

Paclitaxel-Carboplatin Based Therapy in Elderly Patients with Non-Small Cell Lung Cancer

Özlem Özkul¹, Hasan Morcalı², Bayram Kızılkaya³, Gökhan Puşuroğlu³,
Yasemin Bakkal Temi⁴, Cemil Bilir¹

¹ Sakarya University School of Medicine, Department of Medical Oncology

² Recep Tayyip Erdoğan University Hospital, Department of Radiation Oncology

³ Recep Tayyip Erdoğan University Hospital, Department of Internal Medicine

⁴ Şanlıurfa Mehmet Akif İnan Teaching and Education Hospital, Department of Medical Oncology

Abstract

Background: Nonsmall cell lung cancer (NSCLC) is increasingly seen in the elderly population. At the time of diagnosis, more than half of the patients are over 65 years of age.

Methods: We retrospectively analyzed our hospital records. NSCLC patients treated with combination either chemotherapy or combination with radiation according to the stage.

Results: The median follow up period was 20 months and 9 (32%) patients died during this period. Patients with stage IV patients had 7.9 months median OS, patients who had locally advanced stage had 19 months median OS. Serum uric acid levels were significantly correlated with overall survival and overall response rates in locally advanced disease (HR 1.01-2.4, P=0.05 and 0.02, respectively).

Conclusion: Our results showed that combination therapy with taxanes and platinumins can be effective choice for selected elderly patients and we can use serum uric acid levels as a prognostic factor who had advanced NSCLC.

Keywords: elderly patients,uric acid,total bilirubin

Introduction

The elderly population has been increasing steadily thanks to screening strategies and new treatment options. It is estimated that the number of this group will increase 2 times higher in 2030 in the United States¹ and it is expected to find a %70 incidence of cancer in this age group². The incidence of advanced non small cell lung cancer (NSCLC) in the group older than 65 years is higher than %50³. Since, this elderly population is not included in clinical trials, treatment options in this group are limited. Treatment strategies and data in this group are coming from retrospective studies⁴. A recent analysis of the North Central Cancer Treatment Group (NCCTG) demonstrated that in elderly populations, there is a need for further prospective studies for the right patient selection and optimal treatment options⁵. This study aimed to evaluate paclitaxel-carboplatin based treatment in elderly patients.

Methods

In this study, we retrospectively analyzed our hospital data. A totally 28 locally advanced and metastatic NSCLC patients included in the study. All patients were pathologically confirmed with NSCLC. All patients treated with either combination paclitaxel and carboplatin combination or additionally radiation combination according to the stage. The following characteristics obtained from patients' charts: age, gender, histopathology, diagnosis time, type of drug, date of progression time, date of last visit, responses to treatment and survival. Laboratory parameters obtained from the hospital records. Response evaluation made by according to response evaluation criteria in solid tumors-1.1 (RECIST-1.1) criteria every three months. Progression-free survival (PFS) was defined as the time between the diagnosis and disease progression, whichever occurred first. Overall survival (OS) was calculated as the time between the diagnosis and death or last follow-up.

Statistical analyses

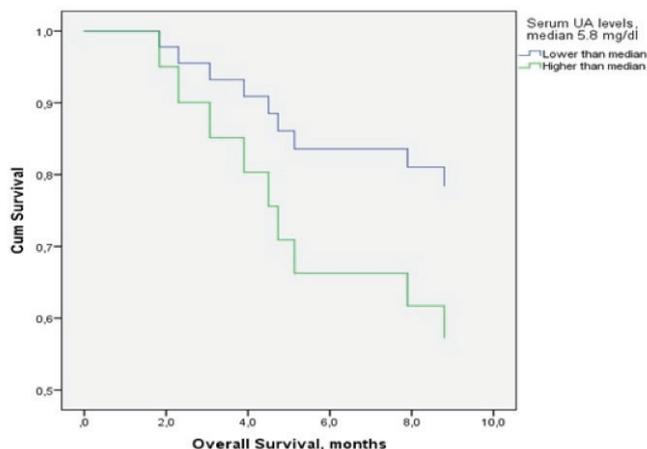
All statistical tests were performed by using software (SPSS 21 inc USA). The distribution of variables normality tested with Kolmogorov-Smirnov test and presented as mean \pm standard deviation (SD) median and interquartile ranges, as appropriate. Differences between survivor and died patient's variables according to distribution evaluated by the unpaired t test, and Mann-Whitney U test, respectively, as appropriate. The Wilcoxon signed-rank test used to compare the change in serum TSH levels between baseline and after first and 3rd month of TKI therapy. For each covariate, the

univariate and multivariable associations with OS and PFS were conducted using the Cox proportional hazards model. A P value <0.05 was considered as statistically significant.

