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ORIGINAL ARTICLE

Does Preoperative Carbohydrate Loading Help Outcomes in Total Knee Replacement Surgery?

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Abstract

Background: Prolonged overnight fasting prior to surgery was advocated to reduce the risk of aspiration during or after surgery. Recent studies suggest prolonged fasting is associated with increased insulin resistance, increased acute phase stress response and decreased well-being among surgical patients. Our hypothesis is that pre-operative oral carbohydrate loading 2 hours prior to surgery is associated with improved patient reported well-being.

Methods: The double-blind randomized control study evaluated 140 patients undergoing elective primary total knee replacement (TKR) surgery. Patients above the age of 55 years, of either gender, were randomized into the study group (that received oral carbohydrate solution up to 2 hours prior to induction of anesthesia) and control group (that received plain water in the same amount as the study group). The well-being of patients in the pre and post-operative period was assessed using visual analogue scores (VAS) for pain, thirst and hunger. Additionally, blood samples were collected in the pre and post-operative period for biochemical assays. The study compared the pre and postoperative changes in the insulin resistance, C-reactive protein and the Prognostic Inflammatory and Nutritional Index (PINI) as secondary outcome measures.

Results: 140 subjects (99 females, 41 males) were enrolled. There was significant reduction in the VAS scores of thirst, hunger and pain in the study group ($p < 0.001$). Post-operative insulin resistance was lower in the study group compared to the control group (10.77 ± 1.11 vs. 11.22 ± 1.43), but not statistically significant.

Conclusion: Pre-operative oral carbohydrate loading before elective TKR surgery was associated with significantly better well-being. Although there was a reduction in insulin resistance, it was not statistically significant. The role of pre-operative carbohydrate loading in reducing length of stay and insulin resistance will require further investigation in patients undergoing orthopedic surgery.

Keywords

Carbohydrate loading, Insulin resistance, TKR surgery, PINI, VAS scores

Introduction

Prolonged or overnight fasting prior to surgery has traditionally been practiced [1] to reduce the perioperative risk of aspiration. However, this results in, significant inconvenience and discomfort for patients.

In the clinical setting, insulin resistance is generally regarded deleterious, since chronically elevated glucose concentrations can be responsible for some of the morbidity associated with surgery, such as infections and prolonged length of hospital stay. Additionally, overnight fasting leads to thirst, hunger, headaches and anxiety [2].

Surgery results in a stress response characterized by a catabolic state with increased energy requirements

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and elevated biochemical markers of inflammation such as C-Reactive Protein (CRP). The Prognostic Inflammatory and Nutritional Index (PINI) is a combination of two positive acute-phase reactants (CRP and α-1-acid glycoprotein) and two negative reactants (albumin and pre-albumin). The PINI has been used to prognosticate morbidity and mortality in the peri-operative period. Machado, et al. [3] have shown reduction, although statistically insignificant, in the PINI in patients receiving pre-operative carbohydrate. A study by Perrone, et al. [4] showed no difference in the PINI in the post-operative period.

Multiple studies [5-7] have shown that prolonged fasting results in increased insulin resistance, lead to hyperglycemia and poor outcomes. Recent studies [7,8] and reports from the ERAS- Enhanced Recovery After Surgery Society and European Society of Anesthesiology (ESA), have concluded that oral carbohydrate (CHO) solution given up to 2 hours prior to induction of anesthesia improves patient well-being in the post-operative period.

Fatos Sada, et al. [9] conducted a study of patients undergoing open colorectal operations and open cholecystectomy, which measured the effect of pre-operative carbohydrate loading on patient well-being, which was assessed using the visual analogue scale (VAS) scores for 7 parameters of thirst, hunger, nausea, pain, anxiety, weakness and mouth dryness. They found significant reduction in the study group in all the parameters.

Our study on preoperative carbohydrate loading in patients undergoing elective total knee replacement surgery was undertaken as part of our “SUN” initiative to identify areas of patient care that might benefit from targeted nutritional intervention. The “SUN” (Scaling Up Nutrition) initiative program is an internal activity taken up in the hospital by the nutrition department. As part of this initiative, the dieticians identify areas where nutrition practices need to be changed as per the global guidelines. Once identified, a research proposal is made and presented to the hospital’s clinical research team for approval and inputs. The research activity would generate evidence among the hospital’s patients and the necessary protocol are drafted and implemented after the study to change the practice.

