Performance variability of commercial jet nebuliser systems measured with European standard and its clinical implication

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Introduction

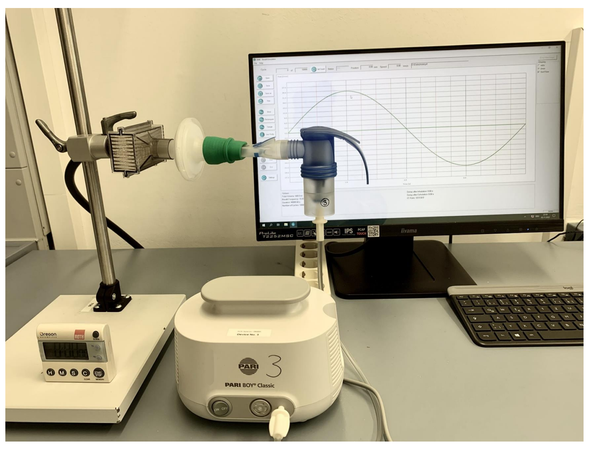
Jet nebuliser systems are widely used to administer aerosolised medicines to patients with respiratory diseases. This therapy option avoids application errors which may occur using e.g., metered dose inhalers (MDIs) or dry powder inhalers (DPIs) [1], [2]. Patients with suboptimal respiratory flow (< 30 l/min), physical and/or cognitive limitations or when higher than routine drug doses are required, particularly benefit from jet nebuliser therapy [4]. The choice of nebuliser system is the clinician's primary approach to optimising deposition to the lungs and is therefore a critical clinical consideration that has an important impact on treatment success. There are many nebuliser systems on the market with very different aerosol performances and therefore it is often difficult for physicians to objectively assess their clinical effectiveness.

Objectives

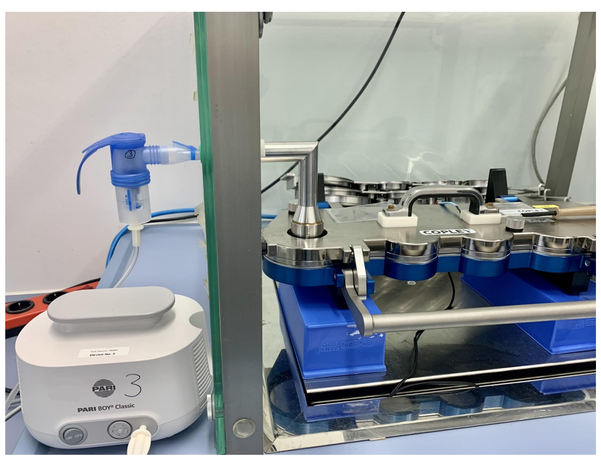
The aim of this study was to evaluate the aerosol performance of 15 commercially available jet nebuliser systems according to the European standard DIN EN ISO 27427:2020, which allows an objective comparison of the devices and that manufacturers should comply with. The clinical importance of the measured parameters was discussed.

Methods

Three different nebuliser systems of one brand were measured in duplicate according to DIN EN ISO 27427:2020 standard. The jet nebulisers were filled with 2 mL of 0.1% (w/v) Salbutamol. Salbutamol contents were determined by HPLC.



Aerosol Output (AO), Aerosol Output Rate (AOR) and nebulisation time (NT) were measured with a PARI COMPAS breath simulator using a tidal volume of 500 ml, 15 breath/min, I:E ratio of 50:50. The nebulised salbutamol solution was collected on inspiratory filters. A filter change was performed after 1 min of nebulisation. The AOR is defined as the amount of Salbutamol deposited on the inspiratory filter within the first minute of nebulisation.



Mass Median Aerodynamic Diameter (MMAD) and Respirable Fraction (RF= % particles < 5 µm) were measured with a cooled (17°C) Next Generation Impactor at 50% RH and 23°C ambient conditions at a flow rate of 15 L/min. Nebulisers were connected (mouthpiece attached) to the conditioned NGI.

For the quantitative determination of salbutamol content, all samples were analysed using a validated standard HPLC-UV system. Respirable Dose (RD) and Respirable Drug Delivery Rate (RDDR) were calculated as follows: RD [µl] = RF [%] x AO [µl]/100 formulation and RDDR [µl/min] = RF [%] x AOR [µl/min]/100 formulation. MMAD and RF [%] was calculated using Copley CITDAS software.

