Titration Approach to Reduce Paclitaxel Hypersensitivity Reactions: A Quasi-Experimental Retrospective Study on Clinical and Economic Outcomes in an Oncology Setting

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Background

- Paclitaxel is a widely used taxane-based chemotherapy agent indicated primarily for the treatment of breast, lung, ovarian, and head and neck cancers.
- **Infusion-related hypersensitivity reactions (HSR)** are a common adverse event, affecting up to **42% of patients**.
- Whilst premedication regimens are standard practice, a significant risk of HSR persists. **Titration protocols**, involving gradual increases in paclitaxel infusion rates, have emerged as a **promising alternative to standard infusion methods**.

Methodology

Quasi-experimental retrospective pre/post study

Titration protocol implementation : April 1st, 2024

Pre-implementation group
- Period : December 2022 to March 2024

Standard infusion protocol
No progressive rate :
- Paclitaxel every week: infused over 1h
- Paclitaxel every 3 weeks: infused over 3h

Post-implementation group
- Period : May 2024 to August 2025

Titration protocol only for first 2 doses
For both 1h and 3h infusions :
- **Step 1 :** 50ml/h x 15 min
- **Step 2 :** 100ml/h x 15 min
- **Step 3 :** 150ml/h x 15 min
- **Step 4 :** Maximum infusion rate (total volume of bag/total time)

Pre-medication received by both groups: famotidine 20 mg IV, diphenhydramine 50 mg IV and dexamethasone 10-20 mg IV

Population

Inclusion criterias
- Adults ≥ 18 years old
- Received all three first paclitaxel doses at the outpatient oncology clinic of the Jewish General Hospital (JGH)
- Taxane-naive
- Standard pre-medications adminisered

Exclusion criterias
- Paclitaxel administered as part of a clinical trial
- Treatment given outside the outpatient clinic (e.g. during hospitalization)
- Paclitaxel titration protocol not respected

Statistical analysis

- Chi-square test, with a significance level of ($p < 0.05$)
- Person's chi-square, except for the outcomes of paclitaxel infusion time and chair time where T tests were used to compare the means.

Outcomes

Primary outcome

Incidence of HSR before versus after implementing the paclitaxel titration protocol at the JGH.

Secondary outcomes

1. Comparison of HSR management (use of rescue meds and its total cost, switch to nab-paclitaxel, use of desensitization protocol, use of allergist consultation)
2. Comparison of chair time and infusion time between groups
3. Comparison of HSR type and severity

Results

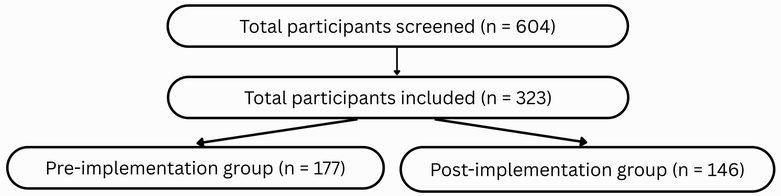


Table 1 : Characteristics of participants pre/post-implementation groups

Characteristics	Pre-implementation (n = 177*)	Post-implementation (n = 146**)	p-value
Age ± SD	61.1 ± 12.7	59,6 ± 13.4	0.060
Sex, no. (%)			0.281
Male	28 (15.8)	17 (11.6)	
Female	149 (84.2)	129 (88.4)	
Allergy to medication, no. (%)			0.078
Yes	36 (20.3)	42 (28.8)	
No	141 (79.7)	104 (71.2)	
Cancer diagnosis, no. (%)			
Breast cancer	103 (58.2)	81 (55.5)	0.624
ENT cancer	21 (11.9)	4 (2.7)	0.002
Gastrointestinal cancer	6 (3.4)	3 (2.1)	0.468
Gynecology cancer	35 (19.8)	39 (26.7)	0.140
Lung cancer	9 (5.1)	10 (6.8)	0.502
Other	3 (1.7)	9 (6.2)	0.035
Cancer stage, no. (%)			
I	36 (20.3)	25 (17.1)	0.480
II	53 (29.9)	33 (22.6)	0.147
III	53 (29.9)	54 (37)	0.167
IV	35 (19.8)	33 (22.6)	0.514
Unknown	0 (0)	1 (0.7)	
ECOG score			
0	105 (59.3)	78 (53.4)	0.843
1	65 (36.7)	50 (34.2)	0.915
2	5 (2.8)	4 (2.7)	0.933
3	2 (1.1)	2 (1.4)	0.779
Unknown	0 (0)	12 (8.2)	
Use of concomitant chemotherapy, no. (%)			0.954
Yes	128 (72.3)	106 (72.6)	
No	49 (27.7)	40 (27.4)	
Dose of dexamethasone received as pre-medication, no. (%)			
10 mg	24 (13.6)	34 (23.3)	0.023
15 mg	0 (0)	1 (0.7)	0.270
20 mg	153 (86.4)	111 (76.0)	0.016
Paclitaxel infusion duration			0.637
1 hour	116 (65.5)	92 (63.0)	
3 hour	61 (34.5)	54 (37.0)	

