CUSTODIOL® HTK Solution The Clear Choice



ORGAN PRESERVATION SOLUTION

KIDNEY • LIVER • PANCREAS



Introduction to Custodiol® HTK Solution

Custodiol[®] HTK Solution is intended for perfusion and flushing of donor liver, kidney, and pancreas (and heart) prior to removal from the donor for preserving these organs during hypothermic storage and transport to the recipient. It is based on the principal of inactivating organ function by withdrawal of extracellular sodium and calcium, together with intense buffering of the extracellular space by means of histidine/histidine HCI, so as to prolong the period for which the organs will tolerate interruption of blood and oxygen.

Advantages of Custodiol[®] HTK Solution include:

- Low viscosity⁽²⁾
- Low potassium content safe for systemic absorption⁽²⁾
- Low sodium⁽³⁾
- No starch
- Buffered with histidine and histidine HCI
- Doubles buffering capacity in transplanted organs which moderates drop pH⁽⁴⁾
- Protects against edema⁽⁴⁾
- Lower biliary complications(5)(8)
- No flush needed⁽¹⁾



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Organ Preservation Solutions: Major Clinical Differences⁽⁶⁾

	HTK (Custodiol [©])	UW (ViaSpan®)	
Composition	K+ low	K+ high	
Viscosity	(1°C) - 2.0 cP, ~water	High: 6.2 cP	
Flow	Higher:x3 Lower		
Cooling	Faster	Slower	
Additives-	Ready to Use	Several: fresh GSH	
Filters (<1–5 μm)	No	Yes: particles 3-25->100 µm	
Flushing Prior to Implant	plant No Yes		
Adverse Events	ts None Cardiovascular complication		
In Situ Protection	Heart, kidney, liver	No	

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LIVER TRANSPLANTATION | Extended Criteria Donors

In a study comparing Histidine-Tryptophan-Ketoglutarate (HTK) and University of Wisconsin (UW) in a large number of SCD and ECD livers, the authors concluded that Custodiol HTK and UW are not clinically distinguishable in the large sample of liver transplants. However, HTK may be protective against biliary complications. Kaplan-Meier graft survival curves failed to demonstrate a significant difference in SCD or ECD livers.⁽⁷⁾







LIVER TRANSPLANTATION

A study concluded that ischemic-type biliary lesions (ITBL) account for a major part of patients' morbidity and mortality after orthotopic liver transplantation (OLT). This study retrospectively evaluated 1843 patients.⁽⁸⁾ A Starter

Organs that were perfused with UW solution developed ITBL significantly more often than Custodiol HTK perfused organs (P=0.036).⁽⁸⁾

The authors of this study mentioned that the clinical consequences of this study for their institution have been the strict limitation of CIT to <10h and the exclusive use of HTK solution.^(B)

In a meta-analysis and systematic review on the effect of preservation solutions for liver transplant, the authors concluded there was no good evidence of any difference in outcomes when comparing Custodiol HTK and either UW solution or Celsior.⁽⁹⁾

Early Dysfunction Comparing HTK with UW Solution in Randomized Trials ⁽⁹⁾						
Author and Year	H.	гк	U	W		Relative Risk
	n	N	n	N		(95% CI)
Ernhard 1994	0	30	1	30	•	0.33 [0.01, 7.87]
Meine 2006	1	37	6	65*	< ∎	0.29 [0.04, 2.34]
Brolese 2008	6	148	2	74		1.50 [0.31, 7.25]
Fixed Effects Mod	lel for	All St	udies			0.73 [0.23, 2.35]
					0.10 1.00 10.00 Relative Risk (log scale)	
Forest plot shows relative risk comparing UW and HTK in randomized controlled studies (<1 favors HTK). $Q = 1.78$, $p = .041$						

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KIDNEY TRANSPLANTATION | Living Donor Data

In a study comparing Custodiol HTK and UW in Renal Transplantation, the authors concluded HTK demonstrated similar efficacy to UW in terms of patient and graft survival. HTK was associated with a significant risk reduction on the incidence of DGF⁽¹⁰⁾

Graft survival did not significantly differ by preservation solution but in living donor patients, HTK showed a trend toward improved long-term graft survival over UW solution.



