AeroChamber® Valved Holding Chamber (VHC)
In Vivo Clinical Summary

The following summaries have been extracted from various journals and resources to produce a comprehensive analysis of in vivo clinical data

- Emergency Department (ED) education of parents with the AeroChamber® VHC improved children’s metered dose inhaler (MDI) adherence at home. (1)

- In adult and pediatric asthma patients use of MDI’s with the AeroChamber® VHC (with and without mask) is equivalent to SVN (with and without mask), and avoids exposing clinicians to fugitive emissions and allows time for patient technique training. (2,3)

- Use of the AeroChamber® VHC and proper technique (slow inhalation with breath hold) can significantly improve lung deposition with HFA beclomethasone. (8)

- The AeroChamber® VHC has a small chamber volume and was chosen for use in this study due to optimal in vitro characteristics and ease of use. (8)

- The AeroChamber® VHC has been extensively studied in vivo with many MDI’s
  - Flovent† (fluticasone propionate) (7,9,10,11,13,16,17,19)
  - Fluticasone was found to be clinically safe and to significantly improve asthma control using the AeroChamber® VHC with children 1-4 years of age. (16,17)
  - Alvesco† (ciclesonide) (4,20)
  - QVAR† (beclomethasone) (8)
  - Serevent† (salbutamol) (12,28)
  - HFA and CFC Albuterol (21)

- The AeroChamber® VHC ComfortSeal® mask design is recognized as superior in terms of fit, dead space, seal, and efficient aerosol delivery. (5,6,26)

- The AeroChamber® VHC improves deposition in 5-9 year olds (with mouthpiece) and 1-4 year olds (with mask) relative to older children using MDIs with no VHC. (13)

- The AeroChamber® VHC design and size is associated with correct usage and improved drug delivery and is the most prescribed VHC by health care professionals. (14,15)

- The anti-static AeroChamber® VHC improved fine particle deposition up to 70% in children. (11,13,19)

- Use of AeroChamber® VHC in ED’s have reduced costs, admissions, decreased treatment time, had fewer complications and lowered readmission rates in adults and children and when compared to SVN’s. (22,23,27,29)

- Properly used, the AeroChamber® VHC with MDI is equivalent to the AeroEclipse® nebulizer in the COPD population. (25)

- The AeroChamber® VHC is recommended for patients with poor coordination. (18,20,24)
DOES PARENTAL INVOLVEMENT IN PEDIATRIC EMERGENCY DEPARTMENT ASTHMA TREATMENT AFFECT HOME MANAGEMENT?
Hussain-Rizvi A, Kunkov S, Crain EF

Study Found

Synopsis
To determine whether parents who deliver albuterol treatments in a pediatric emergency department with a metered dose inhaler with a space (MDIS) report better adherence to MDIS use at home compared to parents whose children undergo standard nebulizer therapy. Children aged 1-5 years were randomized by day to usual treatment with nebulized albuterol (40 children) or to treatment by the parent with albuterol with an MDIS (46 children). All caregivers received standard discharge instructions, a space and an MDI. Two weeks following the visit, a trained research assistant blinded to the child’s group status, administered a brief telephone questionnaire to each caretaker. At follow-up, children in the MDIS group were 7.5 times more likely to be using the MDIS for their albuterol treatments (95%CI 1.6-35.6). Involving parents in treatment of asthma exacerbations in the emergency department using an MDIS may improve adherence to MDIS use at home.

COMPARISON OF VALVED-HOLDING CHAMBER (VHC)-FACEMASK/ MOUTHPIECE WITH SMALL VOLUME NEBULIZER-FACEMASK FOR BRONCHODILATOR DELIVERY

Study Found
Poster Presented at: European Respiratory Society Conference; 2009 Sept 12-16; Vienna, Austria.

Synopsis
Aerosolized medications now represent the standard-of-care for asthma. We report a preliminary study to test the hypothesis that treatment by anti-static VHC-face mask (Aerochamber MAX® Monaghan Medical Corp., Plattsburgh, NY, USA) is as effective as via nebulizer-face mask based on FEV, and dyspnea responses. 8 adult subjects diagnosed with asthma demonstrating a ≥200 ml FEV, response to inhaled albuterol by spirometry were randomized to 5 treatment modalities: (1) 2-actuations by metered dose inhaler (pMDI)+VHC-mouthpiece (2) 4-actuations pMDI+VHC-mouthpiece (3) 2-actuations pMDI+VHC-face mask (4) 4-actuations pMDI+VHC (5) unit dose (3ml, 2.5mg) ampoule via small volume nebulizer. Each subject was evaluated by a different treatment on 5 consecutive mornings withholding their beta-agonist prior to testing. Heart rate, oxygen saturation, perceived work of breathing (BORG), and hand tremor was assessed prior to testing, 15, 30 minutes post treatment. Using BORG as a measure of effective delivery, all methods except (5) were shown to be statistically significant (p<0.05) when comparing mean ANOVA methods at baseline, 15, 30 minutes. Mean FEV, at both 15, 30 minutes post treatment was measurably higher than baseline values across treatment methods correlating with BORG findings. No side effects were noted during the study. Although the study demonstrated substantial equivalence between treatments, additional subjects must be studied to improve statistical power. The pMDI+VHC method avoids exposing the therapist to fugitive albuterol emissions and allows the respiratory therapist time to train the patient in correct inhaler technique.

THE CONVERSION TO METERED-DOSE INHALER WITH VALVED HOLDING CHAMBER TO ADMINISTER INHALED ALBUTEROL: A PEDIATRIC HOSPITAL EXPERIENCE
DiBlasi RM, Crotwell DN, Cowan CA, Carter ER, Salyer JW

Study Found

Synopsis
INTRODUCTION: Inhaled bronchodilators are one of the most frequently prescribed medications for children hospitalized with respiratory disorders. Historically, the most common method of administration has been via the small-volume nebulizer (SVN). The methods and effectiveness by which these medications are administered to pediatric patients has been evaluated extensively over the last decade. There is a large body of literature that indicated that the metered-dose inhaler with valved holding chamber (MDI_VHC) is at least as effective as SVN for the delivery of bronchodilators to infants, children and adults. In the past it was thought that young children were unable to use MDIs because they could not coordinate inhalation and that these devices would not be effective in delivery of bronchodilators. However, with the use of VHCs with face masks, infants and small children can now be successfully treated via MDI.
COMPARISON OF THE EFFICACY AND SAFETY OF CICLESONIDE 160 MICROG ONCE DAILY VS. BUDESONIDE 400 MICROG ONCE DAILY IN CHILDREN WITH ASTHMA


