for 30 min. Diagnosis of VAP was based upon CPIS score and clinical criteria (1). For cytokines determination was used ELISA.
RESULTS. 41 patients were included, 11 (26 %) developed VAP. APACHE II 24 ± 7. Development of VAP was associated with higher ICU stay, time under MV and mortality. *Baseline* Those who developed VAP presented worst pO_2/FiO_2 ratio 152 vs 259 ($p < 0.01$). In 24 % of patients was identified a microorganism, (26 % of non-VAP patients and 18 % in VAP-patients, in which were multi-resistant). VAP-patients, showed significantly higher TNF-α blood levels 7.6 vs 5.5 pg/ml ($p < 0.05$); MBAL TNF-α and IL-6 levels were lower 6.4 vs 19.6 pg/ml (p 0.08) and 5.4 vs 9.2 pg/ml (p 0.06) respectively. There were no differences with other cytokines or biomarkers.CPR or hs-CPR were not detectable in EBC. *Follow-Up*: VAP-patients: in three cases (27 %), causal microorganism was present in previous cultures. With regard to cytokines and biomarkers: blood TNF and MBAL IL-8 levels were significantly lower in samples previous to diagnosis of VAP (6.6 vs 7.7 pg/ml and 446 vs 2,460 pg/ml respectively). Those who developed VAP, at diagnosis, presented significant higher levels of: blood IL-8 and CRP; and MBAL, hs-CRP. PCT was also higher in blood and MBAL but not significantly.
CONCLUSIONS. Only in 27 % of patients who developed VAP, precious cultures were helpful in diagnosis. We could not find a definite profile of any cytokine or biomarker that could anticipate diagnosis of VAP. Blood levels of IL-8 and CRP and MBAL levels of hs-CRP and PCT are elevated in VAP patients.
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0781
HIGH DOSE NEBULIZED AMIKACIN: A PILOT STUDY IN VENTILATED PATIENTS WITH HEALTHCARE ASSOCIATED PNEUMONIA

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INTRODUCTION. High-dose nebulized antibiotics, as a complement to intravenous treatment, may improve pneumonia treatment efficacy, thanks to increased concentrations at the site of infection. Up to 60 mg/Kg of amikacin have been successfully nebulized in animal studies and to healthy subjects undergoing mechanical ventilation[1,2]. However, the pharmacokinetics and safety of such high doses have not been assessed in patients suffering of pneumonia.
OBJECTIVES. To evaluate serum pharmacokinetics and safety of 60 mg/Kg amikacin nebulization during mechanical ventilation
METHODS. Patients undergoing invasive mechanical ventilation with a suspicion of hospital acquired, healthcare- or ventilator-associated pneumonia were included. Aside of an intravenous betalactam antibiotic, each patient received 20 mg/Kg amikacin intravenously at inclusion; thereafter amikacin was administered *qd*. for 3 days: 60 mg/Kg nebulized (prototype jet-nebulizer in a dry circuit or with a heated humidifier) or 20 mg/Kg intravenously. 10 serum concentration of amikacin were measured over 24 h after each administration for non-compartmental pharmacokinetic analysis. Safety/efficacy data were recorded until day 10. Patients in whom pneumonia was not confirmed (amikacin sensitive bacterial documentation) or experiencing a side effect linked to amikacin administration were excluded from the study, but safety assessment was pursued until day 10.
RESULTS. 22 patients were included in the study, after informed consent. Six patients were excluded because pneumonia was not confirmed (n = 5) or because of renal failure before the second amikacin administration (n = 1), leaving 16 patients with at least 2 amikacin administrations: median age 59 years (interquartile range 51–72); n = 2 female; weight 75 Kg (63–78); body mass index 26 Kg/m^2 (24–28); baseline serum creatinine 62 μmol (51–73).
Overall 32 nebulizations were analysed: 4.5 g (4.1–4.9) nebulized over 2h15 (1h31–2h48); the area under the serum amikacin concentration curve (AUC) was 27 mg h/L (13–46), significantly lower than the AUC after intravenous administration: 396 mg h/L (paired $p < 0.01$). Serum bioavailability was 2.8 % (2.1–4.8), not significantly different, wether or not, active humidification was present. Without humidification, two patients experienced tracheal tube obstruction possibly related to amikacin nebulization, whereas this never happened in case of active humidification.
CONCLUSIONS. Nebulization of up to 60 mg/Kg appeared feasible in intubated patients. Systemic toxicity is very unlikely to occur as serum AUC appeared well below those observed after intravenous infusion. Active humidification may prevent tracheal tube obstruction without significant changes in bioavailability and thus in probable alveolar drug deposition.
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0782
PHARMACOKINETICS OF COLISTIN AFTER THE ADMINISTRATION OF A LOADING DOSE OF 4.5 MU OF COLISTIN METHANESULFONATE (CMS) IN OBESE CRITICALLY ILL PATIENTS VERSUS REGULAR WEIGHT CRITICALLY ILL PATIENTS

