in the control group and 9 patients (13%) in the intervention group (p=0.32). No drink related adverse events occurred. In conclusion, taking a carbohydrate drink 2-3 hours before TKA significantly lowers the number of patients with orthostatic hypotension in early mobilization. However, the clinical relevance of the carbohydrate drink has to be studied further.

Keywords: total knee arthroplasty, reduced fasting, orthostatic intolerance, orthostatic hypotension, fast-track, carbohydrate drink.

INTRODUCTION

During the last decades, fast-track rehabilitation protocols have been widely implemented, which improved quality of care, patient outcomes, and safely reduced length of hospital stay after total knee arthroplasty (TKA)[1,2]. One of the key elements in fast-track protocols is early mobilization[3,4]. This can be interfered by orthostatic hypotension and -intolerance which is frequently observed; up to 44% of patients suffer from this after arthroplasty[5-8]. Orthostatic hypotension and -intolerance can be due to various causes, including hypovolemia, and leaves patients unable to mobilize[5]. Therefore, prevention of orthostatic hypotension and -intolerance might improve early mobilization[9,10]. Moreover, postoperative hypotension is one of the reasons for prolonged hospital stay[11-13].

Historically, patients were instructed not to eat or drink after midnight before surgery[14]. This fasting period was maintained to prevent pulmonary aspiration of gastric contents during anesthesia. Literature showed that reduced fasting times are feasible, therefore, the current policy is 2 hours fasting for liquids and 6 hours fasting for solid food before surgery[15-19].

Preoperative carbohydrate drinks reduce anxiety, nausea, vomiting, and increase well-being in non-orthopedic surgery[20-26]. Moreover, consuming a carbohydrate drink 2-3 hours preoperatively, was not associated with increased intake related complications[17,27,28].

In total hip arthroplasty (THA) small positive effects regarding pain and well-being were found for preoperative oral carbohydrate intake[29]. Until now no studies have been performed investigating preoperative carbohydrate drink in TKA.

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The hypothesis of this present study was that consuming a carbohydrate drink 2-3 hours prior to TKA, is a good and feasible option to decrease postoperative orthostatic hypotension.

MATERIALS AND METHODS

A prospective, randomized controlled trial was conducted. The study was initially performed in the Reinier de Graaf Hospital, Delft, the Netherlands and due to the merger of hospitals continued in the Reinier Haga Orthopedisch Centrum, Zoetermeer, the Netherlands. All consecutive patients scheduled for a primary unilateral TKA between December 2019 and December 2021 were reviewed for eligibility. Patients with risk factors for pulmonary aspiration were excluded. Therefore, exclusion criteria were: age above 80 years, American Society of Anesthesiologists (ASA) class >3, an insufficient command of Dutch language, and Diabetes Mellitus (DM). Patients with DM were excluded, since fasting and oral carbohydrate drinks increase glucose variability and insulin resistance in diabetic patients. Patients with previous bariatric surgery or medical treatment for hypertension were not excluded.

All TKAs were performed in a fast-track setting. Two groups were compared, a control group with current fasting times, and an intervention group in which patients consumed a carbohydrate drink 2-3 hours before surgery.

Primary objective was to compare the number of patients with postoperative orthostatic hypotension during first time mobilization after TKA between both groups. Secondary objectives were comparing the prevalence of orthostatic intolerance, nausea, vomiting, and length of stay between both groups.

Patients were randomized into the control- or intervention group by a digital program Castor EDC (Amsterdam, the Netherlands)[30]. Randomization was performed by variable block randomization in the proportions 4, 6 and 8. Patients and outcome assessors were not blinded for treatment allocation.

Patients in the control group were allowed to drink clear liquids until 2 hours before surgery and to eat 6 hours before surgery. Patients in the intervention group consumed 2 bottles of 200ml (total 400ml) carbohydrate drink (Nutrica Preop; Numico, Zoetermeer, the Netherlands) 2-3 hours before surgery. This is a clear, non-carbonated, isomolar carbohydrate drink.