Study Found

Synopsis
Ciclesonide is an onsite-activated inhaled corticosteroid (ICS) for the treatment of asthma. This study compared the efficacy, safety and effect on quality of life (QOL) of ciclesonide 160 microg (ex-actuator; nominal dose 200 microg) vs. budesonide 400 microg (nominal dose) in children with asthma. Six hundred and twenty-one children (aged 6-11 yr) with asthma were randomized to receive ciclesonide 160 microg (ex-actuator) once daily (via hydrofluoroalkane metered-dose inhaler and AeroChamber Plus* spacer) or budesonide 400 microg once daily (via Turbohaler(R)) both given in the evening for 12 wk. The primary efficacy end-point was change in forced expiratory volume in 1 s (FEV(1)). Additional measurements included change in daily peak expiratory flow (PEF), change in asthma symptom score sum, change in use of rescue medication, paediatric and caregiver asthma QOL questionnaire (PAQLQ(S) and PACQLQ, respectively) scores, change in body height assessed by stadiometry, change in 24-h urinary cortisol adjusted for creatinine and adverse events. Both ciclesonide and budesonide increased FEV(1), morning PEF and PAQLQ(S) and PACQLQ scores, and improved asthma symptom score sums and the need for rescue medication after 12 wk vs. baseline. The non-inferiority of ciclesonide vs. budesonide was demonstrated for the change in FEV(1) (95% confidence interval: -75, 10 ml, p = 0.0009, one-sided non-inferiority, perprotocol). In addition, ciclesonide and budesonide showed similar efficacy in improving asthma symptoms, morning PEF, use of rescue medication and QOL. Ciclesonide was superior to budesonide with regard to increases in body height (p = 0.003, twosided). The effect on the hypothalamic-pituitary-adrenal axis was significantly different in favor of ciclesonide treatment (p < 0.001, one-sided). Both ciclesonide and budesonide were well tolerated. Ciclesonide 160 microg once daily and budesonide 400 microg once daily were effective in children with asthma. In addition, in children treated with ciclesonide there was significantly less reduction in body height and suppression of 24-h urinary cortisol excretion compared with children treated with budesonide after 12 wk.

FACEMASKS AND AEROSOL DELIVERY IN VIVO

Erzinger S, Schueepp K, Brooks-Wildhaber J, Devadason S, Wildhaber J

Study Found

Synopsis
It has been shown in vitro that even a small air leak in the facemask can drastically reduce the efficiency of drug delivery. In addition, it has been shown that drug deposition on the face does significantly add to overall drug loss and has the potential of local side effects. The aim of this study is therefore to verify these findings in vivo. Eight asymptomatic recurrently wheezy children, aged 18-36 months, inhaled a radiolabeled salbutamol formulation either from a pressurized metered-dose inhaler through a spacer with attached facemask or from a nebulizer with attached facemask. Drug deposition of radiolabeled salbutamol was assessed with a gamma camera and expressed as a percentage of the total dose. Lung deposition expressed as a percentage of the total dose (metered dose and nebulizer fill, respectively) was 0.2% and 0.3% in children who inhaled with a non-tightly fitted facemask. Lung deposition was 0.6% and 1.4% in screaming children with a tightly fitted facemask and between 4.8% and 8.2% in patients breathing normally. Overall mask deposition was between 0.8% and 5.2%. Overall face deposition was between 2.6% and 8.4%. The results from this pilot study support the results found in in vitro studies, where a facemask leak greatly reduces drug deposition to the patient. “A facemask should have an effective seal, be flexible and soft with a large inward curved rim and have minimal dead space.”

FACEMASKS AND AEROSOL DELIVERY BY METERED DOSE INHALER – VALVED HOLDING CHAMBER IN YOUNG CHILDREN: A TIGHT SEAL MAKES THE DIFFERENCE

Janssens HM, Tiddens HAWM

Study Found

Synopsis
A facemask on a valved holding chamber (VHC) facilitates the inhalation of aerosols from metered dose inhalers (MDI) for young children. Only recently the facemask has been recognized as a vital part for efficient aerosol delivery. Several in vitro and in vivo studies show that a tight seal of the facemask is crucial for optimal aerosol deposition to the lungs. Even a small leak can reduce the dose delivered to the lungs considerably. However, a tight seal is difficult to obtain when a child is not cooperative. Depending on the design of the facemask, it is easier to obtain a good seal. Factors such as dead space, shape, and material should be considered when designing a facemask. However, when a child is upset and not cooperative during the administration, aerosol deposition will be minimal, even with the best-designed facemask.
Therefore, systemic exposure was higher with the VHC in these pediatric patients with asthma.

The primary efficacy measure was mean percent change from baseline to endpoint in 24-hour daily (composite of daytime and nighttime) asthma symptom scores. RESULTS: The FP-treated children had significantly greater (P ≤ .05) reductions in 24-hour daily asthma symptom scores (−53.9% vs −44.1%) and nighttime symptom scores over the entire treatment period compared with the placebo group. Baseline median urinary cortisol excretion values were comparable between the groups, and there was little change from baseline at endpoint. FP plasma concentrations demonstrated that systemic exposure was low. CONCLUSIONS: FP HFA 88 μg twice daily was effective and well tolerated in pre-school-age children with asthma.

SPACER INHALATION TECHNIQUE AND DEPOSITION OF EXTRAFINE AEROSOL IN ASTHMATIC CHILDREN
Roller CM, Zhang G, Troedson RG, Leach CL, Le Souëf PN and Devadason SG

Study Found

Prescribing Information - Flovent® HFA Product Monograph, USA, Jan, 2007

Excerpt from Monograph:
Pediatric: Two pharmacokinetic studies evaluated the systemic exposure to fluticasone propionate at steady state in children with asthma aged 4 to 11 years following inhalation of fluticasone propionate HFA. In an open-label, multiple-dose, 2-period crossover study, 13 children aged 4 to 11 years received 88 mcg of fluticasone propionate HFA twice daily for 7.5 days in one period and 88 mcg of fluticasone propionate CFC twice daily for 7.5 days in the other period. The geometric means (95% CI) of AUC(last) were 28 pg•hr/mL (10, 80) following fluticasone propionate HFA and 65 pg•hr/mL (27, 153) following fluticasone propionate CFC, indicating that systemic exposure was 55% lower using fluticasone propionate HFA. The geometric means (95% CI) of Cmax were 15.1 pg/mL (8.5, 27) following fluticasone propionate HFA and 20.4 pg/mL (13, 32) following fluticasone propionate CFC, indicating that Cmax was 26% lower using fluticasone propionate HFA. Tmax was similar for both treatments. AUClast and Cmax in this pediatric population were 37% and 60% lower compared with the values in adult patients receiving the same dose.

