A Meta-Analysis of Icodextrin versus Glucose Containing Peritoneal Dialysis in Metabolic Management of Peritoneal Dialysis Patients

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Abstract

Objectives: The objective of this article is to study the available works on comparison between icodextrin-based solutions (ICO) and glucose-based solutions (GLU) in peritoneal dialysis (PD) patients. The final aim was to get evidence for potential differences in metabolic management of PD patients by comparing the ICO with the GLU for the long dwell once a day. Methods: A meta-analysis of included reports, identified by MEDLINE and other sources, containing information on fasting plasma glucose, total cholesterol, triglycerides, and so on in PD patients, was performed. Results: Nine randomized controlled trials (RCTs) (553 patients) were included. The ICO did not differ from the GLU with respect to fasting plasma glucose (weighted mean difference (WMD) = −0.76; 95% confidence interval (CI) = −1.79 to 0.28; Z = 1.43; p = 0.15), triglycerides (WMD = −0.66; 95% CI = −1.40 to 0.09; Z = 1.73; p = 0.08), and body weight (WMD = −2.02; 95% CI = −5.06 to 1.03; Z = 1.30; p = 0.20). But peritoneal creatinine clearance (WMD = 0.49; 95% CI = 0.34–0.64; Z = 6.35; p < 0.00001), urea clearance (WMD = 0.40; 95% CI = 0.25–0.55; Z = 5.12; p < 0.00001), and plasma total cholesterol (WMD = −0.40; 95% CI = −0.70 to −0.10; Z = 2.64; p = 0.008) were higher for the ICO versus the GLU. Conclusions: The ICO had been shown to have significant advantages over the GLU in small solute clearance and plasma total cholesterol. Patients, no matter what kind of PD solution was used, had no significant difference of plasma triglycerides, fasting plasma glucose, and body weight.

Keywords: peritoneal dialysis, icodextrin-based solutions, glucose-based solutions, fasting plasma glucose, meta-analysis

INTRODUCTION

The glucose-based solution (GLU) is associated with the peritoneal fibrosis as a low PH, high osmolality and glucose concentration peritoneal dialysis fluid (PDF).¹ The icodextrin-based solution (ICO), which is a mix of different-length polymers of glucose, has become a mainstay regimen in peritoneal dialysis (PD) patients. This glucose polymer PDF has clinical and theoretical advantages over the GLU in fluid (such as ultrafiltration) and in metabolic management of PD patients.² However, these advantages in metabolism have not yet been tested in a plethora of randomized controlled trials (RCTs). So we performed a meta-analysis of the existing data from RCTs to evaluate it.

METHODS

Search Strategy

Relevant RCTs were identified by searching “The Cochrane Library, PUBMED, and MEDLINE” databases (from 1990 to December 2010). The terms “icodextrin,” “glucose (and similar terms),” and “peritoneal dialysis” were used as search terms. RCTs that compared the ICO with the GLU were included.

Selection Criteria

We included in the meta-analysis all RCTs that compared the ICO with the GLU in the outcomes, which we needed for setting in adult PD patients older than 18 years. We have excluded review papers, case reports,
letters, and abstracts. Furthermore, we excluded several potentially useful papers because their limitations lead to erroneous conclusions.

**Data Extraction and Quality Assessment**

The following data were taken from the selected studies by two authors independently: year of publication, the length of treatment time, number of patients, plasma triglycerides, total cholesterol, fasting plasma glucose, body weight, peritoneal creatinine, and urea clearance. Unpublished data from Aiwu3 were also included.

For quality assessment of RCTs, we evaluated them in terms of randomization, allocation concealment, double-blind design, and reasons for withdrawals. And we scored each study based on the Jadad scale, in which scores ranged from 0 to 5. According to the Jadad scale, we could get 0 or 1 points for each of the five items as follows: with or without randomization; whether the investigator used the appropriate randomization methods or not; with or without a double-blind design of experiment; whether the investigator used the appropriate double-blinding design or not; the number of withdrawals and reasons for dropouts. The Jadad score of less than 2 was classified as low-quality studies, 3–4 as good-quality studies, and 5 as excellent-quality studies.4–6 The quality assessment of our meta-analysis of RCTs is given in Table 1.

