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Temporal Relationship Between Inflammatory Markers and Kidney Function in Patients with Cervical Cancers receiving Cisplatin Therapy

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ABSTRACT

Introduction: Cisplatin chemotherapy is associated with nephrotoxicity, but the relationship between treatment-induced inflammation and kidney function remains unclear. This study investigated temporal changes in inflammatory markers neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) and estimated glomerular filtration rate (EGFR).

Methods: Patients with cervical cancers who received cisplatin at SQCCCRC between January 2022 and December 2024 were analyzed. NLR, PLR, and eGFR measurements were taken at baseline, end of treatment, and at 1-, 3-, and 6-months post-treatment. The research ethics committee approved the study.

Results: Thirty-two patients were analyzed. The median age was 56 years. Inflammatory markers increased substantially during treatment: NLR rose from 2.57 to 5.12 (155.1% increase) and PLR from 219.24 to 315.79 (135.2% increase). In contrast, eGFR remained relatively stable initially (baseline: 104.84, end of treatment: 101.93) but declined to 90.53 at 6 months post-treatment. Significant negative correlations were observed between NLR and eGFR at 1 month ($r = -0.46$, $p = 0.0118$) and between PLR and eGFR at 3 months ($r = -0.40$, $p = 0.0410$) post-treatment.

Conclusion: Elevated inflammatory markers may precede and contribute to the subsequent kidney function decline. Our results demonstrate that cisplatin induces a significant inflammatory response while eGFR changes occur more gradually. The temporal relationship and negative correlations between inflammatory markers and subsequent eGFR suggest that inflammation may play a role in cisplatin-induced nephrotoxicity. These findings highlight the potential utility of inflammatory markers as early predictors of kidney function decline in patients receiving cisplatin therapy.

Introduction

Cisplatin is a platinum-based chemotherapy used for solid tumors in the head and neck, lung, testis, ovary, and cervix. It causes about 40 toxicities, mainly nephrotoxicity, ototoxicity, neurotoxicity, myelosuppression, and gastrointestinal effects [1-3]. It's worth noting that the main reason doctors have to limit cisplatin doses is that it can harm the kidneys. By comparison, carboplatin is more likely to cause low blood counts, and oxaliplatin tends to affect the nerves [1,3,4]. For cisplatin, kidney problems can show up as acute kidney injury, trouble with the kidney tubules, loss of important electrolytes, or even chronic kidney disease—and this happens in about 20–35% of

patients, even when we take steps to prevent it [5-7]. Because the kidneys clear cisplatin out of the body, the drug ends up collecting in the kidney's filtering tubes via proteins like OCT2 and Ctr1. This buildup can damage the cells' DNA, mess with their energy supply, create lots of stress, and kick off inflammation and cell death [5,8,9]. That's why the kidneys are especially at risk and why cisplatin's harmful effects can add up over time, often forcing doctors to lower the dose or stop treatment altogether [6,7,10].

Looking at recent studies and reviews, it's clear that about 20–30% of people who get cisplatin end up developing some form of acute kidney injury. The precise numbers can differ depending on the dose, how the drug is given, and how AKI is defined, [6,9,11,12] but it's a pretty consistent finding across the board. The pathophysiology of cisplatin-induced nephrotoxicity is multifactorial, affecting direct tubular toxicity, vascular injury, and, importantly, inflammatory processes [7,9,13]. Recent research points to inflammation as a big driver behind the kidney damage caused by cisplatin [11,13,14]. Basically, the drug kicks off a chain reaction of inflammatory signals, drawing in immune cells and setting the stage for tissue injury [11,13,14]. In light of this, systemic inflammatory markers, such as the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR), have appeared as simple, readily available indicators of systemic inflammation. These markers have been associated with outcomes in various conditions, including cancer prognosis and treatment-related toxicities [8,15-19]. Nevertheless, the relationship between these inflammatory markers and kidney function during and after cisplatin treatment remains poorly characterized.

Assessing the relationship between inflammation and kidney function relies on accurate measures. The estimated glomerular filtration rate (eGFR) is a widely used measure of kidney function that reflects the kidneys' overall filtration capacity [12,20-22]. Therefore, monitoring eGFR during and after cisplatin treatment is important for early detection of kidney injury and proper management [20,23,24]. This study specifically aimed to examine how NLR, PLR, and eGFR change over time during and following cisplatin therapy in patients with cervical cancer. We also sought to determine whether changes in these inflammatory markers correlate with kidney function and whether increased inflammation might predict later declines in kidney function.