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INTRODUCTION. Although it is known the difficulty of the antimicrobial dosing in obese patients so far there are no pharmacokinetic studies of colistin for these kinds of patients.
OBJECTIVES. The aim of the study is to describe the pharmacokinetics (PK) of CMS of two different critically ill populations of patients, obese vs. regular weight using a loading dose of 4.5 MU of CMS.
METHODS. A clinical trial (MagicBullet) is in progress at the ICUs of Virgen del Rocío University Hospital, Seville, Spain, since January of 2012. Critically ill patients who met the following inclusion criteria were enrolled: Age ≥ 18 years, >96 h of mechanical ventilation, ventilator-associated pneumonia, CPIS > 4, tracheo-bronchial culture, non-pregnant women, and normal renal function. The following data was collected: gender, age, weight, height, APACHE II score, body max index (BMI), plasma creatinine (Cr) and creatinine clearance (CL_{CR}) on days 1 (1st CMS dose) and 3 (7th CMS dose), using the Cockcroft–Gault formula. Patients were treated with a loading dose of CMS of 4.5 MU (360 mg, 1 h infusion, followed by 3 MU (240 mg) every 8 h (30 min infusion). Venous blood samples were drawn after the loading dose at 1, 2, 4, and 8 h after the beginning of the CMS infusion and at the steady state (7th dose) at 1, 4, and 8 h after the beginning of the CMS infusion. All blood samples were immediately chilled and centrifuged, and the plasma was stored at − 70 °C until assayed. Plasma colistin concentrations were determined by a HPLC–MS/MS method. A non-compartmental analysis of data was done (PKSolver 2.0). Due to the small number of cases in each group, only descriptive analyses were performed (SPSS 15.0).
RESULTS. Seven patients have been included: four in the obese group and three in the regular weight group. Demographic, clinical, and PK data are shown in Tables 1, 2 and 3. No deterioration of renal function was observed during the study in any of the patients included. With regard to the PK at the steady state important differences in the maximum plasma colistin concentrations (total colistin and unbound colistin) 1.89 vs. 3.42 and 0.62 vs. 1.13 were found between obese and regular weight patients.
CONCLUSIONS. Although a higher number of patients have to be included to confirm these results, it looks like the actual dose regimen used for the treatment of obese patients is suboptimal. If these results are confirmed with the inclusion of more patients a higher dose of colistin for obese patients should be considered to treat severe infections caused by MDR bacteria.
GRANT ACKNOWLEDGMENT. MagicBullet is a project funded by the European Union–Directorate General for Research and Innovation through the Seventh Framework Program for Research and Development (Grant Agreement 278232) and has been running since January 1st 2012 (duration 36 months).

Table 1 Demographic and clinical data

No	APACHE II Score	Demographic data					
		Gender	Age (year)	Weight (kg)	Height	BMI	Diagnosis
1	25	M	68	120	174	39.6	VAP
2	19	M	47	80	178	25.3	VAP
3	17	M	76	110	175	35.9	VAP
4	26	F	67	90	150	40	VAP
5	24	F	57	57	168	20.2	VAP
6	12	M	54	100	185	29.2	VAP
7	15	M	68	150	164	55.7	VAP

Table 2 Renal function data

No	Plasma creatinine (mg/dL)		Creatinine clearance (mL/min)	
	Creatinine level Day 1	Creatinine level Day 3	Creatinine clearance Day 1	Creatinine clearance Day 3
1	0.67	0.54	179.10	222.22
2	0.75	0.75	137.78	137.78
3	1.36	1.29	71.90	75.80
4	0.51	0.39	152.08	198.88
5	0.9	1.16	62.06	48.15
6	0.79	0.99	151.20	120.65
7	0.47	0.35	319.15	428.57

Table 3 Pharmacokinetics data

		Loading dose (1st dose)		Steady state (7th dose)	
		Obese	Regular weight	Obese	Regular weight
Total colistin	Cmax (μg/mL)	2.71	2.62	1.89	3.42
Total colistin	Tmax (h)	2.00	2.00	2.00	4.00
Total colistin	T1/2 (h)	12.37	9.11	14.89	21.38
Total colistin	AUC0–8 h (μg/mL × h)	14.57	15.37	10.99	22.75
Unbound colistin	fCmax (μg/mL)	0.94	0.87	0.62	1.13
Unbound colistin	fTmax (h)	2.00	2.00	2.00	4.00
Unbound colistin	fT1/2 (h)	10.67	8.72	14.59	20.79
Unbound colistin	fAUC0-8 h (μg/mL × h)	4.87	5.06	3.56	7.51

