LETTER TO THE EDITORS

IGL-1 as a preservation solution in intestinal transplantation: a multicenter experience

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Dear Editors,

Intestinal transplantation (ITx) is a lifesaving procedure for complicated intestinal failure. It is still characterized by a high risk of infection and rejection [1]. Of all organs, the intestine is the most vulnerable to ischemia–reperfusion injury (IRI) and the associated cross talk between the innate and adaptive immune response can trigger rejection [2]. A crucial factor in limiting IRI is the organ preservation phase. Currently, static cold storage with University of Wisconsin (UW) solution is the gold standard, although other solutions such as HTK (histidine–tryptophan–ketoglutarate) have also been reported [3]. Due to low numbers, randomized controlled trials are difficult to organize in this field.

Institut Georges Lopez solution (IGL-1) is an extracellular type preservation solution with two characteristics: (i) high sodium and low potassium and (ii) presence of polyethylene glycol as a colloid, resulting in lower viscosity (Table 1). It is used in several European centers for multiorgan preservation and is supported by extensive data [4,5]. Specifically for the intestine, IGL-1 demonstrated improved graft viability and epithelial repair compared to UW in animal experimental models [6]. This may be due to the polyethylene glycol that stabilizes the luminal wall and acts as powerful antioxidant [7]. Despite promising preclinical data, there are currently no reports of IGL-1 in clinical ITx.

We performed a retrospective analysis (January 2014–April 2018) of all ITx, where the graft was preserved with IGL-1 in 4 European ITx centers: Leuven (Belgium), Gothenburg (Sweden), Groningen (The Netherlands), and Berlin (Germany). Thirteen ITx were performed in 13 patients (one child/12 adults, seven

Table 1. Comparison of preservation solutions by composition.

Composition	IGL-1	UW	HTK
Na^+ (mmol/l)	125	30	15
K^+ (mmol/l)	30	125	10
HES (mmol/l)	–	0.25	–
PEG-35 (mmol/l)	0.03	–	–
Histidine (mmol/l)	–	–	198
Tryptophan (mmol/l)	–	–	2
Ketoglutarate (mmol/l)	–	–	1
Osmolarity (mOsm/kg)	320	320	310
pH	7.2–7.4	7.2–7.4	7.02–7.2

IGL-1, Institut Georges Lopez-1; UW, University of Wisconsin; HTK, histidine–tryptophan–ketoglutarate; HES, hydroxyethyl starch; PEG-35, polyethylene glycol-35.

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Table 2. Multicenter donor and recipient characteristics and outcome.

Patient	Center	Donor	COD	Age (years)	Recipient	Graft type	IF Cause	Age (years)	CIT (min)	T0 Biopsy median P/C score (at time of reperfusion)	T1 biopsy median P/C score	Timing of T1 biopsy (Days after ITx)	Induction therapy	Maintenance therapy	Acute rejection (<30 days)	Current status
1	Gothenburg	Donor	Meningitis	9	Recipient	ISB	SBS	42	535	2	1.5	7	ATG	Tac + CS	Yes	Deceased
2	Gothenburg		Cerebral ischemia	30		MvTx	DPMT	54	840	N/A	2	7	ATG	Tac + CS	Yes	Functioning graft
3	Gothenburg		Trauma	34		MvTx	SBS	53	537	4	3	7	ATG	Tac + CS	No	Functioning graft
4	Gothenburg		Trauma	35		MvTx	SBS	38	546	N/A	3	7	ATG	Tac + CS	No	Functioning graft
5	Gothenburg		Trauma	13		MvTx	CIPO	21	483	N/A	3	7	Basiliximab	Tac + CS + MMF	No	Functioning graft
6	Gothenburg		Trauma	16		MvtX	SBS	37	529	N/A	2	7	Basiliximab	Tac + CS + MMF	No	Functioning graft
7	Gothenburg		Trauma	12		MvTx	SBS + CIPO	33	485	N/A	2	7	Basiliximab	Tac + CS + MMF	No	Functioning graft
8	Groningen		Trauma	20		ISB	IND	37	560	N/A	4	7	ATG	Tac + MMF + CS	Yes	Deceased
9	Groningen		Trauma	14		ISB	SBS	46	369	N/A	3	6	ATG	Tac + MMF + CS	Yes	Functioning graft
10	Leuven		Meningitis	17		ISB	CIPO	17	192	3	1	3	Basiliximab	Tac + MMF + AZA	No	Functioning graft
11	Leuven		Trauma	28		MvTx	DPMT	47	331	4	2	6	Basiliximab	Tac + MMF + AZA	Yes	Functioning graft
12	Leuven		Trauma	25		ISB	CIPO	42	195	6	1	4	Basiliximab	Tac + CS	No	Functioning graft
13	Berlin		CVA	41		ISB	SBS	24	363	N/A	N/A	N/A	ATG	Tac + CS	Yes	Functioning graft

ATG, anti-thymoglobulin; AZA, azathioprine; CMV, cytomegalovirus; CIT, cold ischemia time; CIPO, chronic intestinal pseudo-obstruction; COD, cause of death; CS, corticosteroids; CVA, cerebrovascular accidentl; DPMT, diffuse portomesenteric thrombosis; IF, intestinal failure; IND, intestinal neural dysplasia; ISB, isolated small-bowel transplant; MMF, mycophenolate mofetil; MVTx, multivisceral transplant; N/A, not available; P/C, Park/Chiu; RSV, respiratory syncytial virus; SBS, short-bowel syndrome; Tac, tacrolimus.

females/six males) for short-bowel syndrome ($n = 7$), motility disorder (=4), and diffuse portomesenteric thrombosis ($n = 2$) (Table 2). Seven multivisceral and six isolated intestinal grafts were transplanted. All donors were brain-dead with a median age of 22.5 years (9–41 years) and BMI of 21 kg/m^2 (17–22 kg/m^2). Four to six liters of IGL-1 were used through aortic infusion without luminal preservation. Median cold ischemia time was 485 min (192–840 min).

All patients received induction therapy with either anti-thymoglobulin ($n = 7$) or basiliximab ($n = 6$). Immunosuppressive therapy, rejections, and infectious complications are presented in Table 2. In all cases, the bowel appeared macroscopically well vascularized after reperfusion with minimal signs of reperfusion edema. The first surveillance biopsies were taken 6.25 days (min 3 days, max 7 days). (3-7) after ITx and showed an average Park/Chiu score of 2.4 (min 1 to max 4) (Table 2). Two grafts showed histological signs of rejection in the first week after ITx.

One-year graft survival was 76%. Three patients required a transplantectomy (1 for CMV reactivation, 2 for refractory rejection). Two patients died after transplantectomy: one from intestinal failure-associated liver disease and one from bacterial sepsis, resulting in a one-year patient survival of 83% [median survival: 667 days (98–1065)]. Ten patients are alive with a functioning graft, and one requires parenteral nutrition following transplantectomy.

This preliminary experience suggests that IGL-1 can safely be used for preservation of intestinal grafts with good short-term results. Further research is required to compare outcomes with established preservations solutions.

Conflicts of interest

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