Therefore, systemic exposure was higher with the VHC in these pediatric patients with asthma.
LUNG BIOAVAILABILITY OF HYDROFLUOROALKANE FLUTICASONE IN YOUNG CHILDREN WHEN DELIVERED BY AN ANTISTATIC CHAMBER/MASK

Study Found

Synopsis
OBJECTIVE: To determine whether an antistatic valved holding chamber/mask improves lung bioavailability of hydrofluoroalkane (HFA) fluticasone in young children. STUDY DESIGN: Twelve patients, age 1 to 6 years, with well-controlled asthma were treated with an HFA fluticasone metered-dose inhaler (Flovent HFA) twice daily (440 mcg/day). The drug was delivered by tidal breathing through conventional (AeroChamber Plus) and antistatic (AeroChamber MAX) valved holding chambers (VHCs) with masks in a randomized, crossover manner, each for 3 to 7 days. When adherence was 100% at home, blood was collected for measurement of steady-state fluticasone plasma concentration (FPC) 1 hour after the last dose was administered in the clinic. FPC indicates systemic exposure directly and airway delivery indirectly. It was measured by liquid chromatography-mass spectrometry. Data was analyzed by regression analysis. RESULTS: The mean +/- SD FPC was 107 +/- 30 pg/mL after conventional VHC and 186 +/- 134 pg/mL after the antistatic VHC (P = .03). In 5 patients (40%), the antistatic VHC increased FPC by >/= 100%, to potentially excessive levels in 4 of them; it had little effect in 7 patients. CONCLUSIONS: HFA fluticasone was delivered to the airways by both devices even though the patients could not inhale deeply and breath hold. The antistatic VHC variably increased lung bioavailability. To reduce systemic exposure, the dose should be weaned to the minimum required to maintain asthma control.

SYSTEMIC EXPOSURE FOLLOWING FLUTICASONE PROPIONATE METERED DOSE INHALER USING HYDROFLUOROALKANE PROPELLANT WITH VALVED HOLDING CHAMBERS AND FACE-MASKS IN PRE-SCHOOL CHILDREN

Study Found
Poster Presented at: 2006 Annual Meeting of the American College of Clinical Pharmacy; 2006 October 29;; St. Louis, Missouri.

Valved holding chambers with masks are often used with metered-dose inhalers in children with asthma to deliver drug to the lungs. Differences in holding chamber design can influence the amount of drug delivered. Lung deposition of fluticasone propionate (FP) using hydrofluoroalkane (HFA) propellant was examined using the AeroChamber Plus® and Babyhaler valved holding chambers. Children 1 to <4 years old were randomized in an open-label, 2-way crossover design (no washout between treatments) to receive 88 μg (44 μg/actuation) twice daily (every 12 hours) for 7.5 days (15 doses) using the AeroChamber Plus® VHC and Babyhaler with face-masks (FAS10002). The first and last 4 doses were directly observed by study staff. To limit the amount of blood collected from any one patient, children were randomized to one of three groups for blood sampling: Group 1: pre-dose, and 0.5-1, 1.5-2, 2.5-3, 3.5-4 hours post-dose: Group 2: 2.5-3, 3.5-4, 4.5-5, 6.5-7, 7.5-8 hrs post-dose; Group 3: 7.5-8, 8.5-9, 9.5-10, 11.5-12, post-dose, 12.5-13 hrs (0.5-1 hrs hour post dose #16). FP systemic exposure as described by area under the curve (AUC) was determined by population pharmacokinetics. Seventeen and 18 children completed AeroChamber® and Babyhaler treatments, respectively: one child completed only the Babyhaler treatment. Population mean (95% confidence interval) for FP exposure following dosing with the AeroChamber Plus® VHC was 97pg*h/ml (85, 113) and with the Babyhaler was 52pg*h/ml (34, 64). Lung deposition of FP through the AeroChamber Plus® VHC was higher when compared to the Babyhaler. However, systemic exposure for both devices was well below the threshold observed for decreases in cortisol production. Thus, both devices provide safe delivery of FP HFA to young children.
SIMILAR LUNG AND SYSTEMIC DELIVERY CHARACTERISTICS OF SALBUTAMOL FROM AN AEROCHAMBER PLUS* VHC AND A VOLUMATIC

Mazhar SHR, Chrystyn H.

Study Found
Poster Presented at: International Conference American Thoracic Society Conference; 2006 May 23; San Diego, CA.

Synopsis
We have shown that the amount of urinary salbutamol excreted in the first 30 minutes (USAL0.5) represents the relative lung deposition and the 24 hour salbutamol plus its metabolite excretion (USAL24) indicates the total systemic delivery following an inhalation (Hindle and Chrystyn. Brit J Clin Pharmacol 1992; 34: 311-5). We have used these in-vivo methods together with invitro characterisation of the emitted dose using an Andersen Cascade Impactor (ACI) to compare the Volumatic (VOL) and AeroChamber Plus* (AERO). Spacers were attached to a salbutamol CFC free metered dose inhaler (MDI). 13 subjects, mean (SD) 31.2(7.6) years and 64.9 (10.9) Kg completed the in-vivo study. The in-vitro and in-vivo results were: (we will recreate the proper chart to show these results in final version)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>MDI</th>
<th>MDI + VOL</th>
<th>MDI + AERO</th>
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</thead>
<tbody>
<tr>
<td>ACI</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Spacer</td>
<td>74.9(6.1)</td>
<td>90.6(6.7)</td>
<td></td>
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<tr>
<td>TED</td>
<td>176.6(7.6)</td>
<td>94.9(4.6)</td>
<td>85.3(4.5)</td>
</tr>
<tr>
<td>Throat</td>
<td>93.6(7.4)</td>
<td>11.3(1.9)</td>
<td>11.7(1.2)</td>
</tr>
<tr>
<td>FDP</td>
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<td>41.8(2.3)</td>
<td>36.8(1.5)</td>
</tr>
<tr>
<td>MMAD</td>
<td>2.69(0.03)</td>
<td>2.76(0.07)</td>
<td>2.9(0.10)</td>
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<tr>
<td>Urinary salbutamol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>USAL0.5</td>
<td>5.71(1.9)</td>
<td>16.36(8.2)</td>
<td>14.4(7.6)</td>
</tr>
<tr>
<td>USAL25</td>
<td>100.2(16.7)</td>
<td>97.3(12.7)</td>
<td>84.6(25.8)</td>
</tr>
</tbody>
</table>

TED - total emitted dose; Throat - ACI throat+S0+S1; FPD - fine particle dose, ACI S2-filter; MMAD - mass median aerodynamic diameter. Statistical analysis of the USAL0.5 data revealed no difference between the two spacers [mean difference [95% confidence interval] of 1.9[-4.5,8.3]μ g]. USAL0.5 VOL and AERO were each greater (p<0.001) than MDI alone (mean difference [95%CI] of 10.6[4.2,17.1] and 8.7[2.3,15.1]μ g, respectively). USAL24 amounts were all similar. The invitro characteristics suggest that slightly more salbutamol will be delivered to the lungs from a Volumatic than an AeroChamber Plus* VHC. The in-vivo data confirms this but the difference, as predicted by the in-vitro data, is only small. The results are consistent with the smaller size of the AeroChamber Plus*.

RELATIVE AMOUNT OF FLUTICASONE DELIVERED BY HFA-MDI TO CHILDREN OF DIFFERENT AGES

Khan YR.