Results and Discussion

Nebuliser Sytem	AO [µl]	AOR [µl/min]	MMAD [µm]	RF [%]	*RD [µl]*	*RDDR [µl/min]*	NT [min]
PARI COMPACT2	520 ± 30	150 ± 8	3.40 ± 0.20	68.7 ± 3.0	358 ± 26	105 ± 7	5.27 ± 0.37
PARI BOY Classic/Pro (blue attachment)	410 ± 40	160 ± 10	3,80 ± 0.13	62.0 ± 1.7	256 ± 26	99 ± 7	2.89 ± 0.17
PARI BOY Pro/Junior (red attachment)	350 ± 40	100 ± 10	2.80 ± 0.06	80.0 ± 1.0	281 ± 32	81 ± 8	3.43 ± 0.08
PARI BOY Junior (yellow attachment)	490 ± 20	160 ± 10	3.10 ± 0.14	73.0 ± 2.9	363 ± 20	115 ± 9	3.72 ± 0.12
Atomisor® Classic Aerodjinn+ 28NL9MU	300 ± 120	80 ± 30	4.09 ± 0.51	55.5 ± 8.0	165 ± 67	46 ± 15	3.76 ± 0.2
Aponorm Compact Plus (setting: maximum)	190 ± 150	50 ± 40	3.58 ± 0.44	67.1 ± 6.6	122 ± 100	36 ± 27	4.64 ± 0.25
Omron C28P/Omron X105 Advanced	530 ± 40	100 ± 20	4.26 ± 0.11	57.9 ± 1.2	310 ± 28	60 ± 13	7.37 ± 0.68
Omron NE C900/ COMP A-I-R Pro	310 ± 30	60 ± 10	3.38 ± 0.06	69.6 ± 1.2	215 ± 22	44 ± 7	5.60 ± 0.54
BRM-085II	250 ± 20	50 ± 10	3.24 ± 0.33	69.2 ± 4.9	173 ± 12	35 ± 8	5.11 ± 0.62
Innospire Deluxe	420 ± 20	120 ± 10	3.56 ± 0.21	64.9 ± 2.6	274 ± 17	81 ± 6	3.72 ± 0.16
Microdrop Family2	520 ± 50	60 ± 10	4.02 ± 0.16	61.3 ± 2.3	317 ± 36	39 ± 8	8.04 ± 0.85
Yuwell 403H	310 ± 50	120 ± 20	3.48 ± 0.34	66.2 ± 5.5	206 ± 33	79 ± 15	3.18 ± 0.04
Atomisor Classic Aerodjinn+ NL9MP	510 ± 130	110 ± 20	3.82 ± 0.59	59.5 ± 7.0	297 ± 68	67 ± 12	4.73 ± 0.44
Innospire Elegance	310 ± 50	70 ± 20	3.34 ± 0.06	74.1 ± 1.4	230 ± 35	48 ± 15	5.78 ± 0.42
Aponorm Compact Kids	210 ± 30	60 ± 10	3.47 ± 0.13	66.6 ± 1.7	142 ± 18	37 ± 5	4.56 ± 0.52

Table 1: Summary of results: Aerosol parameters of 15 commercial jet nebuliser systems (Data were expressed as mean values ± SD)

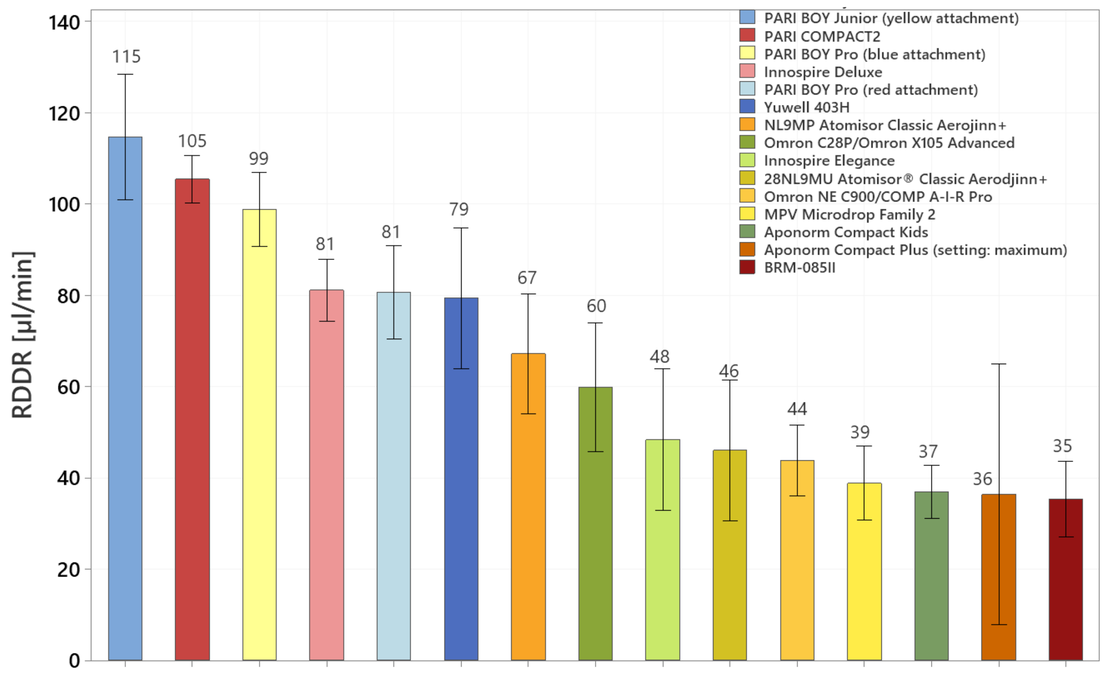


Figure 1: Respirable Drug Delivery Rate (RDDR) for all measured jet nebuliser systems (mean value ± 95% confidence interval, n = 6). RDDR varied by a factor of 3.

- The aerosol performance data measured according to the European standard DIN EN ISO 27427:2020 revealed a high degree of variability (Table 1).
- A high aerosol output (AO) does not necessarily mean a high RD. The combination of both high AO and RF indicates a device with high lung deposition.
- A short nebulisation can positively influence the patient's adherence. An efficient nebuliser system therefore ideally has a high RD and a short nebulisation time. This is expressed by the parameter RDDR.
- The calculated RDDR values differed significantly and varied by a maximum of a factor of 3 (Figure 1). The PARI BOY Junior, the PARI COMPACT2 and the PARI BOY Pro had the highest RDDRs, which were significantly different from all other nebulisers tested.

Conclusion

- RDDR is an objective quality parameter for the performance of a nebuliser.
- Physicians can choose between many nebuliser systems on the market with considerably different performances. The calculated RDDR values differed significantly and varied by a maximum of a factor of 3.
- To ensure that patients receive clinically effective doses and thus achieve the best possible therapeutic effect, it is important that clinicians choose a nebuliser system with a high RDDR.
- Taking this into account, jet nebuliser therapy offers a reliable treatment option particularly for young children and the elderly due to its ease of application.

References

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