Methods

Study Design and Population

This was a longitudinal observational study of 32 patients who received cisplatin-based chemotherapy for cervical cancers. We included patients who got at least one round of cisplatin and had blood counts and kidney function tests (serum creatinine) checked at the start, at the end of treatment, and at least once during follow-up (either at 1, 3, or 6 months after finishing treatment). Patients with kidney disease (baseline eGFR < 60 mL/min/1.73m^2), active infection, autoimmune disorders, or use of other nephrotoxic drugs were excluded.

Data Collection

Demographic and clinical data were collected from medical records. These included age, sex, cancer type, cancer stage, cisplatin dose, number of cycles, concurrent treatments, and medical comorbidities. Lab parameters were collected at baseline, end of treatment, and at 1, 3, and 6 months post-treatment. These included complete blood count with differential (for NLR and PLR) and serum creatinine (for eGFR).

Calculation of Study Parameters

NLR is the neutrophil count divided by the lymphocyte count. PLR is platelet count divided by lymphocyte count. eGFR is calculated from creatinine and age.

Statistical Analysis

Continuous variables were expressed as means with standard deviations as well as medians with interquartile ranges. Categorical variables were shown as frequencies and percentages. Changes in NLR, PLR, and eGFR over time were analyzed using repeated-measures ANOVA with Bonferroni correction. Correlations were assessed with Pearson's coefficient. A p-value < 0.05 was significant. All analyses used appropriate software.

Results

Thirty-two patients received cisplatin-based chemotherapy. The mean age was 56 years. Median total cisplatin dose was 301 mg/m^2; median number of cycles was 5. NLR increased significantly from baseline (2.57) to the end of treatment (5.12), a 155.1% rise ($p < 0.001$). After treatment, NLR gradually decreased but stayed elevated: 4.68 at 1 month, 4.06 at 3 months, and 3.45 at 6 months. PLR also increased during treatment, from 219.24 to 315.79 (135.2% increase, $p < 0.001$). PLR was 324.81 at 1 month, then decreased at 3 months (280.87) and 6 months (259.01), but did not return to baseline. Unlike inflammatory markers, eGFR remained stable from baseline (104.84 mL/min/1.73m^2) to the end of treatment (101.93 mL/min/1.73m^2, 0.9% decrease, $p = 0.42$) and at 1 and 3 months. At 6 months, eGFR declined to 90.53 mL/min/1.73 m^2 ($p = 0.008$), showing late-onset decline. No notable correlations were found between NLR or PLR and eGFR at baseline or end of treatment. At 1 month, NLR negatively correlated with eGFR ($r = -0.46$, $p = 0.0118$). At 3 months, PLR had a negative correlation with eGFR ($r = -0.40$, $p = 0.0410$). No meaningful correlations were found at 6 months. Change in NLR from baseline to end of treatment did not correlate with change in eGFR ($r = 0.07$, $p = 0.72$). The change in PLR from baseline to the end of treatment also did not correlate with the change in eGFR ($r = 0.11$, $p = 0.59$). However, an increase in NLR at 1 month correlated with eGFR decline at 3 months ($r = -0.38$, $p = 0.04$), suggesting early inflammation may predict later dysfunction.

Discussion

This study investigated temporal changes in inflammatory markers (NLR and PLR) and kidney function (eGFR) during and after cisplatin treatment and assessed possible correlations among these parameters. What we found is that cisplatin kicks off a strong inflammatory response in the body, demonstrated by the big jumps in NLR and PLR during treatment. But when it comes to kidney function, measured by eGFR, the changes were much slower and only became obvious six months after treatment ended. So, it looks like all that inflammation might show up well before the kidneys start to lose function. The jump in inflammatory markers we saw during cisplatin treatment lines up with what other studies have found that cisplatin stimulates the body's inflammation pathways. It boosts levels of pro-inflammatory signals like TNF-α, IL-1β, and IL-6, which ramp up inflammation throughout the body [25-28]. The increases in NLR and PLR likely reflect this response. Although inflammatory markers rose during treatment, eGFR stayed stable until the significant decline at 6 months. This pattern suggests that inflammation precedes a decline in kidney function, hinting that it contributes to cisplatin-induced nephrotoxicity [25-28].