Study Found

Synopsis
RATIONALE: We hypothesized that less fluticasone propionate (FP) is delivered by MDI to the airways of children <5 yr who passively inhale through a mask/valved holding chamber (VHC) than to older children who inhale deeply and breath hold. The 1-hr steady-state FP plasma concentration was used as an indirect measure of the relative amount deposited in the lungs and a direct measure of systemic exposure. METHODS: Sixty children with well controlled persistent asthma received FP 2x110 μg BID for ≥ 3 days, delivered by HFA-MDI through a device they used effectively. This higher dose is routine in our clinic. 100% adherence, documented by electronic monitor, was required. Five groups of 12 each were studied; 1) 12-18 yr by actuator alone; 2) 5-9 yr by actuator alone; 3) 5-9 yr by antistatic VHC/mouthpiece (AeroChamber MAX*); 4) 5-9 yr by antistatic VHC/mask; and 5) 1-4 yr by antistatic VHC/mask. FP was measured by an LC-MS/MS assay with a 13% CV for precision at 5 pg/ml. RESULTS: The mean±SD concentrations in pg/mL were: 12-18 yr actuator, 76±61; 5-9 yr actuator, 87±80; 5-9 yr VHC/mouthpiece, 207±149; 5-9 yr VHC/mask, 140±61; and 1-4 yr VHC/mask, 165±58. The mean concentration in the 12-18 yr actuator group was significantly lower than VHC groups (p=0.003), but not different from the 5-9 yr actuator alone group. CONCLUSIONS: There was a device but not an age-related difference in deposition. The antistatic VHC improved deposition of HFA-FP and compensated for passive inhalation in children 1-4 yr.

DO PEDIATRIC HEALTHCARE PROVIDERS KNOW HOW TO USE METERED DOSE INHALER PLUS SPACER DEVICES?

Iheagwara K, Sharif I, Ozuah PO.

Study Found

Synopsis
We tested whether health practitioners correctly used MDI-spacer devices. Of 122 subjects, 89% had instructed a patient on using a spacer. Whilst performance with the Aerochamber was the best, only 3% correctly demonstrated all the steps for that device.

“Results: 122 subjects participated in the study, (30 generalist attendings, 42 nurses and 50 residents). 100% of the physicians had prescribed an MDI-spacer; of these, 23% write a prescription for “spacer” without specifying a particular brand of spacer. Of those who do specify a brand, 94% prescribe the AeroChamber, 3% prescribe the Optihaler, 2% prescribe “other brands” and none prescribe the Optichamber.”
THE EFFECT OF INHALATION TECHNIQUE, SPACER VOLUME AND TRAINING ON AEROSOL DELIVERY FROM SPACERS IN CHILDREN
Devadason SG, Walker SL, Owen J.

Study Found

Synopsis
RATIONALE: Variability in the clinical use of inhaler devices is high, particularly in children. Optimisation of inhalation therapy should ensure more consistent dose delivery to the airways of young children. We assessed the effect of spacer volume, inhalation technique and training of the parent/child on drug delivery to children using pressurised inhalers. METHODS: Albuterol was delivered via large (Volumatic; VOL) and small (AeroChamber Plus*; AC+) spacers to 21 children (2-14yrs). Children ≥ 5yrs either took 5 tidal breaths, or one slow maximal inhalation with 10 sec breath-hold. Children <5yrs used tidal breathing only. Training sessions were scheduled ≥ 12wks apart. Drug delivery was assessed using a low resistance filter attached to the spacer mouthpiece. RESULTS: Mean (SD) drug delivery (% nominal dose) to children of all ages using AC+ [51.5 (14.7)%] was significantly higher (p=0.04) than using VOL [39.3 (10.1)%]. Mean (SD) drug delivery using the single maximal inhalation technique [45.4 (13.7)%] was significantly higher (p=0.01) than that using tidal breathing [32.3 (13.9)]. The improvement in delivery using the single maximal inhalation was most marked in the 5-7yr age group. Training the parent/child to use the spacer correctly gave a small (3.9%) but significant increase (p=0.04) in drug delivery. CONCLUSIONS: AC+ (small volume) delivered more drug than VOL (large volume). This is possibly due to the more efficient construction and design of the AeroChamber Plus* as delivery is normally improved when using large volume spacers. The single maximal inhalation technique increased drug delivery to patients compared to tidal breathing. However, it is easier for children <5yrs to use the tidal breathing technique. Training of the parent/child resulted in a smaller than expected (albeit significant) increase in drug delivery.

SAFETY PROFILE OF FLUTICASONE PROPIONATE HFA IN PRE-SCHOOL AGE CHILDREN WITH ASTHMA
Qaundah PY, Maspero J, Cerutli E, Scott CA, Clements DS, Wu W, Crim C.

Study Found

Synopsis
RATIONALE: To evaluate the safety of fluticasone propionate HFA 88mcg BID (FP) vs placebo HFA (PLA) via MDI with the AeroChamber Plus* spacer with attached facemask for 12 weeks in pre-school age children with asthma. METHODS: One to <4 year-olds with symptomatic asthma, receiving maintenance asthma medications (excluding systemic [SCS] or inhaled corticosteroids [ICS]) plus a short-acting beta-agonist (SABA) or SABA alone, were enrolled in this randomized (120 PLA: 239 FP), double-blind, parallel-group, placebo-controlled trial. Children receiving SCS within 10 weeks prior to randomization and/or ICS within 2 (low dose) or 8 (moderate-high dose) weeks prior to Screening were excluded. Safety assessments included: adverse events (AEs), clinical labs, oropharyngeal/nasal exams, asthma exacerbations, and 12-hour, overnight urinary cortisol excretion (U-Cortisol). RESULTS: No deaths or treatment-related serious AEAs were reported. The percentages and types of AEs were comparable between groups. Events most commonly reported were fever (PLA=24%, FP=28%), nasopharyngitis (PLA=14%, FP=16%) and URI (PLA=11%, FP=13%), events common in this age-group. Baseline lab results were comparable between groups. Few (PLA=0, FP=2) patients had a negative to positive shift in the oropharyngeal/nasal exam. More PLAtreated patients experienced an asthma exacerbation (11%) compared with FP-treated patients (4%). Baseline median U-Cortisol values were similar between groups (PLA=2.3mcg; FP=2.8mcg); and, there was little change from baseline after 12 weeks (PLA = -0.1mcg; FP = -0.4mcg). CONCLUSION: 12-week treatment with FP HFA 88mcg BID was well tolerated in 1 to <4 year-olds with asthma. The safety profile was similar to PLA and there was no evidence of adrenal suppression.

