Clogging Challenge Test on Mesh Vibrating Nebuliser Using Budesonide Suspension

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Summary

In the past few decades, inhalation therapy has undergone a series of changes due to the introduction of new technologies and treatments; among them, vibrating mesh nebulisers have made their way into the field supported by their features that highlight portability and efficiency to deliver respiratory drugs. Although these devices have been proven to produce desired outcomes, there are still limitations to their use. Mesh clogging is one of the top concerning issues caused by device handling and cleaning habits. It can influence aerosol particle size and nebulisation time, the former being particularly relevant to central and peripheral lung deposition. This study investigated potential mesh clogging on a nebuliser and the effects it could cause on the aerosol characteristics. Deepro™ Vibrating Mesh Nebuliser was used to aerosolize budesonide inhalation suspension during several days without washing the device. The results showed that aerosol particle size stayed below 5 µm and fine particle fraction held above 45% even when the device was not washed for up to five days. Some minimal variations in the results were normalized once the device was washed under standard cleaning procedure in both challenge tests. The results supported the hypothesis that the nebuliser did not exhibit significant mesh clogging given that aerosol characteristics remained stable. The assumption that Deepro™ did not exhibit major mesh clogging characteristics highlighted the advantages of its performance. Further research is required to examine data during longer challenge test periods and to compare its performance with other devices.

Key Message

Deepro™ was found not to exhibit substantial mesh clogging during two challenge tests, considering the expected effects of clogging. The performance of the device was described as stable even when it was not washed for up to 5 days. The results contradicted typical concerns about clogging in mesh nebulisers.

Introduction

Vibrating mesh nebulisers have solidified their position in the respiratory drug delivery field and become the primary choice of pharmaceutical companies to conduct clinical trials [1]. Compared to their counterparts, the jet nebulisers, mesh nebulisers present a series of features that make them easy to operate, portable, and energy efficient. Moreover, mesh nebulisers are characterized by a higher aerosol delivery efficiency, which translates into minimal residual volumes [2]. It has also been reported that aerosol from mesh nebulisers can achieve twice as much deposition into the lungs than conventional jet nebulisers [3].

Newer mesh nebuliser models are able to aerosolize a wider range of respiratory drugs. Supported by their improved technologies, aerosolization of suspension drugs, such as budesonide, is attainable at present [4]. On the other hand, there are still some issues to overcome, mesh clogging being one of them. Mesh clogging or blockage has been cited as a recurrent problem in most mesh devices, generating larger particle size and longer nebulisation time [1]. Patients' cleaning habits play a critical role in this issue as some of them might not thoroughly follow the standard cleaning procedure. According to past studies, clogging could be attributed to aggregation of environment organic and inorganic debris [5], while it could also be the consequence of suspension particle aggregation [6]. Aiming to examine the performance of an innovative mesh nebuliser, the device was submitted to two clogging challenge tests. The device used in this study is a modified version of a model commercially available in the Federative Republic of Brazil.

Experimental Methods

In order to investigate mesh clogging, Pulmicort Repsules®, budesonide inhalation suspension from AstraZeneca, with a dose of 1 mg per 2 mL was aerosolized with Deepro™ Vibrating Mesh Nebuliser from HCmed Innovations Co., Ltd. Two clogging challenge tests examined the effects of mesh clogging through periods of 2 and 5 days. In the first test, one nebuliser was used to aerosolize budesonide suspension twice on Day 1 without washing the device in between runs, and twice on Day 2, once before washing the device and another after. For the second test, the same nebulizer was used to carry out three runs on Day 1 without washing the device, and twice on Day 5, once before washing it and another after. No replications were conducted due to sample limitation.

The 2-day challenge test served as an initial study, while the 5-day test assumed that a patient would only use the nebulizer on Day 1 and Day 5 due to lack of compliance with standard use and cleaning. This behaviour allowed the residual medication to completely dry in the reservoir. The mesh nebuliser used in this experiment and the sketch representing standard cleaning procedure are both shown in Figure 1.

Particle size distribution was analysed using Next Generation Impactor (NGI) manufactured by Copley Scientific. The flow rate was set to 15 L/min with nebulisation time of 7 minutes. Samples were collected from the NGI stage trays and HPLC analysis was carried out to compute drug deposition in each tray. Copley Inhaler Testing Data

Analysis Software (CITDAS) was used to calculate the delivered dose (DD), fine particle dose (FPD), fine particle fraction (FPF), and mass median aerodynamic diameter (MMAD) for all NGI tests.

