Modified DHAP Regimen Associated Adverse Events in 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. Hematologic toxicity is universal. Severe (grade 3/4) non-hematologic adverse events include infection (24%) and nephrotoxicity (6%).

Objective This study was intended to estimate the efficacy, outcomes and toxicity profile of modified DHAP protocol (mDHAP) in the treatment of relapsed/refractory (R/R) CHL and NHLs. Herein, we demonstrate the therapy- adverse associated events (TAEs) we encountered during the management and follow up of the included cases.

Patients and Methods This is a prospective cohort study which included 51 R/R patients (34 NHL: DLBCL, FL, MCL, PTCL, T-cell B-cell rich and 17 CHLs) who were diagnosed and treated at Oncology Center, Mansoura University between 2020 and 2022. The mean age was 45.7 years, M/F: 28/23 (54.9%/45.1%). 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 Severe (grade III-IV) hematological toxicities documented were anemia, thrombocytopenia, neutropenia and febrile neutropenia (FN) in 4 (7.8%), 19 (37.2%), 31(60.8%) and 19 (37.2%) of total lymphoma patients, respectively. The median durations of neutropenia grade III-IV were 3 days (range, 2-5) after 1st and 2nd cycles, 2 days (range, 2-3) after 3rd and 4th cycles. The longest median duration of hospital admission due to FN was 4 days (range, 2-7) after the 1st mDHAP [Table 1]. There were no complaints of serious non-hematological adverse events e.g. sepsis, oral mucositis, pulmonary toxicity, neurotoxicity, conjunctivitis or GIT symptoms. Infection with Covid-19 was confirmed in 8 (15.6%) lymphoma patients, (2 HL and 6 NHL) patients [Table 2]. Overall response rate (ORR) was achieved in 33 (68.8%) lymphoma patients [13/17 (76.5%) HL patients and 20/34 (64.5%) NHL patients].
Fifteen (29.4%) patients failed to achieve response and were prescribed another salvage regimen. The median overall survival (OS) was 7 months (95% CI: 4.6-9.4) in HL group, and 8 months (95% CI: 6.5-9.5) in NHL group with no significant difference regarding OS between the 2 groups (P=0.81). There was no significant difference in OS aggressive and indolent NHL cases included (7 months [95% CI: 4.9-9] vs. 7 months [95% CI: 5.2-10.8], respectively with a P-value 0.4) [Figure 1].

Conclusion A modified DHAP regimen with administration of cisplatin 25 mg/m^2 over 4 consecutive days was effective, safe and well tolerated.

Table 1. Analyzing Patients characteristics and response according to m-DHAP cycles