All patients were admitted on the day of surgery. Preoperatively patients received dexamethasone 0.15mg/kg confirming our protocol[31,32]. All patients were operated with either spinal- of general anesthesia. In spinal anesthesia 0,5% isobaric bupivacaine (Marcaine spinal 5mg/mL; Aspen, Gorinchem, the Netherlands) admitted intrathecally. In general anesthesia a larynx mask was used and no muscle relaxant was administrated. Opiates were not administered to rule out possible side effects such as nausea, vomiting, or sedation, which might interfere measurements[9,33]. All patients received additional local infiltration anesthesia with 300mg ropivacaine around the knee joint during end of surgery, conforming to our fast-track regimen. Esketamine (15 mg) was administered to prevent postoperative pain[34,35].

Primary objective was to compare the number of patients with orthostatic hypotension during first postoperative mobilization on day of surgery between both groups. To determine orthostatic hypotension blood pressure was measured with an inflatable cuff around the upper arm; once in supine position and three times (after 1, 3, and 5 minutes) in standing position. Orthostatic hypotension was defined as a systolic blood pressure decrease of at least 20mmHg or a diastolic blood pressure decrease of at least 10mmHg within three minutes of standing compared to supine position[36].

Secondary objectives were orthostatic intolerance, nausea, vomiting, and length of stay in both groups. Orthostatic intolerance was determined by the researcher and positive in case of dizziness, feeling of heat, sweating or syncope during mobilization[36]. Postoperative nausea and vomiting were asked by the researcher. No pain scores were determined. If patients were unable to mobilize this was noted including the reason why. Finally, length of hospital stay was determined.

Power calculation was based on the primary objective, the reduction of orthostatic hypotension. Since it was hypothesized that consuming a preoperative drink will reduce orthostatic hypotension, a superiority design was chosen. A reduction in the number of patients with orthostatic hypotension of 20% was assumed to be clinically relevant.

Based on the results of the study of Lindberg et al. the prevalence of orthostatic hypotension is 40% after total hip arthroplasty[7]. We assumed this is comparable for TKA.

When using an alpha of 0.05 and power of 80% a sample size of 73 patients per group were needed. When taking a dropout of 15% into account, a total of 84 patients per group was needed.

For statistical analyses, IBM SPSS statistics version 28 (IBM Corp. Armonk, NY: IBM Corp.) was used.

A p-value of 0.05 or lower was considered to be statistically significant. Descriptive statistics were used for data analysis. Taking distribution of the data into account chi-square was used for categorical variables and Mann-Withney U test for continuous variables.

The protocol for this randomized controlled trial was approved by the regional Ethical Committee METC-LDD (Z19.025/NL70848.098.19) and was registered in the Netherlands Trial Register (NL7996). All data were handled according to the Helsinki Declaration (version 64, October 2013). All patients signed informed consent.

RESULTS

A total of 395 patients were eligible for inclusion of which 164 patients (168 TKA) were included. The control- and intervention group comprised of 85 and 83 TKA respectively. Most patients were excluded based on DM (66 patients), age >80 years (65 patients), and not willing to participate (61 patients). After inclusion, 1 TKA in the control group and 3 TKAs in the intervention group were excluded before surgery. The study flowchart is presented in figure 1.

Table I presents the baseline patient characteristics of the participating patients. Median age was 69 years[25-80] and 101 (62%) patients were female. Most patients were classified as ASA 2 (117 patients (71%)). Median BMI was 28.7 (19.1-46.1). Median bupivacaine dose was 10mg which was comparable for both groups. The median fasting time in the control group was 12 hours (2.4-19.1) and in the intervention group 5 hours (3.4-6.8). Fasting was defined by the last time that the patient had oral intake. Early mobilization and, as a consequence, blood pressure measurements was not possible in 7 patients of the control group and 4 patients in the intervention group due to wound leakage or sensomotoric impairment. In 2 patients, 1 in each group, the patient had mobilized before the blood pressure measurements took place and were therefore excluded for analysis. Patients with an insufficient dose of dexamethasone, less than 0.15mg/kg, were excluded for analysis which were 5 patients in the control group and 3 patients in the intervention group.

