Influence of Potassium Dichromate on Tracheal Secretions in Critically Ill Patients

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Influence of Potassium Dichromate on Tracheal Secretions in Critically Ill Patients*

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Background: **Stringy, tenacious tracheal secretions may prevent extubation in patients weaned from the respirator. This prospective, randomized, double-blind, placebo-controlled study with parallel assignment was performed to assess the influence of sublingually administered potassium dichromate C30 on the amount of tenacious, stringy tracheal secretions in critically ill patients with a history of tobacco use and COPD.**

Methods: **In this study, 50 patients breathing spontaneously with continuous positive airway pressure were receiving either potassium dichromate C30 globules (group 1) [Deutsche Homöopathie-Union, Pharmaceutical Company; Karlsruhe, Germany] or placebo (group 2). Five globules were administered twice daily at intervals of 12 h. The amount of tracheal secretions on day 2 after the start of the study as well as the time for successful extubation and length of stay in the ICU were recorded.**

Results: **The amount of tracheal secretions was reduced significantly in group 1 ($p < 0.0001$). Extubation could be performed significantly earlier in group 1 ($p < 0.0001$). Similarly, length of stay was significantly shorter in group 1 (4.20 ± 1.61 days vs 7.68 ± 3.60 days, $p < 0.0001$ [mean ± SD]).**

Conclusion: **These data suggest that potentized (diluted and vigorously shaken) potassium dichromate may help to decrease the amount of stringy tracheal secretions in COPD patients.**

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Key words: COPD; double-blind, randomized, placebo-controlled study; extubation; homeopathy; tracheal secretions

Abbreviations: APACHE = acute physiology and chronic health evaluation; BMI = body mass index; CPAP = continuous positive airway pressure; FIO_2 = fraction of inspired oxygen

Weaning from a respirator is a significant problem in patients receiving mechanical ventilation in the ICU.[1] Some factors involved in the assessment for extubation include the severity of the patient's premorbid condition and the extent to which the patient's respiratory muscles have been deconditioned by mechanical support. Most patients are easily weaned and extubated following short periods of mechanical ventilation. While most patients need only a short period of nonaugmented spontaneous breathing through the endotracheal tube before extubation, patients receiving mechanical ventilation as the result of ARDS, pneumonia, exacerbations of COPD, septicemia, pulmonary edema, or other complicated medical conditions often require prolonged periods to be successfully weaned. Besides weaning, extubation may be difficult because of multiple causes, including the presence of profuse, stringy, tenacious tracheal secretions.

COPD is the fourth leading cause of death in the United States, and it accounts for approximately 500,000 hospitalizations for exacerbations each year.[2] One of the problems of COPD and tobacco-use patients encountered in the ICU is difficulty in extubating related to profuse tracheal secretions. Weaning before extubation may be facilitated using different ventilatory modes, such as spontaneous breathing with continuous positive airway pressure

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(CPAP). A problem preventing successful extubation may be profuse tracheal secretions.[3]

Potassium dichromate is a drug that is commonly used in homeopathy for treatment of profuse, stringy, tenacious tracheal secretions. It is prepared according to homeopathic rules and is preferably administered by help of globules.

The aim of this prospective, double-blind, randomized, placebo-controlled study was to evaluate the influence of potassium dichromate on the amount of the described secretions with respect to the time of successful extubation as well as to length of stay in the ICU in these patients after start of the study.

Materials and Methods

The study was approved by the local Institutional Review Board. Patients signed informed consent before enrollment into the study. To ensure patient understanding, information was provided in the presence of their respective relatives and/or next of kins and documented. The study was planned prospectively, randomized, placebo controlled, and double blind.