Methodology

This prospective, randomized double blind study was performed in patients undergoing primary total knee replacement (TKR) surgery. Patients were randomized using automated computer-generated numbers into study and control groups. Similar studies by Ljunggren, et al. who studied the effect of carbohydrate loading in patients undergoing elective hip replacement surgery [10,11] were conducted in the Caucasian population. Analgesic protocols vary between institutions and countries, with greater availability of narcotic analgesics in the western world. Elderly patients undergoing total joint replacement in India are culturally different from the Caucasian population, with decreased activity levels and relatively sedentary lifestyle. We also expected the pain-tolerance threshold to be lower in the Indian population because of these factors. The impact of carbohydrate loading has not been examined in India, and so the present study was taken up to test the effect of carbohydrate loading among Indian population.

Assuming a 95% confidence interval, 80% power and a drop out of 20%, it was calculated that 56 patients would be required in each group (study group with pre-operative carbohydrate loading and the control group) to detect a 30% reduction in the insulin resistance (using the HOMA equation) from baseline after surgery as a result of preoperative nutritional supplementation [12].

Informed consent was obtained from all patients in our study.

Patients of both sexes, over the age of 55 years with primary osteoarthritis of the knee joint, who were advised TKR and were willing to participate were included in the study. Patients undergoing revision TKR for any indication or replacement surgery for inflammatory arthritis, patients having intolerance to carbohydrate drinks, and those who did not give written consent were excluded from the trial.

The Ethics and Scientific Committee of our institute approved the trial (SS/2016/IEC/122, 27/2/2016).

Randomisation and blinding

Randomisation (on a one-to-one basis) was provided by a password-protected web-based randomisation service, with sequence not revealed until data lock. Participants were randomised after appropriate assessment and counselling from a member of the research team.

The investigators, patients, nurses and data-collection staff were all blinded to treatment allocation. Drinks were prepared by a separate member of staff who was not blinded for practical reasons but who was not a part in any aspect of the study apart from preparation of the drinks.

A carbohydrate drink was formulated to meet the carbohydrate loading guidelines [11,12]. Nutrient composition of the carbohydrate drink is recorded in Table 1. The dietitian explained to the patient about the diet protocol, including the carbohydrate drink, before surgery (Table 2). The study group received oral iso-osmolar carbohydrate solution recommended by ERAS, containing 12.5% maltodextrin, in the pre-operative period (800 ml, 100 g of CHO) around 8 PM on the night before the surgery, and 400 ml (50 g of CHO) on day of surgery, up to 2 hours prior to induction of anesthesia. The control group patients received an oral non-caloric liquid in the same amount as the study group, till the induction of anesthesia for the surgery. The carbohydrate drink

is colourless and tasteless liquid which is similar to the plain liquid that is given to the control group. The carbohydrate drink is not sweet to taste. Both the group patients were monitored for the intake of the carbohydrate solution.

Pre-operative anthropometric data was collected, and nutritional status was assessed using the Subjective Global Assessment (SGA) tool. All patients (study and control groups) received the same anesthetic pre-medication before surgery. All surgeries were performed under spinal anesthesia. Intra-operative intravenous fluids were administered at the discretion of the attending anesthesiologist.

Well-being of the patients was the primary outcome measure of this trial. Well-being was assessed in the pre-operative and post-operative period using the Visual Analogue Scores (VAS) for pain, thirst and hunger. The VAS scores were recorded once in the pre-operative period and twice, on the morning of the first and second post-operative days (24 and 48 hours post-operative, respectively). The Cumulated Ambulation Score (CAS) is a score that can be used for daily assessment of developments in basic mobility until independent ambulation is reached. This was assessed for 3 post-operative days for both the groups [13].

Pre-emptive analgesics were not prescribed or used in any of the cases. Post-operatively the analgesia provided was uniform across both groups. All patients received three doses of intravenous paracetamol (1 g IV) on the first post-operative day. From the second post-operative day onwards, all patients were prescribed oral paracetamol (500 mg) thrice a day until discharge.

Table 1: Nutrient composition of the carbohydrate drink.

Nutrients	Composition per 100 ml
Energy	47.5 kcal
Carbohydrate (polysaccharide)	11.8 g
Glucose	0.13 g
Maltose	0.5 g
Protein	0.013 g
Fat	0.013 g
Sodium	28.5 mg

Secondary outcome measures

Change in the insulin resistance of patients was also assessed. Biochemical assays for fasting plasma glucose, insulin, CRP, albumin, pre-albumin, α-1-acid glycoprotein were performed prior to surgery and at 24 hours after surgery. The details of the biochemical tests conducted are depicted in Table 3.