In a study looking at cost effectiveness of preservation solutions in live donor kidneys, it was shown that Custodiol HTK is superior to LR for preventing DGF, HTK and UW are more cost effective than LR and LRD in transplantation.⁽¹¹⁾

In a study by Agarwal et al., it was found that Custodiol HTK is not inferior to UW (as previously suggested by other authors) and may in fact be better protection for the prevention of delayed graft function compared to UW solution.⁽¹²⁾

KIDNEY TRANSPLANTATION | Deceased Donor Data

In a randomized multi-center study on kidney graft preservation comparing Custodiol HTK with UW and Euro Collins, the authors concluded HTK is comparable to UW in its preservative abilities.⁽¹³⁾



Kaplan-Meier Kidney Allograft

In a study comparing Custodiol HTK and UW in Renal Transplantation, the authors concluded HTK demonstrated similar efficacy to UW in terms of patient and graft survival.⁽¹⁰⁾



PANCREAS TRANSPLANTATION

A study prospectively evaluated early graft function in clinical pancreas transplantation after organ perfusion with Custodiol HTK versus UW. This prospective, randomized study, in concordance with the findings of previous retrospective comparisons of pancreas perfusion with HTK versus UW solution demonstrated equally good patient and graft survival for both preservation fluids. HTK solution appears to be equally suitable as UW solution for in situ perfusion and organ preservation in clinical pancreas transplantation.⁽¹⁴⁾



PANCREAS TRANSPLANTATION | Using HTK Preservation: Is it a Cautionary Tale?⁽¹⁵⁾

This study looks at pancreas transplant outcomes. The authors performed 115 PTXs (simultaneous kidney PTX (SKPTs) and 28 solitary PTX's (SPTs) in 114 patients between July 2003 and September 2008.⁽¹⁵⁾

Outcomes in HTK vs UW Group						
	HTK (n = 75)	UW (n = 39)	P Value			
30 Day P Graft Survival	93%	95%	NS			
1 Yr Actual P Graft Survival (for pts 1 Yr FU)	89%	85%	NS			
1 Yr Actual K Graft Survival (for pts 1 Yr FU)	95%	100%	NS			
Conclusion: There is no difference in the kidney and pancreas graft survival rates be- tween HTK and UW preservation solutions in PTX recipients with cold ischemia times up to 15 hrs. ⁽¹⁵⁾						

PANCREAS TRANSPLANTATION

In the following study, the author brought up his data comparing Custodiol, ViaSpan and Celsior solutions in pancreas transplant. It's a retrospective study looking for patient and organ survival after 1 year of transplant.⁽¹⁶⁾

Having donors and recipients with same characteristics as well as cold ischemic times, the postoperative outcomes and graft function after 3 months, 6 months and 1 year were positive among all groups.⁽¹⁶⁾

Donor, Recipient and Graft Characteristics					
	ViaSpan n = 41	Celsior n = 40	Custodiol n = 13	Ρ	
Donor Age	31	31	32	NS	
Donor Body Mass Index	24	24	24	NS	
Male Donor	23 (56)	18 (45)	6 (46)	NS	
Trauma Cause Death	21 (51)	14 (35)	5 (39)	NS	
СІТ	643	750	606	.043	
Recipient Age	39	42	40	NS	
Recipient Weight	68	69	62	NS	
Evolution Diabetes	22	28	26	NS	
Male Recipient	(78)	(63)	(46)	NS	
SPK	36 (88)	32 (80)	11 (85)	NS	
Re-transplant	4 (10)	7 (18)	2 (15)	NS	
Continuous variables mean; categorical variables, absolute value (%). CIT, cold ischemia time; SPK, simultaneous pancreas kidney transplantation					

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PANCREAS TRANSPLANTATION

In a 2016 study, the survival rate was comparable within all groups showing relative rates high with Custodiol in pancreas survival (92%) vs ViaSpan (80%) and vs Celsior (90%). Patient survival rates were relatively higher with Custodiol as well (100%) vs ViaSpan (92%) and vs Celsior (97%).⁽¹⁶⁾

Postoperative Complications						
	ViaSpan	Celsior	Custodiol	Р		
Amylase 1dy	185	188	253	NS		
Pancreatitis	3 (7)	9 (22)	1 (8)	NS		
Pancreatic Fistula	0	1 (3)	1 (8)	NS		
Intestinal Fistula	0	2 (5)	0	NS		
Thrombosis	7 (17)	6 (15)	1 (8)	NS		
Digestive Hemorrhage	5 (13)	7 (18)	2 (15)	NS		
Intra-abdominal Hemorrhage	1 (2)	3 (8)	4 (30)	0.012		
Re-intervention	7 (17)	8 (20)	3 (23)	NS		
Transplantectomy	5 (12)	4 (10)	1 (8)	NS		
Acute Rejection	1 (2)	4 (10)	0	NS		
Humoral Rejection	1 (2)	1 (2)	0	NS		
Dindo Clavien IIIb-IV	8 (20)	8 (20)	3 (23)	NS		
Continuous variables mean; categorical variables, absolute value (%). CIT, cold ischemia time; SPK, simultaneous pancreas kidney transplantation						

The author concluded that all solutions have demonstrated similar quality on pancreas preservation, with a slight advantage towards Custodiol.⁽¹⁶⁾

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About Essential Pharmaceuticals

Owned by Accord Healthcare, Inc., Essential Pharmaceuticals has served the needs of the medical community since 2006 and Custodiol[®] HTK has been used since 2000 throughout heart and organ preservation. Essential Pharmaceuticals has the exclusive sales and distribution rights to Custodiol[®] HTK in the United States and Canada.

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