Measure median (range)	Total N=127	1st cycle N=51	2nd cycle N=48	3rd cycle N=19	4th cycle N=7	5th cycle N=2	P value
Gender Male Female	No. (%) 66 (52) 60 (48)	No. (%) 28 (54.9) 23 (45.1)	No. (%) 27 (56.3) 21 (43.8)	No. (%) 8 (42.1) 11 (57.9)	No. (%) 3 (42.9) 4 (57.1)	No. (%) 1 (50.0) 1 (50.0)	p=0.8
Age at first diagnosis	45 (17-59)	49 (17-59)	48.5 (17-59)	34 (18-58)	44 (23-49)	45 (45-45)	p=0.3
Age at first mDHAP	49 (19-60)	50 (19-60)	50 (19-60)	37.5 (19-60)	44 (26-59)	49 (48-51)	p=0.8
Months between last ttt & 1st mDHAP	N=69 28 (4-104)	N=25 13 (4-104)	N=25 13 (4-104)	N=12 30 (4-104)	N=5 36 (20-104)	N=2 36 (36-36)	p=0.1
Interval between cycles (days)	24 (20-56)	---	23 (21-56)	23.5 (22-26)	25 (20-26)	22.5 (20-25)	p=0.8
Neutropenia	No. (%) 51 (40.5)	No. (%) 31 (60.8)	No. (%) 13 (27.1)	No. (%) 5 (27.8)	No. (%) 2 (28.6)	No. (%) 0 (0.0)	p=0.002
Duration*	3 (2-5)	3 (2-5)	3 (2-4)	2 (2-3)	2.5 (2-3)	---	p=0.3
Neutropenic fever	No. (%) 31 (24.6)	No. (%) 17 (33.3)	No. (%) 8 (16.7)	No. (%) 4 (22.2)	No. (%) 2 (28.6)	No. (%) 0 (0.0)	p=0.3
Duration*	1 (1-2)	1 (1-2)	1 (1-2)	1 (1-1)	1 (1-1)	---	p=0.8
Hospitalization	No. (%) 18 (14.3)	No. (%) 10 (19.6)	No. (%) 5 (10.4)	No. (%) 2 (11.1)	No. (%) 1 (14.3)	No. (%) 0 (0.0)	p=0.7
Duration*	3 (2-7)	4 (2-7)	3 (2-3)	2.5 (2-3)	3 (3-3)	---	p=0.1
Stage at 1st diagnosis II III IV	No. (%) 36 (28.6) 64 (50.8) 26 (20.6)	No. (%) 15 (29.4) 23 (45.1) 13 (25.5)	No. (%) 15 (31.3) 22 (45.8) 11 (22.9)	No. (%) 5 (27.8) 11 (61.1) 2 (11.1)	No. (%) 1 (14.3) 6 (85.7) 0 (0.0)	No. (%) 0 (0.0) 2 (100.0) 0 (0.0)	p=0.4
Stage at enrolment II III IV	No. (%) 20 (15.9) 76 (60.3) 30 (23.8)	No. (%) 8 (15.7) 28 (54.9) 15 (29.4)	No. (%) 8 (16.7) 28 (58.3) 12 (25.0)	No. (%) 3 (16.7) 13 (72.2) 2 (11.1)	No. (%) 1 (14.3) 5 (71.4) 1 (14.3)	No. (%) 0 (0.0) 2 (100.0) 0 (0.0)	p=0.8
Status at enrolment refractory early relapse late relapse	No. (%) 58 (46.0) 24 (19.0) 44 (34.9)	No. (%) 26 (51.0) 11 (21.6) 14 (27.5)	No. (%) 23 (47.9) 11 (22.9) 14 (29.2)	No. (%) 7 (38.9) 2 (11.1) 9 (50.0)	No. (%) 2 (28.6) 0 (0.0) 5 (71.4)	No. (%) 0 (0.0) 0 (0.0) 2 (100.0)	p=0.1
CHOP	No. (%) 65 (51.6)	No. (%) 27 (52.9)	No. (%) 25 (52.1)	No. (%) 7 (38.9)	No. (%) 4 (57.1)	No. (%) 2 (100.0)	p=0.6
Rituximab	No. (%) 23 (18.3)	No. (%) 11 (21.6)	No. (%) 10 (20.8)	No. (%) 1 (5.6)	No. (%) 1 (14.3)	No. (%) 0 (0.0)	p=0.6
Response NR CR PR SD PD	No. (%) 3 (2.4) 67 (53.2) 22 (17.5) 18 (14.3) 16 (12.7)	No. (%) 3 (5.9) 25 (49.0) 8 (15.7) 9 (17.6) 6 (11.8)	No. (%) 0 (0.0) 25 (52.1) 8 (16.7) 9 (18.8) 6 (12.5)	No. (%) 0 (0.0) 11 (61.1) 4 (22.2) 0 (0.0) 3 (16.7)	No. (%) 0 (0.0) 4 (57.1) 2 (28.6) 0 (0.0) 1 (14.3)	No. (%) 0 (0.0) 2 (100.0) 0 (0.0) 0 (0.0) 0 (0.0)	p=0.7

*Duration among those with complications (neutropenia, neutropenic fever, hospitalization)

Table 2 . Covid-19 viral infection status among studied lymphoma patients

Characteristic	Total N=8	HL N=2	NHL N=6
	No. (%)	No. (%)	No. (%)
Severity - Mild - Moderate - Severe	3 (37.5) 3 (37.5) 2 (25.0)	1 (50.0) 1 (50.0) 0 (0.0)	2 (33.3) 2 (33.3) 2 (33.3)
Critical illness	2 (25.0)	0 (100.0)	2 (33.3)
Ventilation requirement	1 (12.5)	0 (100.0)	1 (16.7)
Death	3 (37.5)	0 (100.0)	3 (50.0)

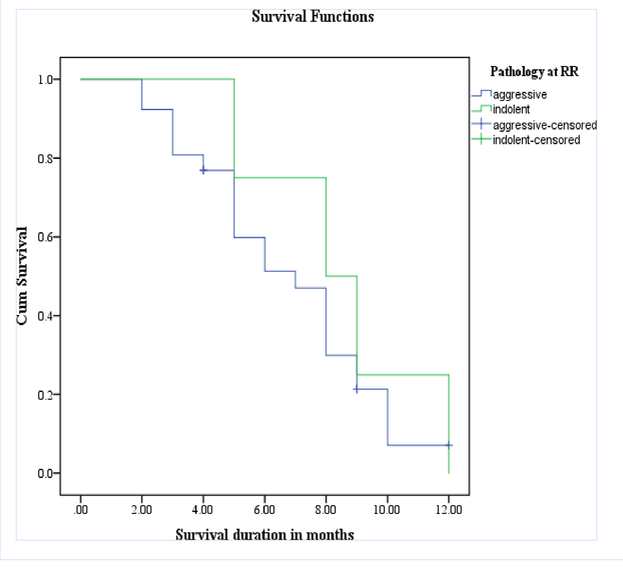


Figure 1. Survival curve for histopathological types of NHL

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