Impact of Intraoperative Cell Savage on Concentrations of Antibiotics used for Surgical Prophylaxis

ID Week 2020
Submission ID: 892004

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ABSTRACT (Revised)

Background: Intraoperative cell salvage (IOCS) is commonly used in complex surgery to administer autologus blood transfusions. While IOCS mitigates the need for allogeneic blood transfusions, an unintended consequence may be drug removal. Herein, we determined the *ex vivo* loss of antibiotics through an intraoperative cell salvage system.

Methods: Packed red blood cells and fresh frozen plasma (300ml) were acquired from banked blood and inoculated with vancomycin, piperacillin, ampicillin, and cefazolin. Inoculated blood was processed through a Cell Saver® Elite™ system. Processed fluid was directed to reinfusion or waste bags. The disposition of each respective drug infused through the Cell Saver® (initial), reinfusion and waste bags was calculated.

Results: Mean initial plasma concentrations for vancomycin, piperacillin, ampicillin, and cefazolin were 61mg/L, 107 mg/L, 172 mg/L, and 132 mg/L. When corrected for volume and hematocrit, concentrations translated to a mean ± SD of 2 ± 1% recovered drug in the reinfusion bag and 97 ± 17% in waste among all antibiotics. These observations were reproduced for ampicillin in two patients undergoing liver transplantation.

Conclusion: These experiments demonstrated significant loss of antibiotics when processed through an IOCS system with approximately 2% of available drug reinfused back to the patient. Further studies measuring the impact of cell salvage on perioperative antibiotic concentrations and infections in patients are warranted.

INTRODUCTION

- Intraoperative cell savage (IOCS), minimizes allogeneic transfusion by collecting, washing, and returning of red blood cells lost during surgical procedures[1-3]
- This technique is used in high risk of bleed procedures including liver transplant and open heart surgery
- The washing and reinfusion process has an unknown effect on the concentrations and disposition of commonly administered drugs during the process, including antibiotics given for prophylaxis of infection

OBJECTIVE

The objective of this study was to determine disposition of four antibiotics commonly used for surgical prophylaxis through an ex vivo IOCS system

METHODS

Antibiotics

- Commercial vancomycin, piperacillin-tazobactam, ampicillin-sulbactam, and cefazolin were studied
- Antibiotics were prepared to stock solutions based on package insert recommendations

IOCS Processing

- Studies for each antibiotic were conducted in duplicate
- Packed red blood cells and fresh frozen plasma were inoculated with clinically relevant plasma antibiotic concentrations (**Table 1**)
- Inoculated banked blood was placed in a warm oscillating bath to allow for protein binding
- Banked blood was processed in a Cell Saver® Elite™ IOCS system (Haemonetics, Braintree, MA) to fill a 125 mL Latham bowl and washed with 500 mL of 0.9% sodium chloride for injection
- Processed volume (estimated by IOCS device) was diverted to waste and reinfusion bags
- Samples were collected for plasma concentration and hematocrit (**Figure 1**)
- Collected plasma was stored at -80ºC until further analysis