Figure 1 : Incidence of all grade HSR

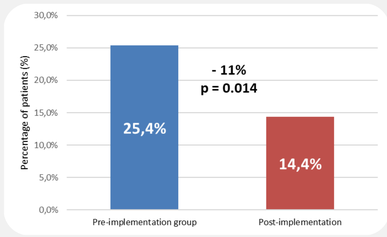


Figure 3 : HSR severity

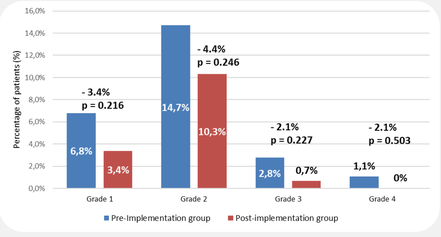


Figure 2 : Timing of first HSR occurrence

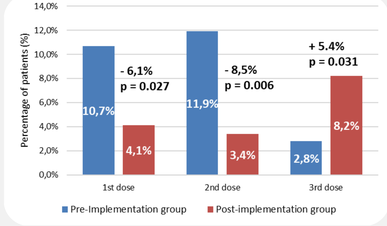
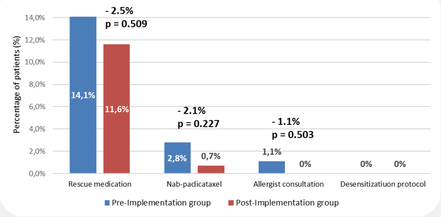


Figure 4 : HSR management



Chair and infusion time

- Mean difference of average chair time :
  - Paclitaxel dose ≤ 80 mg/m² : + 15.3 min (95%CI 8.96 to 21.57, $p < 0.001$)
  - Paclitaxel dose > 80 mg/m² : + 18.9 min (95%CI 7.28 to 30.54, $p = 0.002$)
  - **Average chair time increase of 17.1 min in the post-implementation group**
- Mean difference of average infusion time :
  - Paclitaxel dose ≤ 80 mg/m² : + 24.1 min (95%CI 10.04 to 38.08), $p < 0.001$)
  - Paclitaxel dose > 80 mg/m² : + 13.4 min (95%CI −2.73 to 29.57, $p = 0.102$)
  - **Average infusion time increase of 18.75 min in the post-implementation group**

Discussion

Strengths	Limitations
Comparable baseline characteristics for both groups	Retrospective and single-center
Sensitivity analysis results are consistent with the primary analysis ones	Missing data from paper medication administration records (MAR)
Results are consistent with previous literature [1,2]	Retrospective reaction grading
Pragmatic study design	Cost analysis limited to direct costs

Conclusion

The implementation of a standardized paclitaxel infusion titration protocol
- Decreased HSR incidence
- Decreased the need for rescue medication and nab-paclitaxel substitution
- Increased the total chair time by less than 20 minutes
- Maintained a reassuring safety profile

Future prospective, multicentered studies should confirm these findings, explore an in-depth cost analysis, and evaluate patient satisfaction and feasibility in other chemotherapy regimens.

References

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2. Sefah K, Kilowski KA, Gifford SA, Grove A, Shaffer J, Bryan B, Ahmad S, Holloway RW. Standardized Titration Protocol Reduces the Incidence of Paclitaxel Infusion-Related Hypersensitivity Reactions. J Oncol Pharm Pract. 2020 Jun;26(4):783-791. doi: 10.1177/1078155219895101. PMID: 31856755