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Original Article

Contamination of hypertonic saline solutions in use by cystic fibrosis patients in Israel☆,☆☆

Orit Peled [a,1], Vardit Kalamaro [b,d,f,1], Eitan Kerem [c], David Shoseyov [c], Hannah Blau [d,e], Ori Efrati [f], Colin Block [g,*]

[a] Department of Pharmacy, Schneider Children's Medical Center, 14 Kaplan St., PO Box 559, Petah Tikva 49202, Israel
[b] Cystic Fibrosis Foundation of Israel, 79 Krinitzy St., Ramat-Gan 52423, Israel
[c] Department of Pediatrics and Cystic Fibrosis Center, Hadassah Hebrew University Hospital, PO Box 24035, Mount Scopus, Jerusalem 91240, Israel
[d] Graub Cystic Fibrosis Center, Pulmonary Unit, Schneider Children's Medical Center, 14 Kaplan St., PO Box 559, Petah Tikva 49202, Israel
[e] Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv 69978, Israel
[f] Edmond and Lili Safra Children's Hospital, Chaim Sheba Medical Center, Tel Hashomer, Ramat Gan 52621, Israel
[g] Department of Clinical Microbiology and Infectious Diseases, Hadassah-Hebrew University Medical Center, PO Box 12000, Ein Kerem, Jerusalem 91120, Israel

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Abstract

Background: Treatment of cystic fibrosis (CF) patients with inhaled hypertonic saline (HS) solutions is safe, beneficial and reduces exacerbation rates. We studied contamination of solutions used by Israeli CF patients for prolonged periods.
Methods: The study addressed whether daily opening of previously unopened solutions caused contamination, survival of 6 CF-associated bacteria in artificially inoculated solutions, in-use contamination of solutions and patterns of their use by patients.
Results: Repeated opening did not contaminate solutions and survival of indicator bacteria was variable. *Mycobacterium abscessus* survived in 3% HS solution for 6 weeks and *Burkholderia cenocepacia* and *Pseudomonas aeruginosa* were longer. In 30/76 (39.5%) of used solutions 49 contaminants were found, none being common CF-associated pathogens.
Conclusions: Most CF-related bacteria survived to some degree in HS. Approximately 40% of solutions used by patients were contaminated by organisms of uncertain significance. Our findings highlight the potential risk posed by contamination of HS solutions and support recommendations to use sterile unit-dose formulations.

Keywords: Cystic fibrosis; Hypertonic saline; Sterility; Contamination; Unit dose

1. Introduction

Cystic fibrosis (CF) is caused by mutations in the CFTR gene that result in the absence or dysfunction of the protein that regulates ion transport across the apical membrane at the surface of certain epithelia. In the lungs, CFTR dysfunction leads to airway surface liquid (ASL) depletion and thickened and viscous mucus that adhere to airway surfaces [1]. The result is decreased mucociliary clearance (MCC) and impaired host defenses. Dehydrated, thickened secretions lead to endobronchial infection with a limited spectrum of distinctive bacteria mainly *Staphylococcus aureus* and *Pseudomonas aeruginosa*, and an

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* Corresponding author. Tel.: +972 2 6776543; fax: +972 2 6419545.
E-mail address: colinb@ekmd.huji.ac.il (C. Block).

[1] Orit Peled and Vardit Kalamaro contributed equally to this work.

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exaggerated inflammatory response with subsequent development of bronchiectasis and progressive obstructive airways disease. Pulmonary insufficiency is responsible for most CF-related deaths [2,3].

Inhaled hyperosmolar agents such as hypertonic saline induce osmotic flow of water into the mucus layer, thereby rehydrating secretions and improving mucus rheology and transportability of sputum [4,5], and increased hydration of the airway surface [6,7]. Inhalations of hypertonic saline (4 ml BID following pretreatment with bronchodilators) improved MCC and lung function and reduced exacerbation rate in patients with CF [8–11]. This improvement in mucociliary function may reduce bacterial load and chronic inflammation within the airways with a concomitant stabilization of lung function. Hypertonic saline is inexpensive, safe, and well tolerated in young children [10].

Since HS inhalation has become an acceptable treatment for CF patients, Israeli CF patients have been using it in increasing numbers as long term therapy within the home setting. However, until very recently in Israel, as in many other countries, there were no standardized sterile unit-dose HS formulations. Compounding pharmacies produce large-volume bottled solutions of HS, which patients use for prolonged periods. Furthermore, some patients prepare the HS solution at home by diluting sterile solutions containing higher concentrations of sodium chloride (14.6% and above) with water for injection or normal saline (0.9%) to achieve the desired concentration for inhalations (3–7%). These solutions are used by patients, often for weeks, under non-sterile conditions, with no consideration of the potential for contamination [12–14]. Therefore, concerns regarding the acquisition of potential pathogens by patients with CF through repeated use of pre-prepared HS solutions for inhalations were raised. Based upon prevention as a primary goal for infection control in CF, it is self-evident that any inhaled medication treating CF patients should be sterile. Therefore, the potential for contamination of different HS solutions in use at CF clinics and patients' homes was considered worthy of scrutiny.

The purpose of this study was to investigate bacterial contamination of hypertonic saline solutions under the following circumstances:

1) The effect of simple daily opening and closing of previously unopened hypertonic saline solutions at various concentrations (3%, 7%, 14.6%) under clean conditions and at defined intervals over a one month period.
2) Survival of selected CF-associated bacteria in artificially inoculated hypertonic saline solutions.
3) In-use contamination of hypertonic saline solutions in different settings (out-patient clinics, patients' homes).
4) An additional objective was to document the manner of use of these solutions in the home and clinic settings, in order to identify handling habits that might affect bacterial contamination.

2. Settings

2.1. CF outpatient clinics at three large hospitals

Patients were asked to bring HS solutions they used at home, and were almost finished, for submission to the laboratory. Some patients brought their solutions at several visits (Table 1). The questionnaire was completed once for each patient at a clinic visit. Inhalations were routinely performed at the clinics by CF nurses using the clinics' nebulizers and HS solutions. Each patient was given a decontaminated nebulizer with new solutions for these treatments. There was no standard type of nebulizer in use by all clinics and patients.

2.2. Clinical microbiology laboratory

Laboratory experiments and cultures of solutions in use were performed at the Hadassah-Hebrew University Medical Centre clinical microbiology laboratory.

3. Methods

The institutional review boards of the Hadassah-Hebrew University Medical Center at Mt. Scopus and the Schneider Children's Medical Center in Petah Tikva approved the protocol with verbal informed consent of the patients or their parents. At the Chaim Sheba Medical Center at Tel Hashomer, written informed consent was required.

Table 1
Distribution of 76 HS solutions submitted by 43 patients.

Number of HS solutions per patient	Number of patients	Number of contaminated HS solutions per patient				Total HS solutions [a]
		0	1	2	4	
1	28 [b]	13 [b]	15			28
2	7	2	4	1		14
3	5	2	3			15
4	1	1				4
7	1		1			7
8	1				1	8
Total	43	18	23	1	1	76

[a] Number of patients × number of solutions tested.
[b] 2 solutions were obtained from CF outpatient clinics.