FLUTICASONE PROPIONATE HFA IMPROVES ASTHMA CONTROL IN PRESCHOOL AGE CHILDREN WITH ASTHMA

Study Found

Synopsis
RATIONALE: To evaluate the efficacy of fluticasone propionate HFA 88mcg BID (FP) vs placebo HFA (PLA) via MDI with the AeroChamber Plus* spacer with attached facemask for 12 weeks in pre-school age children with asthma. METHODS: One to <4 year-olds with ≥ 2 episodes of increased asthma symptoms requiring medical attention and pharmacotherapy ≤ 12 months prior to screening and a baseline 24-hr daily asthma symptom score (DASS; scale 0 = none to 3 = severe) of ≥ 1.1 were enrolled in this randomized (120 PLA: 239 FP), double-blind, parallel-group, placebo-controlled trial. Efficacy measures included: mean percent change from baseline to endpoint (last 28 days of treatment) in DASS (primary), mean change from baseline in nighttime asthma symptom scores over the entire treatment period (NASS), change from baseline to endpoint in daily rescue albuterol use (DRAB), and time to treatment failure (TF; i.e., time to first asthma exacerbation). RESULTS: Baseline mean DASS and NASS were comparable between groups (DASS=1.7 PLA, 1.8 FP; NASS = 1.2 PLA, 1.4 FP). At endpoint, FP-treated patients experienced a greater reduction (improvement) from baseline in DASS (54% FP, 44% PLA; p=0.036) and NASS (-0.56 FP, -0.44 PLA; p=0.049). Baseline DRAB use was comparable across groups (4 inhalations/day [IPD] PLA; 5 IPD FP). DRAB decreased by 2 and 3 IPD for the PLA and FP groups, respectively, at endpoint. More PLA patients (12%) discontinued due to TF compared with FP-treated patients (5%) (p=0.034). CONCLUSION: Treatment with FP HFA 88 mcg BID for 12 weeks significantly improves asthma control in 1 to <4 year-olds with asthma.
INHALATION TECHNIQUE AND VARIABLES ASSOCIATED WITH MISUSE OF CONVENTIONAL METERED-DOSE INHALERS AND NEWER DRY POWDER INHALERS IN EXPERIENCED ADULTS
Melani AS, Zanchetta D, Barbato N, Sestini P, Cinti C, Canessa PA, Aiolfi S, Neri M.

Study Found

Synopsis
Background: Pressurized metered-dose inhalers (pMDIs) are often poorly used, but little information is available concerning use of the newer dry powder inhalers (DPIs). Objective: To estimate the inhalation technique and variables associated with the misuse of pMDIs and newer DPIs in clinical practice. Methods: A multicenter, observational survey was used to evaluate the inhalation technique in 1,404 experienced outpatients aged 15 to 88 years affected mostly by asthma (47%) and chronic obstructive pulmonary disease (39%). A total of 1,056 patients were using pMDIs, 190 in conjunction with a large volume spacer (LVS); regarding DPIs, 230 patients were using the Aerolizer Inhaler, 524 were using the Turbuhaler, and 475 were using the Diskus. In each center, a trained observer recorded patients' inhalation techniques for each inhaler used against a standardized step-by-step checklist. Results: Twenty-four percent and 3% of patients used pMDIs poorly, alone or with an add-on LVS, respectively. Failure to correctly perform essential steps for reliable lung delivery with the Aerolizer Inhaler, Turbuhaler, and Diskus was found in 17%, 23%, and 24% of patients, respectively. There was no difference in most variables correlated with poor inhalation between patients using pMDIs and those using DPIs. Conclusions: The use of DPIs is associated with a similar percentage of inadequate inhalation technique as the use of pMDIs in clinical practice. The addition of an LVS to a pMDI and education form health care personnel, rather than simply changing inhalers, represent the best strategies for minimizing poor inhalation technique.

IMPACT OF A NEW ANTI-STATIC VALVED HOLDING CHAMBER ON AIRWAY DELIVERY OF INHALED FLUTICASONE PROPIONATE IN ASTHMATIC CHILDREN

Study Found
Poster Presented at: International Conference of the American Thoracic Society; 2004 May 22; Orlando, FL.

Synopsis
The only effective way to administer fluticasone propionate (FP) to young asthmatic children in the United States is via metered-dose inhaler (MDI) attached to a valved holding chamber (VHC) with mask. Using this method, several factors potentially influence the amount of FP delivered to the patient's airways, including electrostatic charge on the VHC. Since FP peak plasma concentrations are directly proportional to inhaled dose, we used the 1-hour post-dose FP plasma concentration to estimate relative airway delivery in young children from a MDI attached to a conventional VHC with mask, and a new VHC with mask made from electrostatic charge resistant plastic. FP plasma concentrations were determined in 12 children (1.3-6.8 yr) with adequately controlled persistent asthma 1-hour after inhaling 2x110 μg/puffs of FP MDI with HFA-134a propellant BID for at least 3 days through a conventional VHC with mask (AeroChamber Plus*, Monaghan) and the new anti-static VHC with mask (AeroChamber MAX*, Trudell) in a randomized crossover fashion. An electronic monitor confirmed perfect adherence. Subjects and parents were trained to adequately use each device. FP plasma concentrations were quantified by a novel LC-MS/MS assay. A paired student t test was used to compare observed differences in the mean 1-hour FP plasma concentration after each device. Mean ±SD 1-hour FP plasma concentration was 185.6±134.2 pg/ml from the new anti-static VHC with mask, and 106.9±29.5 pg/ml from the conventional VHC with mask (p=0.035). The new anti-static VHC with mask improved delivery of FP to the airways by 70% in young children. FP concentrations after the anti-static VHC were in the same range as those measured in a previous study of older children (6-9 yr) using InspirEase with more efficient inhalation technique.
EQUIVALENT PHARMACOKINETICS OF THE ACTIVE METABOLITE OF CICLESONIDE WITH AND WITHOUT USE OF THE AEROCHAMBER PLUS* SPACER FOR INHALATION
Drollmann A, Nave R, Steinijans VW, Baumgärtner E and Bethke TD.

Study Found
J Allergy and Clin Imm. 2004 Feb;113(2):S120.

Synopsis
Background: Ciclesonide is an inhaled corticosteroid that provides safe and effective control of patient asthma. Ciclesonide is administered as an aerosol solution in a metered-dose inhaler, using hydrofluoroalkane-134a as a propellant. It is activated in the lung to form its only active metabolite, desisobutyryl-ciclesonide (des-CIC). A spacer may be used in combination with the hydrofluoroalkane metered-dose inhaler (HFA-MDI) to maintain inhaled corticosteroid delivery to the lung in patients with poor inhalation technique. Objective: To determine if the pharmacokinetics of des-CIC and ciclesonide are altered when a spacer is used for ciclesonide inhalation. Methods: A randomized, open-label, 2-period crossover, single-center pharmacokinetic study was conducted in 30 patients with asthma (forced expiratory volume in 1 second ≥ 70% predicted). A single dose of ciclesonide (320 μg ex-actuator; equivalent to 400 μg ex-valve) was administered via the HFA-MDI with and without an AeroChamber Plus* spacer (Trudell Medical International, London, ON, Canada). Serum concentrations of ciclesonide and des-CIC were measured before inhalation and at various intervals until 14 hours after treatment using high-performance liquid chromatography with tandem mass spectrometric detection. Results: The pharmacokinetic properties of the active metabolite, des-CIC, were equivalent after inhalation of ciclesonide with and without the AeroChamber Plus* spacer. Point estimates and 90% confidence intervals (CIs) for the ratio of des-CIC pharmacokinetic properties in the presence or absence of a spacer were within the conventional bioequivalence range of 0.80-1.25 (area under the serum concentration time curve from time zero to infinity 0.96 [0.85, 1.07]; peak serum concentration 1.05 [0.94, 1.18]; elimination half-life 1.04 [0.92, 1.18]). Furthermore, there was no relevant difference in the point estimate and 90% CI of the difference of the time to reach peak serum concentration of des-CIC with or without a spacer. Conclusion: The AeroChamber Plus* spacer did not influence the pharmacokinetics of the pharmacologically active des-CIC. Thus, systemic exposure to the active metabolite is similar when ciclesonide is inhaled with or without a spacer.