Patients

Due to the severity of the acute respiratory failure, patients received controlled mechanical ventilation with a respirator (Servo 900C; Siemens Elema; Solna, Sweden) between 3 days and 7 days before study enrollment in a university hospital. The study lasted 18 months. The pulmonary status of the patients did not allow for noninvasive positive airway pressure ventilation during this period. Patients enrolled into the study could be successfully weaned from controlled or assisted mechanical ventilation and were switched to spontaneous breathing with CPAP provided by a continuous flow machine (Dräger CF 800; Dräger; Lübeck, Germany). All patients were intubated with either a conventional endotracheal tube (8-mm inner diameter; Mallinckrodt; Athlone, Ireland) or a tracheostomy tube (8-mm inner diameter; Mallinckrodt). Despite regular suctioning and therapeutic bronchoscopy, extubation for these patients was impossible due to profuse, tenacious, stringy tracheal secretions (equal to grade 3 as described below) for 36 to 48 h before enrollment into the study. Administration of mucolytic agents was avoided due to observation of increased secretions in previous patients. β-Agonist bronchodilators were stopped at the start of the study to avoid any potential influence and/or interaction. A daily screening was performed in accordance with the methods described by Ely et al.[4] Criteria used to decide extubation were that patients should be alert, with stable vital signs, and have an intact gag reflex. Physiologic guidelines were $PaO_2 > 60$ mm Hg during spontaneous breathing with CPAP (fraction of inspired oxygen [FIO_2] < 50%) and positive end-expiratory pressure from 3 to 5 cm H_2O, and respiratory rate < 20 breaths/min. Extubation failure was defined as need for reintubation within the following 72 h except for respiratory deterioration due to newly developed pneumonia. Physicians not involved into the study decided when patients would be extubated.

Inclusion Criteria

Inclusion criteria included a documented history of tobacco use and COPD for at least 10 years before acute deterioration; spontaneous breathing with CPAP with a FIO_2 varying between 0.21 and 0.3, and positive airway pressure from 5 to 7 cm H_2O after weaning from controlled mechanical ventilation. Additionally, extubation was impossible due to profuse tenacious, stringy tracheal secretions according to the criteria listed above.

Exclusion Criteria

Exclusion criteria included signs of additional lung diseases other than COPD at the time of enrollment or during the study observational period; positive blood culture results during the period of controlled mechanical ventilation; concomitant disease of the larynx and trachea obstructing the airway or inhibiting the extubation process; concomitant heart disease; need for catecholamines; pregnancy; and failure to give written informed consent.

Medication

In homeopathic concentrations, potassium dichromate acts primarily by its mucolytic properties.[5] In this study, we used a preparation of C30, which is equivalent to a potentiation of 30 dilutions, in which each of the 30 dilution steps is followed by subsequent vigorous succussions. Therefore, the above-described toxic effects were eliminated. In addition, the original orange-red color disappeared during the preparation. Onset of action may vary from patient to patient but is generally observed within 24 to 48 h.

Potassium dichromate (Deutsche Homöopathie-Union, Pharmaceutical Company; Karlsruhe, Germany) was prepared according to the German Homeopathic Pharmacopoeia[6] by repeated dilution and vigorous shaking. Saccharose globules with a spherical shape and a diameter of approximately 1 mm were impregnated with a C30 dilution of potassium dichromate (group 1). Same-sized globules for placebo in group 2 were impregnated with the same water-alcohol diluent used for the preparation of the globules in group 1, without inclusion of any drug. Placebo globules exhibited the same appearance as the homeopathic globules and were therefore indistinguishable from the globules of group 1 according to the double-blind design of the study. Neither patients nor members of the critical care team or members of the study group knew whether the globules administered to the respective patient belonged to group 1 or group 2.

Randomization Process

Patients were sequentially randomized into two groups: group 1 received the therapeutic agent, and group 2 received according to a computer-generated code. An independent physician not involved into the study held the code. A person not involved in the decision and/or application process of the study filled globules of group 1 and group 2 into separate flasks for each study patient with an increasing number.

Sublingual Administration of the Globules

Globules were administered by pouring five globules into the lid of the flask containing the globules. Then, the globules were poured from the lid directly underneath the patient's tongue. In patients intubated endotracheally, the globules were administered just aside the endotracheal tube. Globules were administered twice daily at an interval of 12 h until extubation of the patient. Fifteen minutes before and after administration of the globules, no oral fluid or oral hygiene was allowed.