0783
EVALUATING THE AMBU® ASCOPE™ 3 SYSTEM FOR BRONCH-ALVEOLAR LAVAGE AND BRONCHIAL WASH IN INVASIVELY VENTILATED PATIENTS

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INTRODUCTION. The Ambu® aScope™ 3 system is a novel disposable bronchoscope (5.5 mm maximum external diameter with 2.2 mm suction/working channel) which connects to a separate portable aView™ monitor. The range of tip movement is 150° upwards and 130° downwards. We report the first observations in practice of this system for bronch-alveolar lavage (BAL) and bronchial wash (BW) in invasively ventilated patients.
OBJECTIVES. To evaluate the functionality and ease of use of the aScope™ 3 system.
METHODS. 20 CE-marked aScope™ three bronchoscopes and two aView™ monitors were supplied by Ambu® for the evaluation. Patients receiving invasive mechanical ventilation via endotracheal or tracheostomy tube who had a clinical indication for either BAL

or BW were included. Ten procedures were carried out by each author, both of whom are experienced bronchoscopists. A 5-point Likert scale was used (1 fully disagree, 3 neutral, 5 fully agree) to evaluate functionality and ease of use of the system, applied to ten statements concerning functionality (see Table 1). Number of major lung segments visualised (out of 6) along with overall impressions of performance (satisfactory: yes/no) and whether the operator felt that the aScope™ three system could replace our existing non-disposable system (yes/no) were also recorded.

RESULTS. All 20 procedures (7 BW only, 4 BAL only, 9 both BW and BAL) were completed between 26/2/13 and 9/4/13 by the 2 authors (10 procedures each). Data were explored using the Shapiro–Wilk test and the results (mean Likert scores for functionality and ease of use) shown in Table 1. All six major segments of the bronchial tree were visualised for all endoscopies. Overall functionality and performance was rated as satisfactory in all procedures and the system was felt to be able to replace the existing non-disposable system in 19 procedures.

Table 1 Mean Likert scores for functionality

	Mean	95 % CI
Easy to advance bronchoscope	4.9	4.6–5.1
Easy to inject via working channel	4.6	4.3–4.8
Ease of performing suction	4.4	4.1–4.8
Suction capability adequate	4.4	4.1–4.7
Functionality of working channel satisfactory	3.7	2.9–4.5
Image quality adequate to perform procedure	4.7	4.4–4.9
Lens clearing was easy	4.3	4.0–4.6
Lightweight handle was a benefit	3.2	2.0–3.4
Easy to record images on aView™ monitor	2.7	1.7–3.6

CONCLUSIONS. Our evaluation by two independent, experienced clinicians has demonstrated that the Ambu® aScope™ three system was assessed as easy to use and performs satisfactorily for BAL and BW in invasively ventilated critically ill patients. The system is portable and easy to assemble and position at the bedside and although the monitor display is smaller and of lower resolution (800 × 480 pixel, 8.5 in. colour TFT LCD screen) than our non-disposable 'stack' system, image quality was good enough to perform the procedures. The suction capabilities were comparable to our non-disposable bronchoscope. The lowest scores were in relation to the functionality of the aView™ monitor, which had pre-release software installed. The lightweight handle was not perceived as a particular advantage in this evaluation, although this did not affect the overall impressions of functionality. The disposable nature of the system may have infection control and cost advantages.

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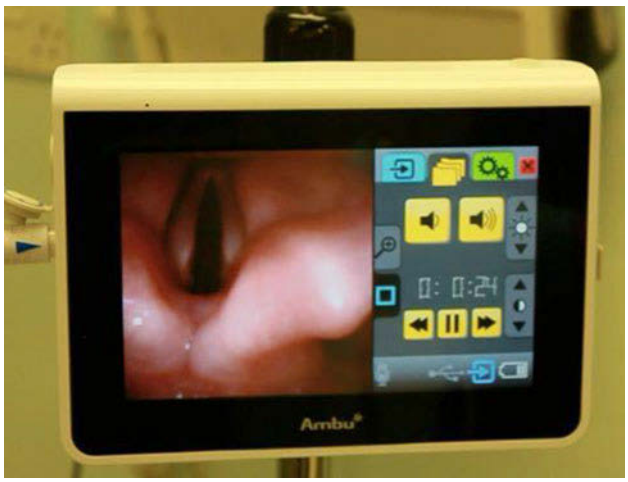

Fig. 1 A view monitor

Fig. 2 A scope 3 and a view monitor

0784
INSPIRATORY FLOW BIAS AND THE INCIDENCE OF VAP

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INTRODUCTION. Ventilator-associated pneumonia (VAP) is the most frequent nosocomial infection in the intensive care unit (ICU). VAP prolongs the duration of mechanical ventilation (MV) and hospital stay, and increases mortality. Since the 1980s, there has been increasing evidence that ventilator settings can produce a flow bias that may clear or embed mucus during MV. The ratio between the peak inspiratory flow (PIF) and the peak expiratory flow (PEF), or the difference between the two, are described as possible critical factors that may influence secretion movement.

