Assessing the clinical impact of intravenous acyclovir dosing in obese patients: should we be using ideal, adjusted, or total body weight?

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INTRODUCTION

- Acyclovir inhibits viral DNA synthesis and replication and has been shown to be effective in treating herpes simplex type 1, herpes simplex type 2, and varicella zoster infections
- Pharmacokinetic studies of intravenous (IV) acyclovir have suggested that dosing obese patients based on their ideal body weight (IBW) may not provide a therapeutic dose, while dosing based on total body weight (TBW) may potentially lead to an increased risk of nephrotoxicity and/or neurotoxicity
- There has been a recent initiative to dose IV acyclovir based on adjusted body weight (AdjBW) in obese patients with severe infections, but this strategy has not been evaluated in clinical studies for safety or efficacy

OBJECTIVES

Primary Objective: To determine the clinical impact of different dosing strategies of IV acyclovir on the outcome of infection, classified as either resolution or treatment failure, in obese patients

Secondary Objectives:

- Duration of IV therapy (DOT)
- Hospital length of stay (LOS)
- Nephrotoxicity or neurotoxicity associated with IV acyclovir use

METHODS

Study design: IRB-approved, single center retrospective observational chart review

Study period: January 2014 – August 2019

Population:

Inclusion Criteria	• Received at least 48 hours of IV acyclovir dosed at 10 mg/kg • Body mass index (BMI) ≥ 30 kg/m^2
Exclusion Criteria	• Pre-existing end-stage renal disease on hemodialysis • Undocumented weight • Undocumented height

Data collection: Utilized the electronic medical record to collect patient demographics, indication for treatment, length of stay, duration of therapy, and incidence of adverse drug reactions

Statistical analysis:

- Patients were included in the safety analysis group if they received at least 48 hours of IV treatment, while the efficacy analysis group included patients who received a full course of therapy for a confirmed viral infection
- Logistic regression was used to predict if weight group was associated with outcome of infection
- Poisson regression was used to determine if length of stay or duration of therapy differed among the groups

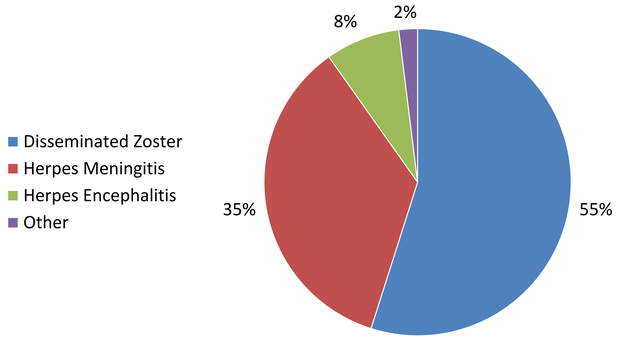
RESULTS

Baseline Characteristics N = 84	IBW (n = 36)	AdjBW (n = 26)	TBW (n = 22)
Mean age (years)	55.7 ± 18.8	52.2 ± 20.6	54 ± 16.9
Sex, Male – n (%)	14 (38.9)	11 (42.3)	7 (31.8)
Race – n (%)			
Caucasian	16 (44.4)	10 (38.5)	6 (27.3)
Black	11 (30.5)	10 (38.5)	7 (31.8)
Asian	3 (8.3)	3 (11.5)	5 (22.7)
Other	6 (16.7)	3 (11.5)	4 (18.2)
Height – cm (median (IQR))	167.6 (158.1-180.3)	163.9 (149.9-182.9)	165.1 (147.3-185.4)
TBW – kg (median (IQR))	100.8 (88.7-110.9)	98.8 (90.3-107.4)	84.6 (81.1-91.5)
BMI – kg/m^2 (median (IQR))	34.6 (32.4-38.6)	35.3 (32.5-39.3)	31.3 (30.4-34.7)

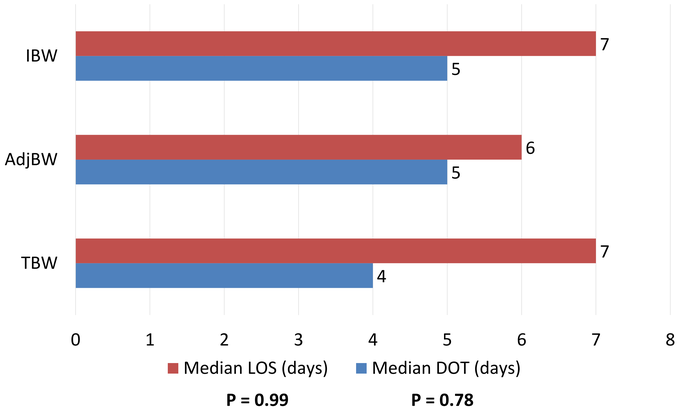
Primary Outcome n = 51	IBW (n = 23)	AdjBW (n = 15)	TBW (n = 13)	P-value
Infection resolution – n (%)	22 (96)	13 (87)	13 (100)	
Treatment failure – n				**P = 0.445**
Stage 3 AKI	1	1	0	
No improvement	0	1	0	

Nephrotoxicity	IBW (n = 36)	AdjBW (n = 26)	TBW (n = 22)	Total (N = 84)
Nephrotoxicity – n (%)	8 (22.2)	5 (19.2)	5 (22.7)	18 (21.4)
AKI stage – n				
Stage 1	7	2	3	12
Stage 2	0	1	1	2
Stage 3	1	2	1	4
Concomitant nephrotoxins – n				
Yes	6	4	5	15
No	2	1	0	3

Indication for Treatment (n = 51)



Secondary Outcomes (n = 51)



STUDY LIMITATIONS

- Retrospective chart review with a small sample size
- Majority of patients presented with disseminated zoster
- Weight of patients not well balanced
- Neurotoxicity hard to identify

CONCLUSION

- No statistically significant difference in the outcome of infection, duration of therapy, or length of stay was observed in this study
- No statistically significant difference in the rate of adverse drug reactions was observed in this study
- Dosing patients with obesity according to their IBW or AdjBW decreases the total drug exposure versus TBW