The insulin resistance and Prognostic Inflammatory and Nutritional Index (PINI) were calculated from the biochemical results obtained.

Insulin resistance was calculated using the HOMA-IR (Homeostasis Model for Assessment for Insulin Resistance) equation proposed by Matthews, et al. [14].

$$\text{Insulin Resistance} = \frac{\text{Serum Insulin} \times \text{blood glucose}}{405}$$

$$\text{PINI} = \frac{\text{CRP} \times \alpha\ \text{glycoprotein}}{\text{albumin} \times \text{pre-albumin}}$$

The acute-phase inflammatory response to surgeries is mediated by acute-phase proteins released by the liver. These proteins increase or decrease within hours after the trauma and may help to predict postoperative complications [15,16]. In this context, the Prognostic Inflammatory and Nutritional Index (PINI) proposed by Ingenbleek and Carpentier has been used to predict the risk for morbidity and mortality [2]. The PINI integrates two positive (C-reactive protein [CRP] and α-1-acid glycoprotein [α-1-GA]) and two negative (albumin and pre- albumin) acute-phase proteins.

The length of stay (LOS) was calculated as the average LOS in both groups and compared.

Table 2: Preoperative carbohydrate loading protocol for patients.

Preoperative day 1	Operative day	Postoperative day 1
Lunch: Regular diet	400 ml of carbohydrate drink until 2 hrs before the induction of anesthesia	Liquid diet 2 hrs after surgery as tolerated
Dinner: Regular diet by 7 PM		Soft diet as tolerated
800 ml of carbohydrate drink thereafter		

Table 3: List of biochemical tests conducted during the study.

Sl. No.	Test Name	Method	Instrument
1.	Plasma Insulin	Chemiluminescent immunoassay (CLIA)	Coulter D × I 800 (Beckmen)
2.	Fasting plasma glucose	Hexokinase	Coulter D × C 800 (Beckmen)
3.	Serum Prealbumin	Nephelometry	MISPA 12 (Agappe)
4.	Serum Albumin	Bromocresol Purple (BCP)	Coulter D × C 800 (Beckmen)
5.	Serum CRP	Nephelometry	MISPA 12 (Agappe)
6.	Plasma α-1 acid glycoprotein	Nephelometry	Agappe

Table 4: Demographic and clinical aspects of the patients in the two groups.

Variable	Control Group	Study Group	P value
Gender (N, %) Male Female	69 19 (27.5) 50 (72.5)	71 22 (30.9) 49 (69.1)	1.0
Age (years) (mean ± SD)	58.9 ± 8.64	60.14 ± 8.45	0.10
Length of hospital stay (mean ± SD, range)	3.25 ± 0.2 (2-6)	3.0 ± 0.18 (2-5)	0.38
BMI (kg/m^2) (mean ± SD)	27.55 ± 4.1	29.33 ± 6.8	0.074
Nutritional Status score (SGA)	7.13 ± 0.54	7.1 ± 0.31	0.54

Table 5: Mean Well-being VAS Scores of the patients in the two groups.

Variable	Preoperative		P value	Postoperative		P value
	Control Group	Study Group		Control Group	Study Group	
VAS Pain Score (mean ± SE)	8.96 ± 0.16	9.28 ± 0.139	0.128	6.19 ± 0.106	4.66 ± 0.119	0.001
VAS thirst Score (mean ± SE)	4.68 ± 0.16	2.63 ± 0.097	0.000	6.456 ± 0.097	2.634 ± 0.97	0.001
VAS hunger Score (mean ± SE)	3.26 ± 0.16	3.11 ± 0.14	0.477	5.56 ± 0.119	3.11 ± 0.143	0.001
Cumulative Ambulatory Score (mean ± SE)	-	-	-	12.02 ± 0.32	12.76 ± 0.33	0.001

Table 6: Mean ± SE of Insulin Resistance, Inflammatory markers between the two groups

