Clinics and Research in Hepatology and Gastroenterology (2017) xxx, xxx–xxx

Available online at ScienceDirect www.sciencedirect.com

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ORIGINAL ARTICLE

Impact of graft preservation solutions for liver transplantation on early cytokine release and postoperative organ dysfunctions. A pilot study

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Abbreviations: AUC, area under the curve; HES, hydroxyethil starch; IGL-1, Institute George Lopez-1; PEG, polyethylene glycol; SCOT 15, *Solution de conservation des organes et tissus 15*; UW, University of Wisconsin.

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http://dx.doi.org/10.1016/j.clinre.2016.12.011
2210-7401/

Please cite this article in press as: Brisson H, et al. Impact of graft preservation solutions for liver transplantation on early cytokine release and postoperative organ dysfunctions. A pilot study. Clin Res Hepatol Gastroenterol (2017), http://dx.doi.org/10.1016/j.clinre.2016.12.011

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Summary
Introduction: During liver transplantation, graft ischemia-reperfusion injury leads to a systemic inflammatory response producing postoperative organ dysfunctions. The aim of this observational and prospective study was to compare the impact of *Solution de conservation des organes et tissus* (SCOT) 15 and University of Wisconsin (UW) preservation solutions on early cytokine release, postreperfusion syndrome and postoperative organ dysfunctions.
Methods: Thirty-seven liver transplantations were included: 21 in UW Group and 16 in SCOT 15 group. Five cytokines were measured in systemic blood after anesthetic induction, 30 minutes after unclamping portal vein and on postoperative day 1.
Results: Following unclamping portal vein, cytokines were released in systemic circulation. Systemic cytokine concentrations were higher in UW than in SCOT 15 group: Interleukin-10, Interleukine-6. In SCOT 15 group, significant reduction of postreperfusion syndrome incidence and acute kidney injury were observed. Alanine and aspartate aminotransferase peak concentrations were higher in SCOT 15 group than in UW group. However, from postoperative day 1 to day 10, aminotransferase returned to normal values and did not differ between groups.
Conclusions: Compared to UW, SCOT 15 decreases systemic cytokine release resulting from graft ischemia-reperfusion injury and reduces incidence of postreperfusion syndrome and postoperative renal failure.

Introduction

Liver transplantation is so far the most effective therapy for end-stage liver diseases. Despite substantial technological, medical and surgical advances, post-transplantation early mortality remains as high as 5 to 12 per cent [1]. The need for identifying interventions in post-recovered liver that potentially decrease postoperative organ failure such as different preservation solutions has been recently outlined [2]. Large retrospective and randomized control trials [3] should be performed together with smaller pathophysiological investigations testing hypotheses aimed at reducing postoperative organ failure.

Liver graft ischemia-reperfusion injury with systemic cytokine release is involved in posttransplantation organ failures affecting circulation [4], lungs [5], heart [6], and kidneys [7]. Ischemia-reperfusion injury results from cold storage of the graft followed by blood reperfusion [8]. After unclamping the portal vein, cytokines are released in systemic circulation and may induce a systemic inflammatory response, producing cellular damage, postreperfusion syndrome and multiorgan failures [4]. The quality of the liver, the length of ischemia and the method of graft preservation determine the degree of liver ischemia-reperfusion and influence remote organ dysfunctions [8,9]. The widely used preservation solution, University of Wisconsin (UW), has been called into question because of high potassium content (intracellular composition), a potent stimulus of vasoconstriction that impairs organ perfusion during washout and reperfusion [10]. In addition, the presence of hydroxyethylstarch (HES) has been shown to produce red blood cell aggregation [11] and renal tubular damage [12]. Therefore, alternative solutions characterized by high-sodium low-potassium extracellular composition and containing polyethylene glycol (PEG) as a substitute for HES, have been proposed [13—15]: The Institute George Lopez-1 (IGL-1) which contains a 35 kDa PEG at 1 g/L, and the Solution de Conservation des Organes et Tissus 15 (SCOT 15), which contains a 20 kDa PEG at 15 g/L. A recent experimental study performed in pigs undergoing kidney transplantation clearly demonstrated that the use of SCOT 15 for allograft preservation provided a higher protection against tissue damage resulting from ischemia-reperfusion injury compared with UW or IGL-1 [16]. A recent clinical study comparing UW to SCOT 15 reported a decrease of cholestasis following liver transplantation from the second postoperative week [14].

The primary objective of this observational and prospective study was to compare the effect of SCOT 15 and UW on postreperfusion syndrome in liver transplanted patients. Secondary objectives were to compare postoperative recovery of liver function and the incidence of postoperative dysfunctions of other organs. Following portal unclamping, the systemic release of cytokines and chemokines was assessed in order to quantify early systemic inflammatory response due to ischemia-reperfusion injury.

Please cite this article in press as: Brisson H, et al. Impact of graft preservation solutions for liver transplantation on early cytokine release and postoperative organ dysfunctions. A pilot study. Clin Res Hepatol Gastroenterol (2017), http://dx.doi.org/10.1016/j.clinre.2016.12.011