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Original research article

Predictors of chemoradiation related febrile neutropenia prophylaxis in older adults – Experience from a limited resource setting

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ABSTRACT

Aim: To identify risk factors that lower efficacy of antibiotic prophylaxis of febrile neutropenia among older patients on chemoradiation.

Background: Audit of institutional data showed that older adults are at higher risk of febrile neutropenia during chemoradiation. In limited resource settings widespread use of Granulocyte-Colony Stimulating Factor (G-CSF) is not economically feasible and antibiotics are used commonly. Despite compliance with antibiotics, prophylaxis is inadequate in many patients owing to patient and tumor related factors.

Materials and methods: Data from records of 219 older patients receiving antibiotic prophylaxis during chemoradiation were studied. Baseline assessment data and predisposing factors for febrile neutropenia were recorded. All patients received prophylactic fluoroquinolones. Incidence of febrile neutropenia and association with predisposing factors at baseline was analyzed by multiple logistic regression.

Results: 38.4% developed febrile neutropenia despite compliance. Multiple logistic regression revealed geriatric assessment (G8) score and tumor stage to be significant predictors of febrile neutropenia while on antibiotics ($p < 0.0001$). Odds ratios for two significant predictors G8 score and tumor stage, respectively, were 2.9 (95% CI 1.8036–4.6815) and 2.7 (95% CI 1.7501–4.1318). Correlation between these two significant predictors was found to be low in our cohort (Spearman's coefficient of rank correlation (rho) – 0.431, $p < 0.0001$).

Conclusion: G8 score and tumor burden are significant predictors of efficacy of antibiotic prophylaxis among older adults receiving chemoradiation. In older patients having poor G8 scores and advanced tumors, antibiotic prophylaxis is unsuitable. Interestingly, comorbidities and poor performance status did not impact efficacy of antibiotic prophylaxis among our elderly patients.

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1. Background

Febrile neutropenia is a major determinant of dose reduction among patients on chemotherapy and is related to the extent and duration of neutropenia.[1] Guidelines suggest that patients at high risk of febrile neutropenia, particularly those receiving chemotherapy regimens that carry greater than 20% risk, should receive prophylaxis.[2] Older adults are identified as being at higher risk than the general population in clinical studies. Findings of the MONITOR-GCSF study reinforce the evidence that patients older than 65 years of age are independently at higher risk of febrile neutropenia; which is further increased by chemotherapy regimens known to have a higher than 20% risk. In a limited resource practice scenario, elderly patients are particularly vulnerable to ill health largely owing to socioeconomic disadvantages that restrict access to adequate healthcare facilities and proper nutrition. Cost intensive treatments are not afforded by most patients and nursing care is mostly inadequate. Prophylaxis with Granulocyte-Colony Stimulating Factor (G-CSF) is not feasible universally among all older adults in our practice owing to financial constraints, and prophylaxis with antibiotics is the mainstay in practice.

A Cochrane review including 109 trials and over 13,000 patients revealed that antibiotic prophylaxis significantly reduced the risk of all causes of mortality, the risk of infection-related death, the occurrence of fever, and clinically documented infection.[3] Prophylactic fluoroquinolones are the preferred choice.[4]

The issue of antibiotic resistance in patients receiving fluoroquinolones prophylaxis is of particular concern with reports of lower benefit in communities where resistance to fluoroquinolones is prevalent.[5] However, studies have shown that patients receiving fluoroquinolone prophylaxis did not fare significantly worse in terms of morbidity and mortality from infection with resistant organisms.[6] A study also revealed that developing fluoroquinolone resistance did not increase incidence and mortality of febrile neutropenia.[7]

The incidence of febrile neutropenia among older adults on chemo radiation at this institute is considerable, warranting antibiotic prophylaxis. An analysis at this tertiary cancer institute has revealed that a considerable number of those who received antibiotic prophylaxis presented with febrile neutropenia despite compliance and many of them required hospitalization and administration of parenteral antibiotics with or without G-CSF. Hospital admission places a considerable burden on the healthcare system; added costs of treatment with parenteral antibiotics and additional G-CSF, as appropriate, often exceed costs of primary prophylaxis with G-CSF. Any additional costs and hospital admissions have a considerable impact on an already burdened healthcare system where economic constraints demand prudent utilization of all available resources.

2. Aim

This study was intended to identify predisposing patient and tumor related factors that may lower the efficacy of prophylactic antibiotics among older adults during chemo radiotherapy.

3. Materials and methods

Data from records for 219 patients over the age of 65 years, who completed chemoradiation at our institute from September 2011 to January 2016, were studied. All these patients were prescribed fluoroquinolone prophylaxis (Table 1).

For every individual, predisposing patient and tumor related factors for febrile neutropenia at baseline were noted; poor performance status, poor nutritional status, previous chemotherapy, advanced disease, low baseline blood cell counts, low body surface area and presence of co-morbidities were taken into account. Nutritional status was assessed using Subjective Global Assessment score (SGA), performance status was assessed according to ECOG (Eastern Cooperative Oncology Group) score and geriatric screening was done by the G8 questionnaire. Among co-morbidities, organ dysfunction, congestive heart failure, chronic obstructive pulmonary disease and thyroid disease were considered most relevant in our practice.

The incidence of febrile neutropenia and consequent hospitalization were recorded in each patient. Concurrent chemotherapy for head and neck and cervical cancer was weekly Cisplatin. 5-Fluorouracil and Mitomycin C was administered concurrently with radiation for all anal cancer patients and 5-fluorouracil and leucovorin was concomitantly administered in rectal carcinoma patients. Accordingly, these patients were considered for fluoroquinolone prophylaxis, particularly

Table 1 – Demographic data of patients in study.

Patient characteristics ($n = 219$)	
Gender	
Male	92
Female	127
Age	65–89 years (median 78 years)
Primary site and stage	
Uterine cervix	121
FIGO stage II	53
FIGO stage III	37
FIGO stage IVA	31
Head and neck	36
Stage III (T3N0, T1–3N1)	19
Stage IVA (T4aN0 or N1, T1–4a N2)	10
Stage IVB (T4b any N, any T N3)	7
Esophagus	5
Stage I, II (T1–3, N0)	2
Stage III A (T1–2 N2, T3N1, T4aN0)	2
Stage IIIC (T4aN1–2, T4b, N3)	1
Anal canal	9
Stage II	5
Stage III	4
Rectum	48
Stage II	19
Stage III	29
Antibiotic prophylaxis	
Ciprofloxacin	72
Levofloxacin	147