Variable	Preoperative		P value	Postoperative		P value
	Control	Study		Control	Study	
Glycemia (mg/dL) (mean ± SE)	121.14 ± 5.66	122.2 ± 5.9	0.896	140.65 ± 4.66	138.38 ± 4.37	0.788
Albumin (g/dL) mean ± SE)	3.97 ± 0.43	4.37 ± 3.9	0.325	3.23 ± 0.045	3.24 ± 0.015	0.813
Pre-albumin (mg/dL) (mean ± SE)	20.2 ± 8.0	21.4 ± 5.9	0.247	16.4 ± 5.2	16.9 ± 5.7	0.458
CRP (mg/L) (mean ± SE)	7.87 ± 1.87	5.4 ± 0.85	0.218	69.8 ± 7.5	70.5 ± 6.7	0.943
Insulin (µU/mL) (mean ± SE)	41.45 ± 5.52	37.8 ± 4.3	0.603	29.69 ± 3.45	28.37 ± 2.41	0.752
α-1 acid glycoprotein (mg/dL) (mean ± SE)	117.83 ± 125	92.03 ± 51.3	0.056	117.89 ± 56.6	124.38 ± 61.8	0.441
HOMA-IR (mean ± SE)	13.1 ± 1.78	12.3 ± 1.6	0.752	11.22 ± 1.43	10.77 ± 1.11	0.803
PINI (mean ± SE)	0.249 ± 0.824	1.19 ± 0.269	0.130	2.13 ± 3.2	2.31 ± 3.9	0.722

CRP: C Reactive Protein; PINI: Prognostic Inflammatory and Nutritional Index.

Statistical Analysis

All the data collected was compiled and tabulated on spread sheets using Excel 2016 (Microsoft). Data analysis was done using SPSS Software Version 16.0 (IBM™ SPSS 16.0). Paired t-test was performed to know the level of significance at 5% (Supplementary File).

Results

The study was conducted with 140 subjects, comprising 41 males and 99 females. The average age in the study group (60.14 ± 8.45 years) was comparable to the control group (58.9 ± 8.64 years). The study recruited 71 patients in the study group and 69 patients in the control group. There was no significant difference in body mass index (BMI) and the pre-operative nutritional status measured with SGA (Table 4). All study patients in both the groups consumed the carbohydrate or non-carbohydrate drink at the prescribed volume.

Post-operative fluid resuscitation was with normal saline, across all patients in both groups. Dextrose Normal Saline (DNS) was not used in any case either pre- or post-operatively. There were no recorded intra-operative or post-operative anesthetic complications or early post-operative infections in study or control groups.

The Visual Analogue Scale (VAS) scores are tabulated in Table 5. Mean post-operative VAS pain score 4.66 ± 0.119 in the study group was found to have significantly reduced compared to the control group 6.19 ± 0.106 ($p < 0.001$) (Table 5).

Mean VAS score for post-operative thirst 2.634 ± 0.97 in the study group was significantly reduced compared to the control group 6.456 ± 0.097 ($p < 0.001$).

Mean VAS score for the patients' reported post-operative hunger 3.113 ± 0.143 in the study group was

significantly reduced compared to the control group 5.56 ± 0.119 ($p < 0.001$). Mean CAS score for post-operative 3-day ambulation in the study group was more as compared to the control group (Table 5).

The difference in the average length of stay (LOS) between the two groups was not statistically significant. Post-operative insulin resistance (Table 6) was lower in the study group compared to the control group (10.77 ± 1.11 vs. 11.22 ± 1.43), but the reduction was not statistically significant (paired t-test at 5% level of significance). A significant increase in CRP was noted in both groups after surgery, but there was no statistical difference in the CRP values in the study group versus the control group (70.5 ± 6.7 vs. 69.8 ± 7.5). There is also no significant difference in the PINI values between the two groups.

Discussion

Few studies are published on patients undergoing elective orthopedic surgery to study the effect of pre-operative carbohydrate loading. As of our knowledge, there are no studies based on the Indian population. In our study we found that, preoperative carbohydrate loading was associated with significantly improved well-being which was assessed by VAS scores for pain, thirst and hunger.

Hausel, et al. [17] reported their findings in a randomized controlled trial involving 252 patients undergoing abdominal surgery. The study concluded that patients who received pre-operative carbohydrate loading had reduced thirst, fatigue and improved concentration.

Ljunggren, et al. [10] conducted a trial to compare oral carbohydrate rich solution versus plain water in patients undergoing total hip replacement surgery. They found that there was no significant reduction in the complication rate or patient well-being in the post-operative period.

