Assessment of Renal toxicity after Modified DHAP (mDHAP) regimen in the salvage treatment of refractory or relapsed Classic Hodgkin's (CHL) and Non-Hodgkin's lymphomas (NHL)

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Background The combination of dexamethasone, high dose cytarabine, and cisplatin (DHAP) is an established salvage regimen for lymphoma patients. Common adverse effect of this protocol is renal toxicity which may result in treatment discontinuation.

Objective This study intended to determine the impact of modified DHAP protocol (mDHAP) on renal functions in relapsed/refractory (R/R) CHL and NHLs.

Patients and Methods This is a prospective cohort study conducted on 51 R/R patients (34 diffuse large B-cell, follicular, mantle-cell, peripheral T-cell, T-cell B-cell rich NHLs and 17 CHLs); attending Oncology Center, Mansoura during the period between 2020 and March 2022.The mean age 45.7(±12.3 SD) years, M/F: 28/23 (54.9%/45.1%). Most patients had advanced stages (III-IV) at time of enrollment (32 (94.1%) NHL and 11 (64.7%) HL). At the end of the study, 46 (90.2%) were alive. All patients received modified DHAP (mDHAP) regimen (**Days 1–4**: dexamethasone 40 mg 15 min-i.v. infusion, cytarabine 0.5 g/m^2/12h 1h-i.v. infusion, cisplatin 25 mg/m^2 3h-i.v. infusion).

Results In total, 127 treatment cycles were administrated. 3 (5.9%), 29 (56.9%), 12 (23.5%), 5 (9.8%) and 2 (3.9%) patients received 1, 2, 3, 4 or 5 mDHAP courses, respectively. Nephrotoxicity did not exceed grade III, which occurred in 8 cycles (6.3%). **In HL patients;** glomerular filtration rate (GFR) significant decrease was observed after each mDHAP cycle. However, in none of the subgroups the mean GFR was <60 ml/min/1.73 m^2 and only after the 4th cycle there was a one stage toxicity according to mean GFR (70.7±15.3) [Table 1 & Figure 1]. In most patients, only renal impairment stage I or II were observed. Renal impairment stage III was seen in 18 % and none had stage IV [Table 2]. **While in NHL patients;** mean GFR significantly decreased after the 1st cycle (*P*=0.022), however it improved significantly with subsequent cycles in the subgroups and even reached a stationary pretreatment mean GFR [Table 1].

Conclusion A modified DHAP regimen with administration of cisplatin 25 mg/m^2 over 4 consecutive days was well tolerated as none of our patients experienced sever renal toxicity or required aggressive medical interference.

GFR mean±SD	HL	Test of significance	P value
Pre 1st mDHAP (n=17)	106.6±18.5		
Post 1st mDHAP (n=17)	104.6±21.5	t=0.66	p=0.52
Post 2nd mDHAP (n=17)	97±18.9	t=2.4	p=0.029
Post 3rd mDHAP (n=11)	91.9±15	t=18.6	p<0.001
Post 4th mDHAP (n=3)	70.7±15.3	t=10.4	p=0.009
GFR mean±SD	**NHL**	**Test of significance**	**P value**
Pre 1st mDHAP (n=34)	97.6±16.6		
Post 1st mDHAP (n=34)	90.6±15.2	t=2.4	p=0.022
Post 2nd mDHAP (n=31)	93.9±18.4	t=0.84	p=0.41
Post 3rd mDHAP (n=7)	97.6±19.6	t=15.1	p<0.001
Post 4th mDHAP (n=4)	97.8±15.6	t=13.1	p=0.001

Table 1. Analyzing renal function tests (glomerular filtration rate, GFR) for assessment of renal impairment or toxicity pre and post m-DHAP according to number of cycles for HL and NHL groups

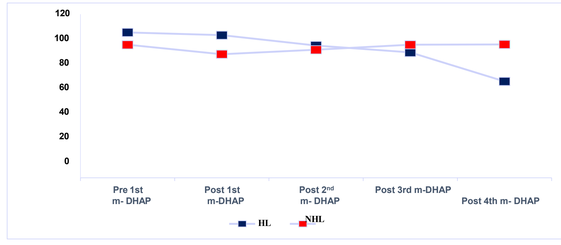


Figure 1. Mean GFR (mL/ min) in m-DHAP cycles in HL and NHL groups

Renal Toxicity Grade	Total	HL	NHL
	No. (%)	No. (%)	No. (%)
Pre 1st mDHAP	**N=51**	**N=17**	**N=34**
Grade I	38 (74.5)	14 (82.4)	24 (70.6)
Grade II	13 (25.5)	3 (17.6)	10 (29.4)
Post 1st mDHAP	**N=51**	**N=17**	**N=34**
Grade I	30 (58.8)	13 (76.5)	17 (50.0)
Grade II	18 (35.3)	3 (17.6)	15 (44.1)
Grade III	3 (5.9)	1 (5.9)	2 (5.9)
Post 2nd mDHAP	**N=48**	**N=17**	**N=31**
Grade I	30 (62.5)	13 (76.5)	17 (54.8)
Grade II	13 (27.1)	3 (17.6)	10 (32.3)
Grade III	5 (10.4)	1 (5.9)	4 (12.9)
Post 3rd mDHAP	**N=18**	**N=11**	**N=7**
Grade I	8 (44.5)	4 (36.4)	4 (57.1)
Grade II	10 (55.5)	7 (63.6)	3 (42.9)
Post 4th mDHAP	**N=7**	**N=3**	**N=4**
Grade I	3 (42.9)	0 (0.0)	3 (75.0)
Grade II	3 (42.9)	2 (66.7)	1 (25.0)
Grade III	1(14.2)	1 (33.3)	0 (0.0)
Post 5th mDHAP	**N=2**	**N=0**	**N=2**
Grade II	2(100)	----------	2 (100.0)

Table 2. Effect of mDHAP on renal functions (WHO toxicity grade scale aster each cycle of m-DHAP for HL and NHL groups).

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