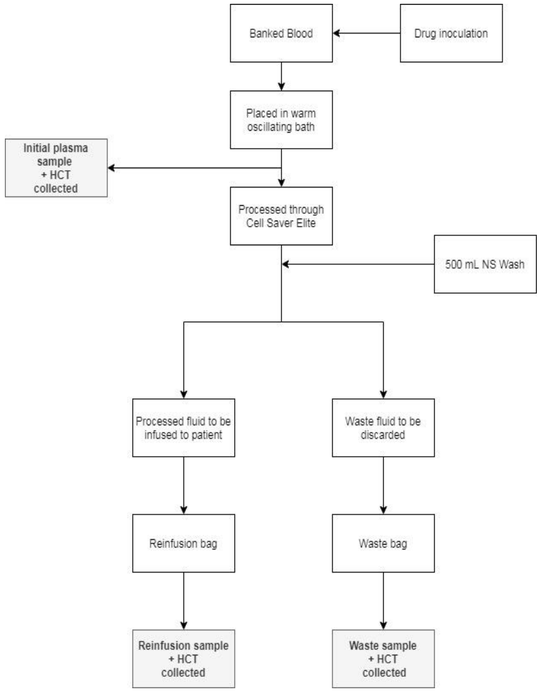
Concentration Determination

- Vancomycin plasma concentrations were determined using Roche Diagnostic Vancomycin Assay
- Piperacillin, ampicillin, and cefazolin concentrations were determined using high performance liquid chromatography (HPLC)
- Percent of recovered drug (± standard deviation) reinfusion and waste bags based on mass was determined

Patient Studies

- Plasma and reinfusion IOCS samples were collected throughout surgery from two patients receiving ampicillin-sulbactam prophylaxis for liver transplantation
- Mean volume of blood (458ml) to fill a latham bowl during surgery and the mean hematocrit of the reinfusion bag (55%) was used during calculations

Figure 1. Flowchart detailing ex-vivo study processing steps



HCT, Hematocrit; NS, 0.9% sodium chloride for injection

RESULTS

Concentration Determination

- Hematocrit ranges
  - Initial: 27-58%
  - Reinfusion: 47-70%,
  - Waste: 0.3-3.9%
- Individual experiment results are available in **Table 1.**
- Mean drug recovery in reinfusion bags was 2±1%
- There was a mean drug recovery of 97±17% in waste bags

Patient Studies

- Patients received 3g of ampicillin-sulbactam every 2-3h
- Plasma concentrations varied from 20-350 mg/L
- A total of 14 and 13 samples were collected from each respective patient
- Reinfused concentrations varied from 3-25 mg/L
- Average percent recovery translated to 2% (IQR: 1-3%)

Table 1. Observed hematocrit, antibiotic concentration data, and calculated percent of drug mass in each container for all experiments

Antibiotic	Exp #	Initial Banked Blood HCT (%)	Target Initial Plasma [C] (mg/L)	Actual Initial Plasma [C] (mg/L)	Processed Blood (mL)	Recovered Reinfusion Bag [C] (mg/L)	Available Drug Recovered in Reinfusion Bag (%)	Recovered Waste Bag [C] (mg/L)	Available Drug Recovered in Waste Bag (%)
Vancomycin	1	47	60	52.4	193	5	3	10	95
	2	32	60	69.2	264	7.2	2	19.1	92
Piperacillin	1	58	122	97.9	230	7.2	3	17.4	93
	2	27	122	115.6	265	4.9	1	27.7	75
Ampicillin	1	58	120	90.3	227	9.1	3	22.2	123
	2	32	120	253.5	201	27	2	72.8	116
Cefazolin [1]	1	32	108	131.6	220	21.1	3	30.8	88

[1] Due to a sample processing error, duplicate observations were not available for cefazolin; [C], concentration

DISCUSSION & CONCLUSION

- There was a consistent antibiotic loss of ~97% observed during ex vivo IOCS studies, while negligible drug amounts were found in reinfusion containers.
- These *ex vivo observations* were further corroborated by results from two patients undergoing liver transplantation who received prophylactic ampicillin-sulbactam.
- When combined with the administration of additional perioperative allogeneic blood or fluid resuscitation without drug supplementation, the risk for sub-optimal antibiotic concentration and infection theoretically increases.
- These observations suggest that IOCS processing could contribute to reductions in plasma antibiotic concentrations below prophylaxis threshold and put the patient at risk for developing a surgical related infection.
- Further studies evaluating the impact IOCS has on intraoperative antibiotic exposure are warranted.

ACKNOWLEDGEMENTS

We acknowledge Elizabeth Martin for assistance with the conduct of these ex vivo experiments. This study was funded in part by a grant from the Hartford Hospital Department of Medicine. The authors have no conflicts to disclose.

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