OBJECTIVES. To investigate in mechanically ventilated patients the effect of flow bias on the incidence of VAP.

METHODS. Participated in the study patients under MV for <24 h and that were expected to continue under MV for >72 h. Exclusion criteria were: suspicion of pneumonia prior to MV, aspiration during intubation and severe hypoxemia. Respiratory mechanics were registered at the time of entering in the study and every each 12 h during the first 60 h using $CO_2SMO^{®}$ monitor. VAP diagnostic was made based on new or worsening radiographic infiltrates and leukocytosis or leucopenia, fever or purulent sputum. Total time of MV, ICU and hospital lengths were registered. Patients that developed VAP were classified as VAP group and patients that did not presented VAP as control group. Statistical analysis was performed using unpaired t-test or Mann–Whitney and a two-way analysis for repeated measures as appropriate.

RESULTS. 30 patients were included in the study, 17 of them presented VAP (Table 1). Although the differences were not significant, the VAP group compared to the control group was older and had a slightly higher APACHE score. Total time of MV, ICU and hospital lengths were significantly higher in the VAP group compared to the control.

Table 1

	Age (years)	APACHE	Total MV time (days)	ICU length stay (days)	Hospital length stay (days)
VAP (n17)	60±18	13,8±5,1	12 [8-21]*	15 [9-23]*	21 [9-42]*
Control (n13)	50±18	12,2±5,0	6 [5-8]	7 [5-10]	11[6-21]

Data are expressed as mean±DP or median [IQR].
*P<0,05 vs control.

There were no differences between the PIF/PEF ratio ($p = 0.080$) and the PEF − PIF difference ($p = 0.110$) during the first 60 h of MV between the two groups. The mean ± SE PIF/PEF ratio and PEF − PIF difference were in the VAP group 1, 5 ± 0.5 and − 14.1 ± 1.5 and in the control 1.6 ± 0.7 and − 17.5 ± 1.4, respectively.

CONCLUSIONS. These preliminary results of a current study suggest that an inspiratory flow bias during the first 60 h of MV does not influence the incidence of VAP. Both groups, VAP and control, were ventilated with a PIF/PFE ratio much higher than the threshold described in the literature—PIF/PFE ratio > 0.9—which, theoretically, is sufficient to move mucus towards the lungs. The negative mean PEF–PIF differences, in both groups, also indicated that secretion was moved deeper into the lungs. As expected, patients with VAP had longer time of MV, ICU and hospital length.

0786
EFFECT OF DIFFERENT TRACHEAL TUBE CUFF MATERIAL, SHAPE AND SIZE FOR FLUID LEAKAGE ACROSS THE CUFF

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INTRODUCTION. Micro aspiration of oral secretions across the tracheal tube cuff is one of the most important causes of ventilator-associated pneumonia (VAP). The formation of folds in the inflated cuff is the major cause of micro aspiration and the cuff material and shape affect the leakage volume across the cuff. Although there are various types of tracheal tubes, the effects of each tube size to cuff leakage are not clear. Even if the internal diameter is same size, cuff size and shape are different greatly in each tube type.

OBJECTIVES. To compare fluid leakage across the cuff in each different tracheal tube type and size in a bench-top model.

METHODS. We compared fluid leakage across the cuff in a bench-top model. Tracheal tubes were inserted into a vertical artificial glass trachea with 22 mm internal diameter. Four different types of tracheal tubes with secretion drainage, SealGuard Evac with polyurethane cuff (Covidien), TaperGuard Evac (Covidien) with polyvinylchloride cuff, Hi-Lo Evac with polyvinylchloride cuff (Covidien), Portex BlueLine SACETT with polyvinylchloride cuff (Smiths Medical), and five different sizes (6.5, 7.0, 7.5, 8.0, 8.5 mm internal diameter) of each tube type were used in this study. Intracuff pressure was set at 25 cmH_2O. 20 ml dyed water was applied above the unlubricated tube cuff and fluid leakage was measured at 2 min. Each experiment was carried out five times. Data were shown as mean ± SEM (ml).

RESULTS. Figure 1 showed the relation between the tube size and fluid leakage across the cuff in different tube types. Tube size to minimize the cuff leakage was different by each tube type. Taper shape cuff with both polyvinylchloride and polyurethane showed similar property.

CONCLUSIONS. Each tracheal tube has its own property in the view of cuff fluid leakage. These results indicate that the best tracheal tube size to prevent VAP is different in each tube type. We need to pay attention not only to tube internal diameter but also to cuff size in each tracheal tube to avoid trachea–cuff size mismatch.