Clinical outcomes of empirical versus pre-emptive broad spectrum antifungal therapy in patients with acute myelogenous leukemia receiving antimold prophylaxis

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BACKGROUND

- Since antimold prophylaxis has been widely used in induction chemotherapy for acute myelogenous leukemia (AML), it should be re-evaluated whether broad spectrum antifungal therapy should be empirically used in prolonged febrile neutropenia.
- Therefore, we compared clinical outcomes of empirical versus pre-emptive antifungal therapy in patients with AML receiving antimold prophylaxis.

METHOD

- From September 2016 to December 2020, all adult AML patients (≥ 18 years) receiving antimold prophylaxis who had febrile neutropenia for ≥ 4 days during induction or re-induction chemotherapy at Seoul National University Hospital were retrospectively reviewed.
- They were classified into the empirical group (therapeutic broad spectrum antifungal agents had been used without evidence of invasive fungal infection [IFI]) or the pre-emptive group (antimold prophylaxis had been maintained until the emergence of IFI's evidence by one or more radiologic or mycologic factors).
- We compared clinical outcomes between the two groups after 1:3 propensity score matching with age, gender, induction or re-induction chemotherapy, and worst qSOFA score.

Table 1. Clinical characteristics and outcomes of empirical versus pre-emptive groups in unmatched and matched cohort.

	Total cohort			Propensity score-matched cohort			
Characteristics	Empirical (n=36)	Pre-emptive (n=193)	*P*	Empirical (n=36)	Pre-emptive (n=97)	*P*	Standardized mean difference
Age (median, IQR)	50 (42-56)	55 (45-63)	0.278	50 (42-56)	50 (43-57)	0.754	0.0641
Male	25 (69.4)	92 (47.7)	0.016	25 (69.4)	64 (66.0)	0.706	-0.0633
CCI score (median, IQR)	3 (2-4)	3 (3-4)	0.209	3 (2-4)	3 (2-4)	0.619	0.0963
Characteristics of AML							
Re-induction chemotherapy (*vs.* Induction)	14 (38.9)	80 (41.5)	0.774	14 (38.9)	38 (39.2)	0.976	0
HSCT before the episode	7 (19.4)	27 (14.0)	0.398	7 (19.4)	12 (12.4)	0.300	0.1994
Failure of achieving CR at the end of the episode	21 (58.3)	86 (44.6)	0.128	21 (58.3)	41 (42.3)	0.099	0.3214
Severity of FN							
Quick SOFA (median, IQR)	0 (0-1)	0 (0-0)	0.029	0 (0-1)	0 (0-0)	0.608	0.1008
PBS (median, IQR)	0 (0-1)	0 (0-0)	0.071	0 (0-1)	0 (0-0)	0.808	0.0437
Duration of FN (median, IQR)	20 (11-25)	12 (7-18)	0.003	20 (11-25)	12 (7-19)	0.015	0.4842
Duration of antifungal use (median, IQR)	30 (26-35)	32 (27-38)	0.717	30 (26-35)	31 (26-39)	0.701	0.0804
Clinical outcomes							
Probable/Proven IFI	0 (0.0)	8 (4.1)	0.249	0 (0.0)	5 (5.2)	0.323	-0.2631
All-cause mortality	3 (8.3)	7 (3.6)	0.195	3 (8.3)	4 (4.1)	0.388	0.1784
IFI-related mortality	0 (0.0)	1 (0.5)	0.843	0 (0.0)	1 (1.0)	1.000	-0.1145

Data are shown as number (%), not otherwise specified.

Abbreviation: IQR (interquartile range), CCI (charlson comorbidity index), FN (febrile neutropenia), LAmB (Liposomal amphotericin B), SOFA (Sequential Organ Failure Assessment), PBS (Pitt Bacteremia Score), IFI (invasive fungal infection).

RESULTS

- A total of 229 chemotherapy episodes, 36 in the empirical group and 193 in the pre-emptive group, were analyzed.
- In the pre-emptive group, broad spectrum antifungal therapy was administered in 45 (23.3%) episodes.
- Incidence of proven or probable IFI (0/36 [0%] in the empirical group *vs.* 5/97 [5.2%] in the pre-emptive group, *P*=0.323) and all-cause mortality (3/36 [8.3%] in the empirical group *vs.* 4/97 [4.1%] in the pre-emptive group, *P*=0.388) were not different between the two groups (Table 1).

CONCLUSION

- Clinical outcomes of empirical versus pre-emptive broad spectrum antifungal therapy were comparable in patients with AML receiving antimold prophylaxis.
- Broad spectrum antifungal therapy could be delayed until the emergence of evidence of IFI, in the current era of antimold prophylaxis.

REFERENCE

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