A COMPARISON OF THE BRONCHOPROTECTIVE EFFECT OF CFC AND HFA ALBUTEROL METERED-DOSE INHALERS (NDIS) USED IN COMBINATION WITH THE AEROCHAMBER PLUS*
Ahrens RC., Teresi ME., Lux CR., Tan Y.

Study Found
Poster Presented at: International Conference of the American Thoracic Society ; 2003 May 17; Seattle, WA.

Synopsis
Previous studies have documented equivalent clinical efficacy of directly inhaled CFC and HFA albuterol MDIs but not whether use of a holding chamber alters this relationship. We compared albuterol delivery to the lungs by an HFA MDI with that of a CFC MDI when used in combination with an AeroChamber Plus* valved-holding chamber (VHC) using a methacholine challenge based bioassay. Seventeen subjects completed this double-blind, randomized, balanced cross-over study. Treatments were 1 or 2 actuations of albuterol CFC MDI (90mcg/puff) or HFA MDI (100 mcg/puff). One of 4 treatments was administered during each study period with the AeroChamber Plus* VHC. A methacholine challenge (modified Juniper method) was initiated 15 minutes after albuterol administration. Results: (geometric mean PC20FEV1)

<table>
<thead>
<tr>
<th></th>
<th>1 Puff CFC</th>
<th>2 Puffs CFC</th>
<th>1 Puff HFA</th>
<th>2 Puffs HFA</th>
</tr>
</thead>
<tbody>
<tr>
<td>16.96</td>
<td>18.81</td>
<td>15.06</td>
<td>20.79</td>
<td></td>
</tr>
</tbody>
</table>

The dose-response relationship was significant (p=0.034) and parallelism and preparation contrasts were not significant (p=0.93, 0.27, respectively). The relative potency estimated using Finney 2-by-2 bioassay statistics was 0.97 (90% confidence interval [CI] 0.41-2.14). The 90% bias-corrected and accelerated percentile bootstrap CI for this estimate was 0.58-1.75. Removing an outlier from the data, the estimated relative potency was 1.04 (90% CI 0.65-1.73). Conclusion: HFA-and CFCMDIs deliver equivalent quantities of albuterol to the lung when used with the AeroChamber Plus* VHC.
NEBULIZERS VS METERED-DOSE INHALERS WITH SPACERS FOR BRONCHODILATOR THERAPY TO TREAT WHEEZING IN CHILDREN AGED 2 TO 24 MONTHS IN A PEDIATRIC EMERGENCY DEPARTMENT
Delgado A, Chou KJ, Johnson Silver E, Crain EF.

Study Found

Synopsis
OBJECTIVE: To determine if administration of albuterol by a metered-dose inhaler with a spacer device (AeroChamber*) is as efficacious as administration of albuterol by nebulizer to treat wheezing in children aged 2 years and younger. DESIGN: Double-blind, randomized, placebo-controlled clinical trial. SETTING: Pediatric emergency department. PATIENTS: From a convenience sample of wheezing children aged 2 to 24 months, 85 patients were enrolled in the nebulizer group and 83 in the spacer group. INTERVENTIONS: The nebulizer group received a placebo metered-dose inhaler with a spacer followed by nebulized albuterol. The spacer group received albuterol by a metered dose inhaler with a spacer followed by nebulized isotonic sodium chloride solution. Treatments were given every 20 minutes by a single investigator blinded to group assignment. MAIN OUTCOME MEASURES: The primary outcome was admission rate. Pulmonary Index score and oxygen saturation were measured initially and 10 minutes after each treatment. RESULTS: The nebulizer group had a significantly higher mean (SD) initial Pulmonary Index score compared with the spacer group (7.6 [2.5] vs 6.6 [2.0]; P =.002). With the initial Pulmonary Index score controlled, children in the spacer group were admitted less (5% vs 20%; P =.05). Analyses also revealed an interaction between group and initial Pulmonary Index score; lower admission rates in the spacer group were found primarily in children having a more severe asthma exacerbation. CONCLUSION: Our data suggest that metered-dose inhalers with spacers may be as efficacious as nebulizers for the emergency department treatment of wheezing in children aged 2 years or younger.

A COMPARISON OF ALBUTEROL ADMINISTERED BY METERED-DOSE INHALER AND SPACER WITH ALBUTEROL BY NEBULIZER IN ADULTS PRESENTING TO AN URBAN EMERGENCY DEPARTMENT WITH ACUTE ASTHMA
Newman KB, Milne S, Hamilton C, Hall K.

Study Found
Chest. 2002 April;121:1036-1041.

Synopsis
STUDY OBJECTIVES: To determine the efficacy of albuterol by metered-dose inhaler (MDI) and spacer (AeroChamber*) compared to a nebulizer. DESIGN: A prospective, open-label study. SETTING: Large urban emergency department (ED). PATIENTS: All consecutive adult asthma patients over a 2.5-year period. INTERVENTIONS: ED personnel used a standardized treatment algorithm, which included albuterol administered by nebulization, for patients presenting to the ED during the first 12 months of the study. The treatment algorithm then was switched to one that utilized albuterol administered by MDI/spacer as the primary mode of delivery for the following 18 months. As part of the conversion to MDI/spacer, ED staff counseled patients on self management and supplied patients with a peak flowmeter, an MDI/spacer, and an inhaled steroid for home use. MEASUREMENTS: Pulmonary function, clinical outcome, laboratory data, and financial data were assembled and analyzed from 2,342 ED visits and 1,420 patients. RESULTS: While there was no significant difference in hospital admission rates between patients in the MDI/spacer group and the nebulizer group (13.2% and 14.6%, respectively), there was a statistically greater improvement in peak flow rates in the MDI/spacer group (126.8 vs 111.9 L/min, respectively; p = 0.002). The MDI/spacer group also spent significantly less time in the ED (163.6 and 175 min, respectively; p = 0.007), had a lower total albuterol dose (1,125 microg and 6,700 microg, respectively; p < 0.001), and showed a greater improvement in arterial oxygen saturation (p = 0.043). Relapse rates at 14 and 21 days were significantly lower (p < 0.01 and p < 0.05, respectively) among patients treated with the MDI/spacer and were associated with asthma education and the provision of a peak flowmeter, a spacer, and an inhaled corticosteroid for patients’ home use. CONCLUSIONS: Albuterol administered by MDI/spacer is an efficacious and cost-effective alternative to nebulization in adults with acute asthma who present at a large urban ED.
MISUSE OF CORTICOSTEROID METERED-DOSE INHALER IS ASSOCIATED WITH DECREASED ASTHMA STABILITY
Giraud V, Roche N.