Suctioning Procedures and Classification of Sputum Volume

An open suctioning system was used during this study. Suctioning was performed routinely every 6 h and in addition when

patients had profuse secretions. Flow-volume loops could not be used during spontaneous breathing with CPAP. The quantity of tracheal secretions during routine suctioning was distinguished by volume of suctioned sputum in a graduated vial interposed between suctioning catheter and the tubes leading to the suctioning pump. Tracheal secretions were classified into three grades (grade 1, 0 to 5 mL; grade 2, 6 to 10 mL; grade 3, 11 to 15 mL). Sputum did not exceed 15 mL in the investigated patients. The amount and viscosity of sputum production prior to study enrollment were not different between both groups as evaluated three times in subsequent order within 24 h. In this study, sputum was classified as grade 3 in all patients before administration of medication. Furthermore, the volume of sputum was evaluated again on day 2 after administration of the globules. The mean of three grades was used for classification.

Parameters Recorded

Prehospital historical and demographic information included age, sex, weight, height, BMI, FEV_1, stage of COPD (1, mild; 2, moderate; 3, severe), tobacco use, need of long-term oxygen therapy, and home noninvasive ventilation before admission.[7] In the hospital prior to entry into the treatment period, APACHE (acute physiology and chronic health evaluation) II, Pao_2/Fio_2, and $Paco_2$ were measured. During the treatment period, suctionings per day and therapeutic bronchoscopies in hospital after randomization, antibiotic regimen during the period of controlled mechanical ventilation, time to extubation, and length of stay in the ICU after enrollment into the study were recorded.

Statistical Analysis

Statistical analysis was done at the Department of Medical Computer Sciences, University of Vienna, using a software package (Statistical Analysis System; SAS Institute; Cary, NC). All statistical analyses were done before breaking the randomization code. Statistical analysis of the data was performed using Kruskal-Wallis test for comparing the two groups. Values are expressed as mean ± SD.

Results

Fifty-five patients were evaluated for the study. Five patients (two patients in group 1 and three patients in group 2) had to be excluded because of the development of pulmonary infiltrates described as pneumonia by independent radiologists within 2 days after enrollment into the study. Therefore, 25 patients remained in each group. Three patients in each group were breathing via a tracheostomy tube. No patients refused to participate in the study.

With respect to parameters recorded before hospitalization and historical and demographic information, three was no difference in age, sex, height, weight, BMI, FEV_1, stage of COPD, and need of long-term oxygen therapy, as well as home noninvasive ventilation (Table 1). Severity and duration of COPD and tobacco use was equal in both groups.

With respect to parameters recorded in the hospital prior to entry into the treatment period, no differences were found between both groups for APACHE II, Pao_2/Fio_2, and $Paco_2$ (Table 1). There was no difference in the number of regular suctionings and therapeutic bronchoscopies between both groups (Table 2).

With respect to parameters recorded during treatment period, there was no significant change of the amount of tracheal secretions between both groups on day 1 after start of the study; tracheal secretions were reduced significantly in group 1 ($p < 0.0001$, Table 2) on day 2. Extubation could be performed significantly earlier in group 1 ($p < 0.0001$, Table 2). Similarly, length of stay at the ICU was significantly shorter in group 1 ($p < 0.0001$, Table 2).

All patients underwent a trial of extubation. None of the patients in group 1 had to be reintubated or needed noninvasive ventilation. In group 1, the amount of secretions remained stable and did not increase. Similarly, blood gas analyses after extubation remained stable in group 1 and did not show