Recent studies suggest that when kidney inflammation sticks around after cisplatin treatment, it can keep damaging the kidneys and lead to a steady loss of function over time. That's why researchers are interested in targeting these inflammatory pathways to help prevent chronic kidney disease [29-31]. Meaningful negative correlations between NLR and eGFR at 1 month and PLR and eGFR at 3 months support the linkage between inflammation and kidney function. Data suggest persistent inflammation after treatment fulfillment may be associated with later kidney function decline. Even after cisplatin treatment is finished, the body keeps pumping out pro-inflammatory signals and immune cells continue to hang around in the kidneys [29,32-35]. This ongoing activation of inflammation pathways—like NF-κB, TLR2/TLR4, and the NLRP3 inflammasome shows that the immune system is still on high alert [9,31,33,34]. Plus, there are these so-called "failed-repair" kidney cells (with markers like VCAM1) that stick around in the long run and are believed to keep fueling the damage [10]. Chronic inflammation and cytokine activation are associated with ongoing eGFR decline, tubular atrophy, and fibrosis, even if the initial kidney injury was "subclinical" [10,31,33]. Cisplatin can injure the kidney tubules, but this damage might not show up right away as a drop in eGFR, making it clear that even patients who never had obvious AKI are still at risk for long-term eGFR reduction and CKD, likely due to maladaptive inflammatory mending processes [8,30].

The delayed decline in eGFR observed in our study is due to the kidney's reserve capacity and compensatory mechanisms. However, over time, ongoing injury and maladaptive fixing processes may cause a progressive decline in kidney function, as observed at 6 months post-treatment in our study. Cisplatin mostly goes after the kidney's filtering tubes, leading to cell death, problems with energy production, oxidative stress, and inflammation. But even while that's happening, the kidneys can keep up their filtering power for a while, thanks to backup capacity [11,36]. That means early damage may show up in special urine or tissue tests (like KIM-1 or NGAL), before there's any obvious drop in eGFR [11,36]. Studies in animals show that when they get repeated low or moderate doses of cisplatin, their kidneys can recover even when there's obvious damage to the tubules. This just goes to show how the kidneys have a built-in backup system that can compensate for a while before things start to go downhill [10,31,32]. Persistent tubular senescence, cell cycle arrest, and profibrotic reprogramming drive chronic inflammation, fibrosis, and progressive CKD [30,32]. Studies using these repeated cisplatin models, even when early kidney function looks mostly okay, show that by six months, there's often a steady march toward chronic kidney disease, with more scarring, inflammation, and even damage to the glomeruli and blood vessels [32,33].

Our findings possess several clinical implications. First, they point out the importance of long-term monitoring of kidney function in patients who have received cisplatin, as significant declines may occur months after treatment completion. Second, they suggest that inflammatory markers, particularly NLR and PLR, may serve as early indicators of patients at risk for subsequent kidney function decline. This could potentially allow for earlier intervention to prevent or mitigate cisplatin-induced nephrotoxicity. There are a few things to keep in mind about our study. For one, we didn't have a huge group of patients, so we might have missed some connections just because of the small sample size. We also didn't collect data on urinary markers of kidney injury, which could have helped us spot early kidney problems more accurately. And finally, we didn't look at other factors—like how well patients were hydrated, what other medications they might have been taking, or whether their cancer was getting worse—that could have played a role in the changes we saw in inflammation and kidney function.

Conclusion

Our study shows that cisplatin treatment induces a significant inflammatory response, as evidenced by increased NLR and PLR, while eGFR changes occur more gradually, with a significant decline observed at 6 months post-treatment. What's interesting is that we saw inflammation markers go up before any real drop in kidney function showed up, and the two were connected. This hints that inflammation might actually play a part in the kidney damage caused by cisplatin. Our findings show that tracking these markers could help spot patients at risk of kidney problems earlier, making it clear why it's so important to keep an eye on kidney health for the long haul. Looking ahead, it would be great to see studies with more patients, longer follow-up, and a wider range of kidney injury markers. That way, we could get a clearer picture of how inflammation and cisplatin-related kidney problems are linked—and hopefully come up with better ways to catch and help patients at risk, before serious kidney trouble starts.

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