A total of 142 patients, 70 control group and 72 intervention group, were analyzed for postoperative orthostatic hypotension. Orthostatic hypotension was present in 24 patients (34%) in the control group and in 14 patients (19%) in the intervention group (p=0.05). (Table II)
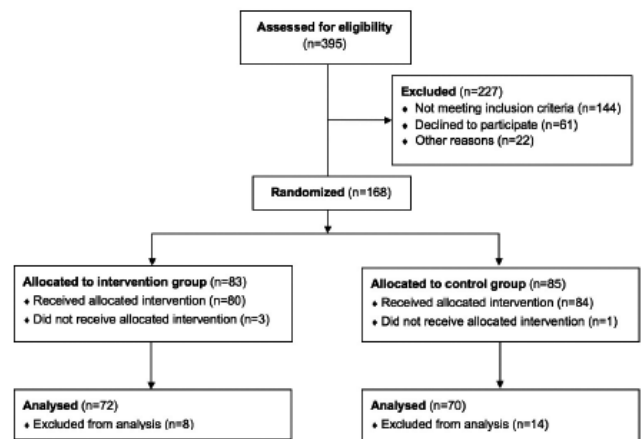

Figure 1 — Flowchart.

Table I. — Patient demographics

	Control group (n=84)	Intervention group (n=80)
Age, years, median (IQR) [range]	70 (9) [25-80]	68 (11) [52-80]
Females, n (%)	52 (61.9%)	49 (61.3%)
Side left, n (%)	43 (51.2%)	34 (42.5%)
ASA class, n (%)		
I	8 (9.5%)	8 (10.0%)
II	54 (64.3%)	63 (78.8%)
III	22 (26.2%)	9 (11.3%)
BMI, median (IQR) [range]	27.7 (6.0) [19.2-38.8]	29.4 (5.8) [22.5-46.1]
All data were presented as (median, Interquartile Range (IQR)), [range]) or (n, %). Abbreviations: ASA: American Society of Anesthesia; BMI: Body Mass Index.		

Orthostatic intolerance occurred in 13 patients (19%) in the control group and in 9 patients (13%) in the intervention group (p=0.32). Mean time between surgery and first mobilization was 3.8 hours (1.6-7.9). The median length of hospital stay was 2 nights (0-6) for both groups (p=0.92). (Table II) No difference was found for nausea between the control and intervention group, 3 patients (4.3%) and 4 patients (5.6%) respectively (p=0.73). In both groups 2 patients vomited early after surgery.

None of the patients disliked the carbohydrate drink, a single patient had troubles with the amount of fluid. No drink related adverse events occurred during the study.

DISCUSSION

The primary goal of our study was to investigate the effect of a preoperative carbohydrate drink on the

Table II. — Primary and secondary outcomes

	Control group (n=70)	Intervention group (n=72)	P †
Orthostatic hypotension, n (%)	24 (34.3%)	14 (19.4%)	0.05
Orthostatic intolerance, n (%)	13 (18.6%)	9 (12.5%)	0.32
Nausea, yes, n (%)	3 (4.3%)	4 (5.6%)	0.73
Vomiting, yes, n (%)	2 (2.9%)	2 (2.8%)	0.98
LOS, nights, median (IQR) [range]	2 (1) [0-5]	2 (1) [1-6]	0.92

Anesthesia technique, n (%)
   Spinal anesthesia
   General anesthesia
	
	64 (91.4%)
	6 (8.6%)
		
		62 (86.1%)
		10 (13.9%)
			0.32

Surgery time, minutes, median (IQR) [range]	84 (28) [58-155]	86 (31) [48-128]	0.90
Time to mobilize, hours, median (IQR) [range]	3.7 (1.0) [1.6-6.4]	3.9 (1.6) [1.6-7.9]	0.30
All data were presented as (median, Interquartile Range (IQR)), [range]) or (n, %). †Chi-square test in categorical data, Mann-Whitney U test in continuous data. Abbreviations: LOS: length of hospital stay.			

prevalence of orthostatic hypotension during first time mobilization after unilateral primary TKA. The number of patients with orthostatic hypotension in the intervention group was significantly lower compared to the control group.

Despite the significant reduction in orthostatic hypotension by consuming a carbohydrate drink preoperatively, still 19% of the patients in the intervention group experienced orthostatic hypotension which might interfere early mobilization. No significant reduction in orthostatic intolerance was found. Since orthostatic hypotension and -intolerance are multifactorial symptoms[5], other interventions besides adding a carbohydrate drink might be successful and need to be further studied. Previously midodrine and high dose glucocorticoids has been studied in THA with no reduction in orthostatic hypotension[7,37]. Recently Hristovska et al. found that impaired orthostatic cardiovascular responses might be the explanation for orthostatic intolerance after TKA[8].