Results

In this study, there were 28 patients with mean age 71 (65-85) years old. Ten patients had stage IV NSCLC and treated with paclitaxel carboplatin combination, remaining 18 patients had stage III A/B and treated with paclitaxel carboplatin concomitant radiation therapy. Median chemotherapy counts were 4 and 5, respectively. The median follow up period was 20 months and 9 (32%) patients died during this period. Eleven (40%) patients diagnosed with adenocarcinoma histology and remaining 17 (60%) diagnosed with squamous cell carcinoma. Patients with stage IV patients had 7.9 months median OS, 3 (30%) patients had regression, 5 (50%) had progression. Patients who had locally advanced stage had 19 months median OS, 9 (50%) patients had regression and 3 (33%) patients had stable disease.

Serum uric acid levels were significantly correlated with overall survival and overall response rates in locally advanced disease (HR 1.01-2.4, $P=0.05$ and 0.02 , respectively). Higher serum UA levels correlated lower response rate and lower survival (showed in graph 1). In metastatic patients, serum total bilirubin levels significantly correlated with OS and ORR ($P=0.008$ and 0.02 , respectively), higher bilirubin levels showed lower OS and ORR rates.



Graph 1. Overall survival in higher and lower of the median levels for serum uric acid levels.

Discussion

In this study we showed that elevated serum uric acid levels are correlated with shorter overall survival in patients diagnosed with locally advanced NSCLC. In addition, median OS was longer in locally advanced group than metastatic patients which similar to data. Lung cancer is the most common cancer causing death in the World and % 80 is inoperable at the time of diagnosis^{6,7}. Lung cancer is roughly divided into small cell lung cancer and non-small cell lung cancer, of which %85 constitute NSCLC⁸. %33 of patients with NSCLC are diagnosed at 75 years of age or older and there was a relationship between the diagnosis and the age⁹. Despite the increasing prevalence of this elderly population, there is a need for further options for treatment and appropriate patient selection¹⁰. The present study showed that locally advanced NSCLC patients treated with paclitaxel-carboplatin concomitant radiation therapy had 19 months of median OS. Langer et al. performed a retrospective analysis of 104 patients, they were 70 years or older and had been treated with concomitant chemoradiotherapy, the median overall survival was 22.4 months¹¹. In another study Atagi et al. performed a phase 3 trial included elderly patients with stage 3 NSCLC, the median survival time was 18.5 months with concomitant chemoradiotherapy arm¹². Despite the increased toxicity, elderly patients treated with concurrent chemoradiotherapy had survival rates similar to younger patients. Lastly, Gridelli et al. showed higher survival rates in combination chemotherapy with paclitaxel and carboplatin than single agent chemotherapy, such as gemcitabine or vinorelbine in elderly patients diagnosed with NSCLC but, they also had higher toxicity rates¹³. Although the number of patients was small in our study, we found similar median OS rate compared with other studies.

Patients with stage 4 disease had 7.9 months of median OS in our study. A recent phase 3 presented by Hainsworth et al. compared the efficacy of single agent versus combined chemotherapy, the trial showed that combination chemotherapy resulted with a modest improvement in time to progression (4,8 vs.2,9 months; $p:0,004$) without an impact on overall survival (5,5 vs.5,1 months; $p:0,65$)¹⁴. Although the design of this study is different, demonstrated the effectiveness of combined treatment in an appropriately selected elderly patients. In another study, which was performed Kim et al. 43 of 48 patients received platinum -based combination chemotherapy for advanced NSCLC, and one of complete response and 15 partial responses had been observed. Five patients had

progression¹⁵. In our study 3 patients (%30) had regression and 5 patients (%50) had progression. The rate of progression was higher in our study compared to Seung's study, but the addition of a different chemotherapeutic to the platinum in the Seung's study may have produced this difference.

In our study, there was a significant correlation between serum uric acid levels and overall survival rate in patients with locally advanced NSCLC. In a study, there was an inverse relationship between serum uric acid levels and general survival of NSCLC¹⁶. In this study, there was 384 stage 3-4 NSCLC patients and most of them were diagnosed with adenocarcinoma. Serum uric acid levels were divided into 4 categories and uric acid levels higher than 7.49 mg/dl were associated with worse overall survival.

In summary, platinum based chemotherapy was found effective in the elderly population. Despite the fact that comorbid diseases are more common in elderly patients and decreasing tolerance of chemotherapy, the choice of appropriate patients and chemotherapy efficacy is similar to that of the young patients. According to our results we should advise that combination therapy with taxanes and platinum can be effective choice for selected elderly patients and we can use serum uric acid levels as a prognostic factor who had advanced NSCLC.



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