Study Found

Synopsis
ABSTRACT: This study assessed whether the improper use of pressurized metered dose inhalers (pMDIs) is associated with decreased asthma control in asthmatics treated by inhaled corticosteroids (ICS). General practitioners (GPs) included consecutive asthmatic outpatients treated by pMDI-administered ICS and on-demand, short-acting β2-agonists. They measured an asthma instability score (AIS) based on daytime and nocturnal symptoms, exercise induced dyspnea, β2-agonist usage, emergency-care visits and global perception of asthma control within the preceding month; the inhalation technique of the patient also was assessed. GPs (n=915) included 4,078 adult asthmatics; 3,955 questionnaires were evaluable. pMDI was misused by 71% of patients, of which 47% was due to poor coordination. Asthma was less stable in pMDI misusers than in good users (AIS: 3.93 versus 2.86, p<0.001). Among misusers, asthma was less stable in poor coordinators (AIS: 4.38 versus 3.56 in good coordinators, p<0.001). To conclude, misuse of pressurized metered-dose inhalers, which is mainly due to poor coordination, is frequent and associated with poorer asthma control in inhaled corticosteroid-treated asthmatics. This study highlights the importance of evaluating inhalation technique and providing appropriate education in all patients, especially before increasing inhaled corticosteroid dosage or adding other agents. The use of devices which alleviate coordination problems should be reinforced in pressurized metered-dose inhaler misusers.

THE DELIVERY TIME, EFFICACY AND SAFETY OF BETA AGONIST BRONCHODILATOR ADMINISTRATION WITH THE AEROECLIPSE® BREATH ACTUATED NEBULIZER (BAN)
Pikarsky RS, Farrell T, Acevedo R, Fascia W, Roman C.

Study Found
Poster Presented at: The American College of Chest Physicians (ACCP); 2001 November 4-8; Philadelphia, PA.

Synopsis
PURPOSE: Aerosol delivery consumes the highest level of Respiratory Care resources. This study evaluated the delivery time, efficacy, and safety of rapidly nebulized Albuterol with the use of the AeroEclipse® Breath Actuated Nebulizer as compared to both an MDI with AeroChamber® VHC (both from Monaghan Medical Corp., Plattsburgh, N.Y.) and the Airlife Misty-Neb Nebulizer (SVN) (Allegiance Healthcare Corporation). Methods: A consecutive, non-randomized, mostly COPD population receiving pre & post bronchodilator testing in our Pulmonary Function Lab were studied. Three different Albuterol medication dosages were administered with the BAN: 0.5 ml Albuterol (2.5 mg) with 0.5 ml Normal Saline, 1.0 ml (5mg) of undiluted Albuterol, and 0.75 ml Albuterol (3.75 mg) using an oxygen flow rate of 8 L/min. Two puffs of Albuterol were administered by MDI with AeroChamber® VHC. Treatments with the SVN consisted of nebulizing 2.5 mg of Albuterol diluted with 3 ml of Normal Saline Unit Dose (UD) using an oxygen flow rate of 8 L/min. The Sensormedics Vmax 22 Pulmonary Function System was utilized to measure FEV1. A standardized subjective questionnaire to determine side effects was completed. Results: The table shows the Albuterol dosages, mean % change of FEV1 from pre-treatment and 10 minute post treatment, mean administration time and tremulousness. The mean treatment time with all BAN patients was 2.78 minutes as compared to 8.33 minutes with SVN (p<0.001)*. The mean treatment time with the MDI was 2.86 minutes as compared to 8.33 minutes with the SVN (p<0.001)**. The changes in FEV1 were not significant. There was no difference in heart rate, respiratory rate or nausea. Seventeen patients receiving the 1.01 undiluted Albuterol indicated an increase in tremulousness.

<table>
<thead>
<tr>
<th>Nebulizer (n)</th>
<th>Dose</th>
<th>% Change FEV1</th>
<th>Time (min)</th>
<th>Tremulousness</th>
</tr>
</thead>
<tbody>
<tr>
<td>AeroEclipse™BAN (12)</td>
<td>0.5ml +0.5ml NS</td>
<td>8.20%</td>
<td>2.67*</td>
<td>0</td>
</tr>
<tr>
<td>AeroEclipse™BAN (64)</td>
<td>1.0 ml undil.</td>
<td>10.90%</td>
<td>3.29*</td>
<td>17</td>
</tr>
<tr>
<td>AeroEclipse™BAN (23)</td>
<td>0.75ml undil.</td>
<td>5.60%</td>
<td>1.30*</td>
<td>5</td>
</tr>
<tr>
<td>MDI (21)</td>
<td>2 puffs</td>
<td>8.50%</td>
<td>2.86**</td>
<td>1</td>
</tr>
<tr>
<td>Misty-Neb (52)</td>
<td>2.5mg UD</td>
<td>9.10%</td>
<td>8.33</td>
<td>2</td>
</tr>
</tbody>
</table>

Conclusion: The rapid administration of Albuterol in the 0.5 ml + 0.5 ml NS and 1.0 ml undiluted doses using the BAN was equally efficacious as the MDI with AeroChamber® VHC and SVN UD. The 1.0 ml Albuterol dosage has the highest incidence of tremulousness. The 0.75 ml Albuterol dosage under-performed. Delivering 0.5 ml Albuterol (2.5 mg) with 0.5 ml Normal Saline using the BAN offered the best delivery time, efficacy and safety profile of the nebulizer trials. The BAN performance was comparable to the MDI with AeroChamber® VHC. Clinical Implications: In a health care facility that delivers large volumes of aerosol treatments, the decrease in delivery time could have a significant impact on resource utilization. The results supported changes in the Respiratory Care practice throughout Crouse Hospital. Further studies evaluating additional medication dosing regimens measuring safety, efficacy and resource utilization are needed.
AEROSOL THERAPY WITH VALVED HOLDING CHAMBERS IN YOUNG CHILDREN: IMPORTANCE OF THE FACEMASK SEAL

Amirav I, Newhouse MT.

