A Retrospective Study Evaluating the Effect of Hepatic Steatosis on Paclitaxel Tolerability in Patients with Breast Cancer

Rambo Le[1], Joshua Peters[1], Mario Sanchez[1], Heather Tran[1], Jennifer Segar[2], MD, Lisa Davis[1,2], PharmD.

The University of Arizona R. Ken Coit College of Pharmacy[1]

The University of Arizona Cancer Center – Banner University Medical Center Tucson[2]

Introduction

- According to the World Health Organization, 2.3 million women were diagnosed with breast cancer in 2020.[1]
- Paclitaxel is a chemotherapeutic agent commonly used for the treatment of breast cancer.[2]
- Significant side effects of paclitaxel include peripheral neuropathy, cytopenias, fatigue, and elevated liver transaminases.
- Paclitaxel is associated with hepatic toxicity, but the underlying mechanisms are not well described.
- Hepatic metabolism and biliary excretion play pivotal roles in elimination and distribution of paclitaxel and its metabolites.
- Hepatic steatosis has been linked to alterations of transporter proteins and changes in the pharmacokinetics of certain medications, which may include paclitaxel.[3]

Objectives

- Determine if hepatic steatosis in patients with breast cancer affects paclitaxel tolerability.
- Evaluate the incidence of hepatic steatosis in the setting of patients with breast cancer who have metabolic syndrome or other risk factors

Methods

- Retrospective chart review using EMR to identify patients with breast cancer treated with paclitaxel at the University of Arizona Cancer Center from September 1st, 2017 to October 15th, 2022.
- Inclusion criteria: breast cancer diagnosis, treatment with paclitaxel, and abdominal imaging with MRI, CT, or PET scan.
- Patient demographics, past medical records, cancer staging, liver function tests, and details of paclitaxel treatments were extracted from medical records and collected in RedCap.
- Patient tolerability was defined based on paclitaxel dose reductions
- Metabolic syndrome was based on the presence at least 3 of the following: BMI ≥ 30 kg/m^2, diabetes, hypertension, and dyslipidemia.
- Statistical analysis: t-Test Two-Sample Assuming Equal Variances on Microsoft Excel.

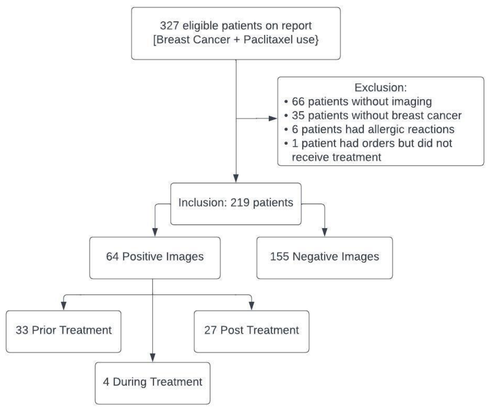


Figure 1. Patient Selection Flowchart

Results

	Positive (n = 64)	Negative (n = 155)	P-value
Age (mean)	54. 45	57.17	
Female	98.46%	99.38%	0.507
Race			
American Indian or Alaska Native	3.08%	1.24%	0.346
Asian	0%	1.86%	0.270
Native Hawaiian or other Pacific Islander	0%	0.62%	0.526
Black or African American	3.08%	3.11%	0.991
White	89.23%	90.06%	0.852
Other Race	4.62%	1.24%	0.120
Unknown	0%	1.86%	0.270
Ethnicity			
Hispanic	38.46%	19.88%	0.003
Not Hispanic	60%	80.12%	0.002
Unknown	1.54%	0%	0.116
Stage			
1 to 3	77.78%	65.84%	0.082
4	21.54%	34.16%	0.082
Therapy Setting			
Neoadjuvant	60%	50.31%	0.203
Adjuvant	10.77%	11.18%	0.918
Metastatistic	29.23%	37.89%	0.208
BMI Classification			
< 18.5	1.54%	3.11%	0.663
18.5 - 24.99	16.92%	33.54%	0.009
25 – 29.99	33.85%	31.68%	0.754
≥ 30	47.69%	31.68%	0.023
Comorbidities			
Diabetes	20%	9.94%	0.041
Hypertension	47.69%	34.16%	0.058
Hyperlipidemia	27.69%	20.5%	0.243
None	4.54%	57.14%	0.033
Presence of LFT elevation			
Prior to paclitaxel use	41.54%	16.15%	<0.001
During paclitaxel use	46.15%	36.65%	0.187
Post paclitaxel use	46.15%	36.65%	0.187
No elevation	30.77%	44.10%	0.064
Reasons for dose adjustment or discontinue			
Neuropathy	21.54%	24.84%	0.600
Disease progression	7.69%	16.15%	0.095
Fatigue	9.23%	10.56%	0.766
Cytopenias	10.77%	18.01%	0.179
Elevated LFTs	6.15%	3.73%	0.424
Other	32.31%	52.80%	0.005