**Statistical Analysis**

Data were analyzed using Review Manager Software (version 4.2 for Windows; The Cochrane Collaboration, Oxford, UK). We assessed the heterogeneity of the trials’ results by calculating the $\chi^2$-test $p$ value. Statistically significant heterogeneity was defined as a $\chi^2$-test $p$ value less than 0.1 or an $I^2$ statistic greater than 50%, in which case a random-effects model was used. On the contrary, a fixed-effect model should have been chosen. We tabulated the mean values, the standard deviation (SD), and the number of patients ($N$) separately for the ICO and the GLU and computed the weighted mean difference (WMD) and the 95% confidence interval (CI). We then tested its significance by the Z-test, and $p$ values less than 0.05 were considered statistically significant.11

**RESULTS**

**The Characteristics of RCTs**

Nine English articles were included. Patients in four articles8,9,12,13 were in automated peritoneal dialysis (APD), including continuous cycling peritoneal dialysis (CCPD). Others were in continuous ambulatory peritoneal dialysis (CAPD). All the patients in the work of Paniagua14 were diabetic patients. The characteristics of the RCTs are given in Table 2.

**Body Weight**

Six RCTs (436 patients) were included. No significant difference of body weight was found between the two groups (WMD $= -2.02$; 95% CI $= -5.06$ to 1.03; $Z = 1.30$; $p = 0.20$; Figure 1). A random-effects model had been used because of the high heterogeneity ($p < 0.00001$; $I^2 = 94.9\%$). If we excluded the work of Posthuma,9 which used CCPD, the conclusion we get is not different (WMD $= -2.40$; 95% CI $= -5.57$ to 0.77; $Z = 1.48$; $p = 0.14$).

**Table 1. Quality assessment of RCTs.**

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Note: RCTs, randomized controlled trials.
When the article of Posthuma9 was excluded, we got

\[ Z = \frac{WMD - WMD_0}{SE} \]

was observed among the trials (\( I^2 = 8.05\); GLU compared with the ICO (WMD = 0.25; 95% CI = 0.27–0.66; \( p = 0.24\)).

The results did not change when the work of Aiwu3 was excluded (WMD = 0.44; 95% CI = 0.23–0.66; \( Z = 4.13\); \( p < 0.0001\)).

**Triglycerides**

Three RCTs (241 patients) were included. There was a high heterogeneity for these trials (\( p = 0.002; \ I^2 = 83.3\%\)). Thus, a random-effects model was used, which showed no significant difference in plasma triglycerides between the two types of PDF (WMD = −0.66; 95% CI = −1.40 to 0.09; \( Z = 1.73\); \( p = 0.08\); Figure 5). If the work of Paniagua14 in which the patients were all diabetic, was excluded, the result was as follows: WMD = −0.31; 95% CI = −0.77 to 0.14; \( Z = 1.34\); \( p = 0.18\).

**Total Cholesterol**

Two RCTs (205 patients) were included. The result showed that patients who were using the ICO got significantly lower plasma total cholesterol compared with patients who received the GLU (WMD = −0.40; 95% CI = −0.70 to −0.10; \( Z = 2.64\); \( p = 0.008\); Figure 6). There were not enough data resource and additional data from RCTs were needed.

**DISCUSSION**

In this meta-analysis, the ICO had been shown to have significant advantages over the GLU in terms