We did not find any significant reduction in the average length of stay in patients receiving carbohydrate supplementation. Alito, et al. [11] also conducted a study based on the ACERTO Protocol in patients undergoing total hip arthroplasty. They compared outcomes between groups receiving oral carbohydrate solution versus a group kept fasting as per conventional practices. They reported reduced average length of stay in the study group receiving oral carbohydrate drink in the pre-operative period.

Awad, et al. [18] published a meta-analysis of twenty-one randomized trials involving 1685 patients, to analyze the effect of carbohydrate loading on average length of stay (LOS). There was no overall reduction in the LOS across all the studies, however they reported significant reduction among patients undergoing major abdominal surgery.

Bilku, et al. [19] conducted a meta-analysis of two randomized controlled trials of pre-operative oral carbohydrate loading and reported a significant difference in patient comfort post-operatively. However, these findings were not consistent with a review of the Cochrane database by Smith, et al. [12], where the improvement in patient comfort was marginal or insignificant.

Overnight fasting results in a catabolic state, which adds to the acute stress response of surgery and results in increased insulin resistance and elevated acute phase inflammatory markers like C-Reactive Protein (CRP) and Interleukin-6 (IL-6) [20]. Nygren, et al. [21] reported that insulin sensitivity was reduced in the post-operative period, causing deranged glucose metabolism and hyperglycemia. In their study, patients treated with pre-operative carbohydrate drink showed improved insulin sensitivity as compared to the overnight fasting group. Insulin resistance and insulin sensitivity, were inversely proportional.

In our study, post-operative insulin resistance was lower in the study group (10.77 ± 1.11) than the control group (11.22 ± 1.43), but this was not statistically significant.

The Prognostic Inflammatory and Nutritional Index was proposed by Carpentier and Ingenbleek, et al. [2] in 1985 to stratify critically ill patients in ICU by risk of complications or death based on nutritional and inflammatory parameters. There was no significant improvement of PINI in our study. There is also some evidence from elective surgery that spinal anaesthesia may diminish the impact of carbohydrate loading, presumably due to the reduction in the stress response [19].

Thorell, et al. [22] reported that increased insulin resistance was associated with longer post-operative stay in the hospital and increased morbidity. It was hypothesized that pre-operative oral carbohydrate loading reduces insulin resistance, which was an independent factor causing increased hospital stay.

Soop, et al. [23] conducted a study to determine effect of changes in the insulin resistance and its relation to factors like length of stay. They reported decreased insulin resistance with pre-operative oral carbohydrate. However, they reported no significant difference in the average LOS. A study by Mathur, et al. [24] failed to show any significant reduction in the average LOS in their study population.

There was no significant difference in the average LOS between the study or control groups in our study.

Route of carbohydrate administration produces varied responses. Oral carbohydrate supplementation produced the desired effects of improved patient wellbeing. Helminen, et al. [25] reported that pre-operative intravenous administration of carbohydrate did not produce the same results.

Limitations of the study

Visual analogue scores for various parameters are patient-reported and are bound to be subjective parameters. A greater sample size and comparison will be required to draw inferences on objective parameters like insulin resistance and other inflammatory markers. The effect of oral carbohydrate loading on complications like infections will require a longer follow-up duration.

Conclusion

Pre-operative oral carbohydrate solution, given up to 2 hours prior to induction of anesthesia, is associated with significantly better well-being and comfort of patients in the post-operative period. There was no meaningful reduction in the average length of stay with carbohydrate loading. We witnessed a reduction of insulin resistance which was not significant. Further studies are required to assess significance of changes in insulin resistance, inflammatory markers and average length of stay in patients receiving oral carbohydrate.

Transparency Declaration of Authors

I, as the primary author, and also on behalf of all the authors, affirm that this manuscript is an honest, accurate, and transparent account of the study being reported. I also declare that no important aspects of the study have been omitted, and that any discrepancies from the study as planned have been explained.

Financial Disclosures

None declared. No author has any financial interests.

Conflict of Interest

None declared. No author in this study has any conflicts of interest to declare.

Statement of Authorship

Radha Chada contributed to the conception and design of the study. Radha Chada, Praharsha Mulpur, Anita Maska, and Veena Diggikar contributed to the acquisition, analysis and interpretation of data. Radha Chada and Praharsha Mulpur drafted the manuscript. Radha Chada, Venkateshwar Reddy Maryada and Annapareddy V Gurava Reddy critically revised the manuscript. All the authors gave final approval.

All authors revised the manuscript and agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

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