Table 1—*Patient Characteristics

Parameters	Group 1, Potassium Dichromate (n = 25)	Group 2, Placebo (n = 25)	p Value†
Pre-hospital information			
Age, yr	69.2 ± 9.1 (49–89)	68.4 ± 10.1 (45–88)	0.748
Male/female gender, No.	19/6	20/5	
Weight, kg	81.0 ± 9.8 (59–102)	78.8 ± 10.2 (59–101)	0.599
Height, cm	170.2 ± 6.3 (157–179)	171.2 ± 5.8 (161–183)	0.763
BMI	28.0 ± 2.8 (21.7–33.3)	26.8 ± 2.8 (21.1–32.6)	0.174
FEV_1, %	54.0 ± 5.3 (32–60)	52.4 ± 5.5 (32–59)	0.152
Stage of COPD‡	1.08 ± 0.4 (1–3)	1.20 ± 0.5 (1–3)	0.178
Need for long-term oxygen therapy, No.	5	9	
Home noninvasive ventilation, No.	1	1	
In-hospital (prior to study entry) information			
APACHE II	21.2 ± 2.2 (18–25)	21.6 ± 2.2 (18–26)	0.583
Pao_2/Fio_2	222.5 ± 18.6 (178–250)	219.4 ± 22.4 (176–250)	0.985
$Paco_2$, torr	61.6 ± 4.5 (53–69)	59.8 ± 4.1 (51–67)	0.140

*Data are presented as mean ± SD (range) unless otherwise indicated.
†Kruskal-Wallis test.
‡COPD stage: 1 = mild, 2 = moderate, 3 = severe.

Table 2—*Parameters Recorded During Treatment Period (Secretions and Suctionings per Day on Day 2)

Variables	Group 1, Potassium Dichromate (n = 25)	Group 2, Placebo (n = 25)	p Value†
Secretions	1.52 ± 0.59 1 (1–3)	2.44 ± 0.65 3 (1–3)	< 0.0001
Grade 1	13	2	
Grade 2	11	10	
Grade 3	1	13	
Suctionings per day	7.2 ± 0.7 (6–8)	6.9 ± 0.8 (6–8)	0.206
Therapeutic bronchoscopies	0.64 ± 0.57 (0–2)	0.76 ± 0.66 (0–2)	0.555
Extubation, d	2.88 ± 1.20 (1–6)	6.12 ± 3.13 (3–14)	< 0.0001
Length of stay, d	4.20 ± 1.61 (2–8)	7.68 ± 3.60 (4–17)	< 0.0001

*Data are presented as mean ± SD (range).
†Kruskal-Wallis test.

significant differences as compared to pre-extubation values. Four patients in group 2 had to be reintubated because of deterioration of blood gas analysis results due to recurrence of tracheal secretions grade 2 to 3.

Discussion

Potassium dichromate (kalium bichromicum, $K_2Cr_2O_7$) is a drug widely used in natural and homeopathic medicine. One of its features is its efficacy to treat patients with stringy, tenacious nasal and tracheal secretions. An open-label, practice-based homeopathic study[5] described the efficacy and safety of a fixed-combination homeopathic medication containing potassium dichromate in 119 male and female patients with clinical signs of acute sinusitis not previously treated. At the first visit, after a mean of 4.1 days of treatment, mucolysis had increased significantly and typical sinusitis symptoms, such as headache, pressure pain at nerve exit points, and irritating cough, were reduced. Adverse drug effects were not reported.[5]

The physical properties of potassium dichromate are its appearance as bright orange-red crystals, a melting point of 398°C, and a specific gravity of 2.67. When swallowed undiluted, it can be harmful or fatal.[8–11] As a systemic poison, it may be primarily toxic to kidneys,[8] liver,[8–9] and GI tract.[10] Furthermore, it can cause severe irritation of the eyes and conjunctivitis. Contact with breaks in the skin can cause "chrome sores" (skin ulcers). Dichromates are skin sensitizers.[12] In the construction industry of Northern Bavaria, potassium dichromate is still the most important allergen. Potassium dichromate caused roughly half of all cases of sensitization such as allergic contact dermatitis and irritant contact dermatitis found to be occupationally relevant in the construction industry.[12]

The use of *in vitro* release of interferon-γ in the diagnosis of contact allergy to potassium dichromate was studied in 20 patients who had positive patch test results to chromate and in 30 control subjects (10 patients with contact dermatitis, allergic to other allergens, 10 patients with other dermatologic diseases, and 10 healthy subjects).[13] The release of interferon-γ in the supernatants of the peripheral blood lymphocytes was significantly higher in the patients with proven allergy to chromate ($p = 0.001$).[13] In an animal toxicity study,[14] a protective effect of $SnCl_2$ on $K_2Cr_2O_7$-induced nephrotoxicity could be observed in rats.