In previous studies, preoperative carbohydrate drinks in THA have only minor or no influence on postoperative well-being[29,38]. This might partially be explained by the small patient groups (60 patients) which make both studies possibly underpowered to determine well-being. In this present study well-being was not investigated and has to be studied further.

At the time of our power calculation, to the best of our knowledge, no literature was available for the prevalence of orthostatic hypotension after TKA. Therefore, we used the prevalence of orthostatic hypotension in THA which has been reported up to 40%[7]. This is in accordance with our findings of 34.3% in the control group and consequently we presume that our power calculation is sufficient.

Recently Hristovska et al. found that 44% of TKA patients experienced orthostatic intolerance with standing 6 hours after surgery[8]. However, in a recently published retrospective analysis of Kurkis et al. an orthostatic intolerance of 11% was found in TKA patients[39]. This is more in accordance with our findings of 18.6% in the control group. We have no clear explanation for these differences since all studies used the same definition for orthostatic intolerance, which was that orthostatic intolerance was characterized by dizziness, nausea, vomiting, visual disturbances, feeling of heat or syncope[36]. However, symptoms of orthostatic intolerance are subjective and might lead to interviewer bias.

Previously Husted et al. and Bundgaard-Nielsen et al. showed that orthostatic intolerance is one of the reasons for prolonged hospital stay[9,13]. The importance of our present study was further stressed by the multiple articles which stated that postoperative hypotension is a modifiable factor to reduce length of hospital stay after arthroplasty[10-12]. Therefore, further research is needed to reduce orthostatic hypotension and -intolerance in joint arthroplasty.

The exclusion criteria were mostly based on patient characteristics that were thought to be associated with increased intake related risks and are therefore debatable. Excluding patients of 80 years and older was arbitrary since literature is not clear regarding the risk of age on gastric emptying[40].

The exclusion of patients with DM was not based on increased intake related risks with preoperative carbohydrate drinks, since it was found this was safe to administer 180 minutes before surgery in DM patients[41]. The reason for exclusion of DM patients was that the effect of preoperative carbohydrate drink might

differ between patients with and without DM which eventually could bias the results.

The effects of dexamethasone on orthostatic hypotension and -intolerance are unclear, although this might influence the measurements[7]. In our study dexamethasone was in the majority of patients administered according to our protocol. Since dexamethasone might influence our outcome, we excluded patients for analysis in which less than 0.15mg/kg dexamethasone was administrated as prescribed in our protocol. In the study of Harsten et al. general anesthesia showed less symptoms of orthostatic hypotension and -intolerance compared to spinal anesthesia[42]. However, in this study high dose of spinal anesthesia (15mg) was used which is notably higher than the dosage used in our study (median 10 mg). We presumed that type of anesthesia has only minor influence on the outcome, which makes our findings more generalizable.

There are some limitations to this study, which need to be addressed.

First, this study was not blinded; therefore, patients and investigators were aware of treatment allocation. Since the primary outcome was an objective measurement (blood pressure) it was presumed that not blinding does not influence the outcome.

The baseline characteristics were statistically significant different for BMI and ASA between the control- and treatment group. More ASA 2 patients and higher median BMI was present in the intervention group. We presume that the difference in baseline characteristics has only minor influence on the outcome.

Patients who used medication (diuretics or ACE inhibitors) for hypertension were instructed not to use this medication at the day of surgery. This is thought to have no influence on orthostatic hypotension and -intolerance[5,8,43].

Finally, the time of carbohydrate drink intake was preoperatively determined. Due to logistical reasons, the surgery schedule incidental changed and not all patients took the carbohydrate drink exact 2-3 hours before surgery. Median time between carbohydrate drink and surgery was 5 (3.4-6.8) hours which was a significantly reduced fasting period compared to the control group (p <0.001).

CONCLUSION

Taking a carbohydrate drink 2-3 hours before TKA significantly lowers the number of patients with orthostatic hypotension in early mobilization. However, orthostatic intolerance was not different between groups and therefore clinical relevance of the carbohydrate drink has to be studied further.

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