

CHARACTERIZATION OF A COMPOUNDED VORICONAZOLE SOLUTION FOR NEBULIZATION AND DESCRIPTION OF ITS USE IN THE CLINICAL SETTING (4CPS-152)

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BACKGROUND

- **Voriconazole** is the primary treatment for invasive pulmonary aspergillosis.
- **Antifungal nebulization** involves advantages, but there are no commercial antifungal pharmaceutical presentations for nebulization.

AIMS AND OBJECTIVES

- **Characterize a compounded voriconazole solution for nebulization.**
- **Describe its use in a cohort of patients.**

MATERIALS AND METHODS

- Voriconazole solution for nebulization was prepared in the Pharmacy Department. Accord®, Kern® and Normon® vials of voriconazole powder for solution for infusion were used.
- Clinical data from patients treated with nebulized voriconazole in our hospital was retrospectively collected.
- Voriconazole concentration in plasma was determined using high-performance liquid chromatography.

RESULTS

- Vials containing 200mg were diluted with sterile water for injection (19ml).
- Syringes containing 40mg/4ml were dispensed.
- Doses (40mg for adults, 10mg for children) were administered every 12-24h.
- **No adverse events were reported** (mild pruritus in a patient with history of allergy).
- There were 11 voriconazole plasma measurements for 6 patients.
->> Voriconazole was only detected in 2 patients receiving oral voriconazole

Comercial product	pH	Osmolarity (mOsm/kg)
Accord®	4.97	359
Kern®	7	503
Normon®	5	313

Voriconazole solution physicochemical characteristics

Age (years)	Comorbidities	Fungal pathogen in bronchoalveolar lavage	Treatment site	Justification	Days of treatment	Outcome
35	CF	<i>Scedosporium prolificans</i>	Hospital ward Outpatient	Lack of response to other treatments	122	Clinical, radiological and microbiological response
21	CF	<i>Aspergillus citrinoterreus</i> <i>Aspergillus terreus</i>	Hospital ward Outpatient	Symptomatic liver toxicity to systemic azoles	420	Resolved liver toxicity. Fungal colonization remains present
35	CF	<i>Scedosporium prolificans</i> *	Hospital ward Outpatient ICU	Antifungal prophylaxis after LT	170	Successful LT
69	Interstitial pneumonia	<i>Aspergillus flavus</i>	Hospital ward Outpatient	Lack of response and toxicity to other treatments	911	<i>Aspergillus flavus</i> showed resistance to voriconazole.
60	Pulmonary fibrosis	<i>Scedosporium apiospermum</i> complex	Outpatient	Booster systemic treatment.	156	Microbiological response Oral treatment was stopped due to visual and liver toxicity
65	Chronic obstructive pulmonary disease	<i>Aspergillus fumigatus</i> <i>Aspergillus flavus</i>	Hospital ward	Avoiding drug-drug interactions	26	Patient died due to graft failure
64	Chronic obstructive pulmonary disease	<i>Purpureocillium lilacinus</i>	Hospital ward	Toxicity to systemic treatment. Avoiding drug-drug interactions	30	Patient died, <i>P. lilacinus</i> was not found in the last bronchoalveolar lavage.
18	CF	<i>Scedosporium apiospermum</i> complex	Outpatient	Toxicity to systemic treatment	840	Colonization remained
30	CF	<i>Aspergillus flavus</i> complex <i>Aspergillus terreus</i> complex	ICU	Lack of response to other treatments	28	Patient died due to invasive pulmonary aspergillosis
5	Interstitial neumopathy	<i>Aspergillus flavus</i> complex	P-ICU	Lack of response to other treatments	81	Microbiological response

Patients' basal characteristics and nebulized voriconazole treatment description (CF: cystic fibrosis, LT: lung transplantation, ICU: intensive care unit, P-ICU: pediatric intensive care unit). * Pathogen was isolated from the graft transportation medium.

CONCLUSIONS AND RELEVANCE

- The characteristics of the compounded voriconazole solution are adequate for nebulization.
- Compounded voriconazole solution is well tolerated and it is not absorbed to the systemic circulation.
- Nebulized voriconazole could be an interesting therapeutic option to treat pulmonary infections and/or colonizations.