The data suggest that potassium dichromate may be a substance allowing earlier extubation due to a reduction in stringy, tenacious tracheal secretions. While the basic parameters were comparable in both groups, the group receiving potassium dichromate showed a statistical significant improvement within a short time period.

The presence of one or more of the following findings defines acute COPD exacerbation: increase in sputum purulence, increase in sputum volume, and worsening of dyspnea.[15] Patients with COPD typically present with acute decompensation of their disease one to three times a year, and 3 to 16% of these will require hospital admission. Hospital mortality from these admissions ranges from 3 to 10% in severe COPD patients, and it is much higher for patients requiring ICU admission.[15] One of the problems encountered in the ICU is difficulty in extubating the patient because of profuse tracheal secretions. This is a special problem in patients with tenacious, stringy tracheal secretions who have tobacco use and COPD in their history. In some patients, these secretions are resistant to antimicrobial and mucolytic therapy, administration of glycopyrroniumbromide is contraindicated because it may worsen the patient's situation. There is no evidence for mucolytic agents or chest physiotherapy in the acute exacerbation setting of COPD.[2]

Weaning before extubation may be facilitated using different ventilatory modes. One of them, spontaneous breathing with CPAP, is used frequently for weaning from mechanical ventilation. Heart-lung interaction, fluid retention, and renal dysfunction can be observed with CPAP too, although the extent of these alterations is generally lower when compared to mechanical ventilation with positive end-expiratory pressure. Interestingly, protocol-guided weaning of mechanical ventilation, as performed by nurses and respiratory therapists, is safe and leads to extubation more rapidly than physician-directed weaning.[16] In contrast with adult patients, the majority of children are weaned from mechanical ventilator support in ≤ 2 days. Weaning protocols did not significantly shorten this brief duration of weaning.[17]

If a patient tolerates successive decreases in ventilator support, that patient is successfully weaned.[1] It is important to separate weaning from extubation. A patient may tolerate being on a minimum amount of ventilator support for an extended period of time from which no further decreases are considered necessary. However, a physician may refuse to extubate the patient for other reasons. Some reasons may be related to the patient, such as the inability to tolerate profuse secretions, the need for sedation for a scheduled diagnostic study, or the concern that another organ system is deteriorating.

Profuse stringy, tenacious tracheal secretions may be responsible for postponed extubation. While the weaning process was successful and the patient was able to breathe spontaneously with CPAP, extubation sometimes may be postponed because of the presence of intense tracheal secretions.

The present study suggests that potassium dichromate C30 may be able to minimize the amount of tracheal secretions and therefore to allow earlier extubation when compared to placebo. Since the potentiation (dilution and vigorously shaking) of the study drug beyond the Avogadro number imposes no interaction with the patient's metabolism, and due to the low cost of the drug, its use in the ICU may be beneficial, minimizing morbidity and mortality.[18,19] Studies give some insight into the potential way of action of homeopathically prepared drugs. Cluster-cluster aggregation phenomena in aqueous solutions of fullerene-cyclodextrin conjugates, b-cyclodextrin, sodium chloride, sodium guanosine monophosphate, and a DNA oligonucleotide revealed that there are larger aggregates existent in dilute aqueous solutions than in more concentrated solutions.[20] In another study, ultra-high dilutions of lithium chloride and sodium chloride (10^{-30} g cm^{-3}) have been irradiated by x-rays and gamma-rays at 77 K, then progressively rewarmed to room temperature.[21] During that phase, their thermoluminescence has been studied and it was found that, despite their dilution beyond the Avogadro number, the emitted light was specific of the original salts dissolved initially.

This is the first scientific study of the effect of potassium dichromate on tracheal secretions. While the mechanism of potentized (diluted and vigorously shaken) drugs still remains subject to research, several articles describe its clinical usefulness.[22–24] The effect may be best explained by cybernetics, which means that the information of the homeopathic drug acts consensually on the regulator. Thereby, the body regains its original property to regulate physical parameters.

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