(a) (b)

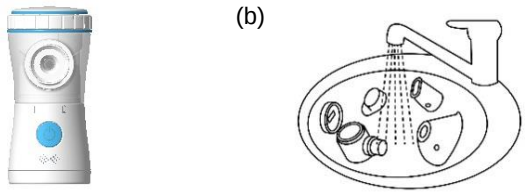

Figure 1. (a) Deepro™ Vibrating Mesh Nebuliser and (b) Standard cleaning procedure using tap water to rinse the device

Results

The results for both the 2-day and 5-day clogging challenge tests calculated with CITDAS are displayed on Table 1 and Table 2, respectively. The delivered dose stayed within the range 0.467 and 0.475 mg during the 2-day challenge test. FPD for the first nebulisation and after washing were calculated as 0.220 mg with only a slight difference in FPF. The values recorded during the two runs in which the device was not washed reported similar results to the initial and after wash runs. MMAD was recorded below 5 µm in all cases.

Table 1. Results from NGI for 2-day Challenge Test

	Delivered Dose (mg)	FPD (mg)	FPF (%)	MMAD (µm)
Day 1 NGI Test 1	0.470	0.220	46.89	4.93
Day 1 NGI Test 2 (w/o wash)	0.467	0.219	46.91	4.91
Day 2 NGI Test 1 (w/o wash)	0.475	0.214	45.10	4.99
Day 2 NGI Test 2 (after wash)	0.471	0.220	46.73	4.91

Table 2. Results from NGI for 5-day Challenge Test

	Delivered Dose (mg)	FPD (mg)	FPF (%)	MMAD (µm)
Day 1 NGI Test 1	0.486	0.223	45.81	4.98
Day 1 NGI Test 2 (w/o wash)	0.468	0.216	46.23	4.91
Day 1 NGI Test 3 (w/o wash)	0.465	0.216	46.05	4.92
Day 5 NGI Test 1 (w/o wash)	0.544	0.258	47.40	4.75
Day 5 NGI Test 2 (after wash)	0.471	0.218	46.28	4.91

There were no major differences observed during the first three runs on Day 1 of the 5-day challenge test. The delivered dose slightly decreased after tests 2 and 3 on Day 1, while the FPF increased and it was associated to smaller MMAD values.

On Day 5, the delivered dose increased meaningfully attributing to a larger reservoir retention after not washing the device for five days. FPF was found to be higher while particle size was smaller. The delivered dose and other indicators normalized on Day 5 after washing the device according to the standard cleaning procedure.

Figure 2 shows two plots containing delivered dose and fine particle dose values for both challenge tests. It can be observed that values remained mostly constant throughout the testing periods when washing or not the nebuliser in between runs. The consistency of these indicators led to the conclusion that expected effects of mesh clogging did not affect the performance of the mesh nebuliser.

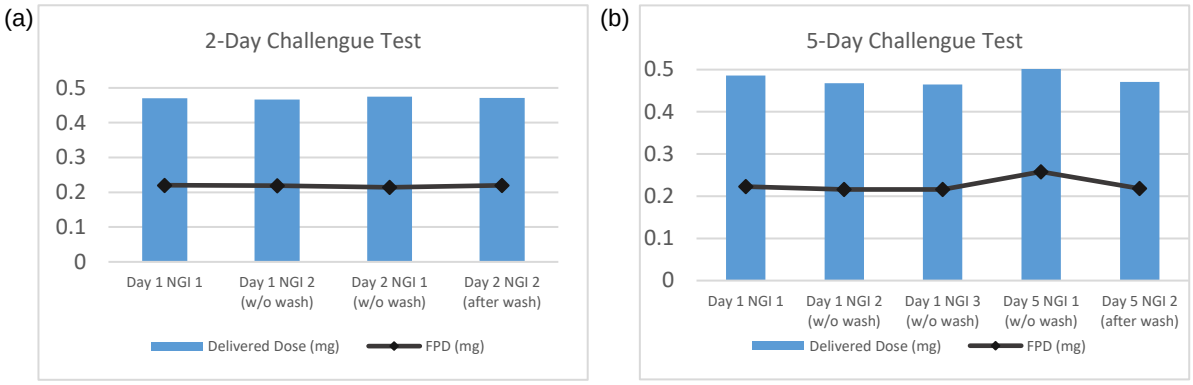

Figure 2. Delivered dose and fine particle dose comparison during (a) 2-day and (b) 5-day challenge tests

Discussion

The results of the clogging challenge tests showed that the mesh nebuliser could operate steadily even when the device was not washed for up to five days. In the 5-day test, the delivered dose was observed to increase on Day 5, which similarly increased FPD. Higher delivered dose could imply different degrees of clinical relevance; therefore, patient adherence to cleaning standards is advisable in all situations. Research on the implications of higher intake of budesonide suspension are recommended to acquire a better understanding of the scenario as well as the effects that could be caused by other formulations.

Further research can also be conducted to examine the implications associated to prolonging the period of the challenge test. Comparison with other mesh nebulisers is equally suggested to garner more information about the performance of other devices.

Conclusion

The clogging tests demonstrated that Deepro™ Vibrating Mesh Nebuliser could operate normally even when the device was not washed for several days. The vibrating pattern characteristics of the device enabled it to resist clogging for an extended period. Nonetheless, the results of this study could be investigated in more depth by replicating the conditions and running tests.

References

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