![Image](https://via.placeholder.com/150)
of important clinical outcomes, such as plasma total cholesterol, peritoneal clearance of creatinine and urea. Because the absorption of icodextrin from the peritoneal cavity was significantly slower than that of dextrose, the ICO produced sustained positive peritoneal ultrafiltration and reduced the concentration of plasma glucose. The study by Gokal et al. showed an improvement in insulin resistance with icodextrin. However, contrary to expectations, there was no significant difference in the impact of fasting plasma glucose in our meta-analysis. We included four RCTs, but only the study of Paniagua reported significant difference in fasting plasma glucose between the two groups. The patients of the study were all diabetic in high and high-average transport, which using 7.5% ICO or 2.5% GLU for the long dwell exchanges in nighttime. Even...
though the dose of insulin reduced significantly in the ICO than in the GLU (−9.1 ± 4.7 U/day vs. 3.6 ± 3.4 U/day, p < 0.01), we could find the control of plasma glucose was better in the ICO. We did not see the same outcome in rest of the three studies, whose patients were nondiabetic or partially diabetic. Why the GLU did not affect the level of fasting plasma glucose in normal people? Maybe it was due to our normal islet function, which could secret much more insulin when we needed to keep our plasma glucose normal. If we always get higher concentration of insulin in blood, what kind of impact would it cause to our health in the long term? Insulin resistance or abnormal glycometabolism in the end? But the concentrations of plasma glucose was susceptible and it was relevant to the concentrations of the GLU, the different dwell times in peritoneal cavity, the different food and the different dialysis methods, for instance. It only represented the level of plasma glucose at that time. So maybe the outcome of HbA1C was more representative and stable than plasma glucose in glycometabolism. There were many limitations in this part of meta-analysis: The studies used 2.5% glucose PD solution compared with 7.5% icodextrin for the long dwell. The other two studies used different concentrations of glucose PD solution (1.36%, 2.27%, and 3.86%). Four studies had different dwell times in peritoneal cavity (8–16 h), which could impact the plasma glucose too. The patients in the studies by Lin et al., Paniagua et al., and Bredie et al. were in CAPD, and the patients in the study by Posthuma et al. were in CCPD. But, even though we excluded the study by Posthuma in which the patients were in CCPD, there was no significant difference in fasting plasma glucose between the two groups.

PD patients were at high risk of developing cardiovascular disease, which was the major cause of death, such as congestive heart failure, cerebrovascular disease, and myocardial infarction. High glucose concentration solutions could cause insulin resistance and dyslipidemia, which were extremely common in PD patients, and potentially had an impact on cardiovascular outcome. Many studies demonstrated that the ICO could improve the lipid metabolism. In our meta-analysis, we found that the ICO did not have statistically significantly lower blood triglycerides than the GLU, but had the different conclusion in blood total cholesterol. There were still not certain whether we could reduce the mortality of vascular complications by controlling the blood total cholesterol. There was no definite answer. One study reported that the relation of triglycerides with coronary heart disease was not influenced materially by total cholesterol levels. But many people did not agree with this view. Did the blood triglyceride play an independent role in cardiovascular disease? Did the ICO have an advantage on reducing vascular complications? Some further researches were needed.

Although the ICO had shown to have significant advantages over the GLU in terms of important clinical outcomes, there were some side effects of the ICO. First, as we all know, the ICO had an almost three-time increase in the risk of new skin rash than the GLU (5.5 vs. 1.7%), although severe cutaneous hypersensitivity reactions were reported rarely. Second, there was a concept that the ICO did not seem to be more biocompatible than the GLU in peritoneal sclerosis. The mesothelial cells, peritoneal fibroblasts, and inflammatory cells were the cellular elements that could promote peritoneal sclerosis. When these cells were stimulated by some factors, it could lead to peritoneal fibrosis, neoangiogenesis, and development of peritoneal sclerosis. In their study, Gotloib et al. pointed that 7.5% ICO induced, through lipid peroxidation, substantial genomic damage, which retard mesothelial cell repopulation after experimentally induced injury in vitro. Moreover, they found that the increase in carbonyl stress compounds (RCOs) in the effluent of patients treated with the ICO might be the source of the persistent peritoneal inflammatory reaction. Another study showed that patients who used the ICO got a higher level of IL-6, which might induce an inflammatory reaction in the peritoneum.

In conclusion, the ICO could improve small solute clearance due to the higher ultrafiltration and did not show a significant difference on fasting plasma glucose or triglycerides. Even though the PD patients who were using the ICO could get lower total cholesterol, there was no evidence that could prove its effect on long-term survival. But maybe the diabetic using the ICO could get better plasma glucose level than those using the GLU.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

REFERENCES