Table 1. Patient Characteristics

Figure 1 – Adverse Effects During Paclitaxel Treatment

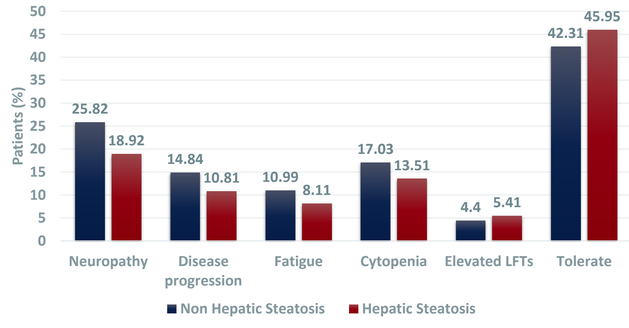


Figure 2 – Patient Comorbidities

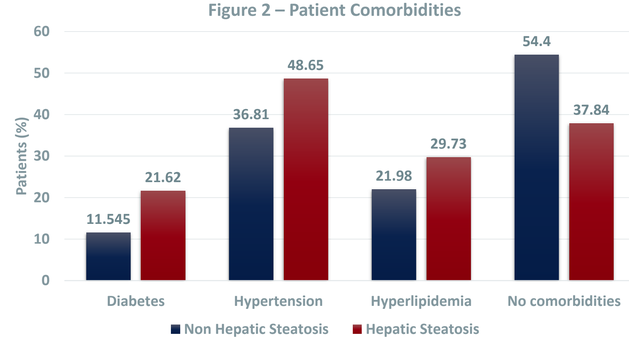
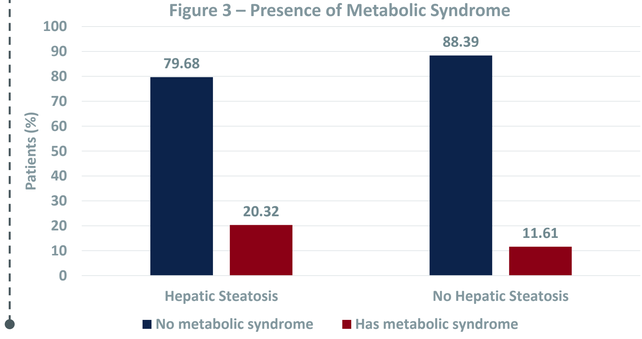


Figure 3 – Presence of Metabolic Syndrome



Discussion

- The findings in this study showed no significance in hepatic steatosis affecting tolerability of paclitaxel in patients with breast cancer. Most patients did not require dose reduction and were not factored into the analysis.
- 100% patients had side effects from paclitaxel, with the 42.92% not requiring dose reduction. Of these patients not dose reduced, 81.91% did not have hepatic steatosis compared to 18.09% with hepatic steatosis. This suggests that patients without hepatic steatosis may tolerate paclitaxel better or have less pronounced toxicity.
- LFT elevation was noted in both groups during paclitaxel treatment and remained elevated after post paclitaxel dosing.
- Significant risk factors for hepatic steatosis: Hispanic ethnicity, diabetes, increased BMI
- A diagnosis of hepatic steatosis was less common in patients without a diagnosis of diabetes, hypertension, or hyperlipidemia.
- There was no correlation between metabolic syndrome and development of hepatic steatosis. However, there was a higher prevalence of metabolic syndrome in the patients with hepatic steatosis, but this was not statistically significant.

Limitations

- Retrospective chart review is limited what is available in EMR.
- Routine liver imaging not performed on this patient population and the timing of imaging varied.
- Did not include abdominal ultrasound in imaging.
- Did not further evaluate toxicity in those who did not require dose reduction.
- Metabolic syndrome was challenging to determine based solely on home medication list and physician notes.

Conclusion

- This is the first study to look at hepatic steatosis affecting paclitaxel tolerability.
- Recognition of steatosis and risk factors for developing steatosis in patients receiving paclitaxel is important.
- Patients without hepatic steatosis may tolerate paclitaxel better and require fewer dose modifications.
- Patients treated with paclitaxel should be closely monitored for LFT alterations and baseline liver imaging should be considered for patients with elevated LFTs.
- There is an unmet need to perform more randomized prospective trials in this area

References

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