Study Found

Synopsis
OBJECTIVE: Masks are an essential interface between valved holding chambers (VHCs), or spacers, and a small child’s face for providing aerosol therapy. Clinical experience suggests that many young children do not cooperate with the VHC treatment or tolerate a mask of any kind. This might impair the mask-face seal and reduce the dose delivered to the child. The objective of this study was to evaluate the ability of parents to provide a good mask-face seal in infants and toddlers using 3 masks provided with commonly used pediatric VHCs and compare this with the seal obtained with the Hans Rudolph pediatric anesthesia mask. METHODS: A preliminary in vitro filter study was conducted to validate the assumption that reduced 9 ventilation as a result of increased facemask leak reduces the drug aerosol dose delivered to the mouth. Facemask leak then was studied in vivo for NebuChamber, AeroChamber, BabyHaler, and Hans Rudolph masks by measuring ventilation with an in-line pneumotachograph while the facemask was held in place by experienced parents who were asked to demonstrate how they deliver medication to their children without any additional instruction. Thirty children (mean age: 3.2 +/- 1.4 years) performed 4 repeat studies with each mask. The first 10 patients performed the tests once again within 1 month. On the second occasion, the parents were coached continuously and encouraged to hold the mask tightly against the child’s face. RESULTS: The AeroChamber and Hans Rudolph masks provided the best seal as reflected in the magnitude of the ventilation measured through them. The NebuChamber provided the poorest seal, with 45% less ventilation than the AeroChamber and Hans Rudolph masks. There was considerable intraindividual variability for all masks (24% to 48%); however, the variability with the NebuChamber mask was 2-fold greater than the other masks. All ventilatory volumes during the coached session were significantly greater than during the uncoached session. CONCLUSIONS: VHCs with masks designed for use with small children may provide a poor seal with the face, leading to reduced or more variable dose delivery. The facemask seal is critical for efficient aerosol delivery to infants and young children, and this should be stressed to parents.

COSTS AND EFFECTIVENESS OF SPACER VERSUS NEBULIZER IN YOUNG CHILDREN WITH MODERATE AND SEVERE ACUTE ASTHMA

Leversha AM, Campanella SG, Aickin RP, Asher MI.

Study Found

Synopsis
OBJECTIVE: To compare the costs and effectiveness of albuterol by metered dose inhaler (MDI) and spacer versus nebulizer in young children with moderate and severe acute asthma. DESIGN: Randomized, double-blind, placebocontrolled trial in an emergency department at a children’s hospital. The participants were children 1 to 4 years of age with moderate to severe acute asthma. Patients assigned to the spacer group received albuterol (600 microg) by MDI by spacer (AeroChamber*) followed by placebo by nebulizer (n = 30). The nebulizer group received placebo MDI by spacer followed by 2.5 mg albuterol by nebulizer (n = 30). Treatments were repeated at 20-minute intervals until the patient was judged to need no further doses of bronchodilator, or a total of 6 treatments. RESULTS: Clinical score, heart rate, respiratory rate, auscultatory findings, and oxygen saturation were recorded at baseline, after each treatment, and 60 minutes after the last treatment. Baseline characteristics and asthma severity were similar for the treatment groups. The spacer was as effective as the nebulizer for clinical score, respiratory rate, and oxygen saturation but produced a greater reduction in wheezing (p =0.03). Heart rate increased to a greater degree in the nebulizer group (11.0/min vs 0.17/min for spacer, p <0.01). Fewer children in the spacer group required admission (33% vs 60% in the nebulizer group, p =0.04, adjusted for sex). No differences were seen in rates of tremor or hyperactivity. The mean cost of each emergency department presentation was NZ$825 for the spacer group and NZ$1282 for the nebulizer group (p =0.03); 86% of children and 85% of parents preferred the spacer. CONCLUSION: The MDI and spacer combination was a cost-effective alternative to a nebulizer in the delivery of albuterol to young children with moderate and severe acute asthma.
**EFFECTS OF SALBUTAMOL DELIVERY FROM A METERED DOSE INHALER VERSUS JET NEBULIZER ON DYNAMIC LUNG MECHANICS IN VERY PRETERM INFANTS WITH CHRONIC LUNG DISEASE**

Gappa M, Gartner M, Poets CF, von der Hardt H.

**Study Found**

**Synopsis**
Treatment of chronic lung disease of prematurity requires effective aerosol delivery of different therapeutic agents. Aerosols can be generated by a metered dose inhaler (MDI) or a jet nebulizer. An MDI combined with a spacer device is easier to use and avoids undesirable effects noted in conjunction with jet nebulization. We compared the clinical effectiveness of 200 micrograms (2 puffs) salbutamol delivered from an MDI in conjunction with a valved spacer device (AeroChamber*), and 600 micrograms given via jet nebulizer (PariBaby) on 2 consecutive days, the order being randomized. Thirteen spontaneously breathing very pre-term infants [mean (SD) gestational age 27.2 (1.8) weeks; birth weight 0.90 (0.34) kg] were studied at a corrected age of 37 (2.3) weeks. Mean (SD) study weight was 1.83 (0.38) kg. Dynamic lung compliance and resistance were determined from measurements of flows, volumes, and transpulmonary pressures, using a pneumotachometer and a small esophageal microtransducer catheter before and 20 min after salbutamol application. Baseline values before salbutamol administration were similar on both occasions: the mean (SD) compliance was 7.7 (3.0) mL.kPa-1.kg-1 pre-MDI plus-spacer and 8.4 (3.1) pre-jet nebulizer; the resistance was 10.4 (4.0) kPa.L-1.s pre-MDI plus-spacer and 9.7 (3.4) pre-jet nebulizer. Following salbutamol, compliance did not change significantly with either MDI plus spacer or jet nebulizer. Resistance fall significantly with MDI plus spacer (mean -2.2; 99.9% CI -0.35, -4.35) and jet nebulizer (-2.4; 99% CI -0.39, -4.42). We conclude that even in small pre-term infants 200 micrograms salbutamol via MDI plus spacer improves dynamic resistance as effectively as 600 micrograms via jet nebulizer and may therefore be a preferable mode of aerosol administration.

**METERED-DOSE INHALATIONS WITH SPACERS VS. NEBULIZERS FOR PEDIATRIC ASTHMA**

Chou KJ, Cunningham SJ, Crain EF.

**Study Found**

**Synopsis**
OBJECTIVE: To determine whether the administration of β-agonists by metered-dose inhaler (MDI) with a spacer device is as effective as the administration of β-agonists by nebulizer for the treatment of acute asthma exacerbations in children. Design: Randomized trial with two arms. Setting: Urban pediatric emergency department (ED) in Bronx, NY. Patients: Convenience sample of 152 children 2 years and older with a history of at least two episodes of wheezing presenting to the ED with an acute asthma exacerbation. Interventions: Patients were randomly assigned to receive standard doses of an β-agonists (albuterol) by an MDI with spacer (AeroChamber*) or by a nebulizer. Dosing intervals and the use of other medications were determined by the treating physician. Measurements/ Main Results: Baseline characteristics and asthma history were recorded. Asthma severity score, peak expiratory flow rate in children 5 years or older, and oxygen saturation were determined at presentation and before admission or discharge. The groups did not differ in age, sex, ethnicity, age of onset of asthma, or asthma severity score, and peak expiratory flow rate, oxygen saturation, number of treatments given, admission rate. Patients given MDIs with spacers required shorter treatment times in the ED (66 minutes vs. 103 minutes, p<0.001). Fewer patients in the spacer group had episodes of vomiting in the ED (9% vs. 20%, p<0.04), and patients in the nebulizer group had a significantly greater mean percent increase in heart rate from baseline to final disposition (15% vs. 5%, p<0.001). Conclusions: These data suggest that MDIs with spacers may be an effective alternative to nebulizers for the treatment of children with acute asthma exacerbations in the ED.