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SEPARATUM

THE USE OF PARENTERAL AUGMENTIN IN THE TREATMENT OF RESPIRATORY TRACT INFECTIONS: CLINICAL, BACTERIOLOGICAL AND LUNG FUNCTION STUDIES.

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Augmentin formulations contain the antibiotic amoxycillin and the beta-lactamase inhibitor clavulanic acid. Clavulanic acid is able to protect amoxycillin from inactivation by the beta-lactameses of various gramnegative bacilli and staphylococci. Serum peak concentrations in men following intravenous infusion over 30 min of augmentin vials 3.2 g occur between 2o and 45 min. Maximal values of 123 µg/ml for amoxycillin and 10.8 µg/ml for clavulanic acid are obtained. The post-infusion half-lives for both compounds are about 7o minutes. Urinary recovery over the 6 hours after dosing is 52.4% for amoxycillin and 39.6% for clavulanic acid (1,2).
To evaluate the clinical efficacy of augmentin a study was initiated in patients with acute lower respiratory tract infections.

Patients and methods

15 consecutive inpatients were treated with parenteral (2.2 g augmentin with 2.0 g amoxycillin and 2oo mg clavulanic acid; t.i.d.) and oral (625 mg augmentin with 500 mg amoxycillin and 125 mg clavulanic acid; t.i.d.) formulations of augmentin. The criteria for entry into the open, non-controlled study were the exacerbation of chronic bronchitis and/or broncho-pneumonia and/or bronchiectasis. Patients with penicillin allergy, treatment with other antibiotics, pulmonary infarction and tuberculosis were excluded. Other non-antibiotic drugs were applied as due to the necessity of the underlying diseases (digitalis, diuretics, bronchodilators, cortison, antidiabetics ect.). Clinical symptoms were monitored and sputum bacteriology, blood chemistry, thoracic X-ray and lung function tests were performed when appropriate.

Results

Pertinent data of the patients are given in table 1. 8/15 were older than 70 years (range 29 - 80). 8 patients suffered from bronchopneumonia (PN), 7 patients were admitted to the hospital as emergency cases due to cardio-respiratory insufficiency complicated by acute bronchitis and airway obstruction (BR).

Table: 1 Clinical data of patients (N = 15; 1 female, 14 male)

No	age	b.w. kg	days at hospital	pneumonia bronchitis	augmentin (days) i.v.	oral	concomitant diseases	lung function RV % TLC	flow-25/50%-FVC l/sec
1	74	75	22	pneum	5	4	emphysema	57.1	0.4/0.6
2	71	79	22	pneum	9	16	n. bronchi	39.9	1.0/2.2
3	56	55	24	pneum	8	14	---	33.5	1.5/3.5
4	59	56	20	bronch	9	9	COLD	----	-------
5	79	52	11	bronch	3	5	COLD, CHF	----	-------
6	75	54	15	pneum	6	9	COLD, CHF	----	-------
7	46	57	19	bronch	9	10	COLD	55.8	0.3/0.8
8	80	67	29	bronch	5	24	COLD, CHF	65.3	0.6/1.2
9	66	61	12	bronch	5	8	COLD	54.0	0.4/1.4
10	29	49	14	pneum	8	12	---	23.6	2.0/4.2
11	73	73	14+)	pneum	12	7	meta hepat.	----	-------
12	74	75	18	bronch	9	11	COLD, CHF	61.3	0.3/0.5
13	63	65	7++)	pneum	7	-	n. bronchi	----	-------
14	78	56	31	pneum	9	21	CHF, AS/AI	41.2	0.7/2.4
15	72	67	19	bronch	7	11	COLD, CHF	61.3	---/0.8
$\bar{x}$	66.3	62.7	19.3	PN = 8	7.4	11.5			
s	14.0	9.5	6.0	BR = 7	2.3	5.7			
N	15	15	14		15	14			

+) demission on request; ++) transferred
COLD chronic obstructive lung disease, CHF congestive heart failure, E emphysema
AS/AI aortic stenosis/insufficiency

Severe airway obstruction was evident in 8/15 cases (BR-group 5/7; PN-group 3/8). The respiratory tract infection was complicated by signs of congestive heart failure in 7/15 patients (BR-group 4/7; PN-group 3/8). The patients were treated for 19 days on the mean (range 11 - 31; N = 14) at the internal medicine department. One patient (excluded; No 13) was transferred to a lung clinic at the end of the parenteral augmentin phase because of bronchopneumonia of the left lower lob, empyema and bronchial carcinoma. The mean parenteral augmentin treatment period lasted for 7.4 days on the mean, the oral formulation was given for 11.5 days, partly on an outpatient basis. There is no statistical difference between the two groups (PN/BR) with respect to the periods of treatment. In all cases the parenteral treatment with augmentin improved the clinical signs and symptoms of the lower respiratory tract infection as judged by clinical investigation and chest X-ray. In one case (No 14) only another antibiotic (gentamycin) was added to the oral augmentin because of a very slow disappearance of the radiologic signs of the infiltration.
In two cases a peripheral bronchial carcinoma (2/15) was identified as the reason for the bronchopneumonic infiltration.
The leading symptoms as rated by the patients diminished rapidly and/or disappeared completely within 8 - 10 days of treatment (s. table 2).

Table 2: Incidence of clinical symptoms

GRADE	I	II	III
	dyspnea (8)	cough (9)	fever (5)
	cough (3)	sputum (2)	sputum (2)
	respir pain (2)	dyspnea (1)	cough (1)
	sputum (1)	fever (1)	
	fever (1)	malaise (1)	
		respir pain (1)	

cough (13/15), dyspnea (9/15), fever (7/15), sputum (5/15).

Local effects at the site of injection, hypersensitivity reactions and adverse effects were not reported. Sufficient data on sputum bacteriology before, during and after parenteral augmentin treatment were not available. Pretreatment bacteriological assessment in 10/15 patients failed. The elderly patients were less able to produce bronchial sputum and in urgent cases the antibiotic treatment had to be initiated

without delay. The bacteriological analysis at the end of the parenteral augmentin treatment revealed in one case the pretreatment pathogen (Klebsiella pneumoniae). This patient received gentamycin in addition to oral augmentin (No 14). In 8/15 patients Enterobacter cloacae was isolated, other findings include Serratia marescens (1/15), Escherichia coli (1/15), Candia (3/15), Haemophilus parainfluencae (1/15), Proteus vulgaris (1/15) and Proteus aeroginosus (1/15).
The lung function analysis included blood gas analysis on admission, spirometry, bodyplethysmography and flow-volume-pressure-analysis when the patient was able to walk to the lung function lab.
In accordance with the clinical diagnosis patients with chronic obstructive lung disease and emphysema showed abnormal lung function data with an excessive increase of the residual volume (RV, range 54.0 - 65.3% of TLC, total lung volume) and minimal exspiratory flow rates during the forced vital capacity maneuver (FVC, s. tabl. 1).

From a clinical standpoint of view parenteral and oral augmentin proved to be very effective to cure the acute respiratory tract infections in 15 patients and to prevent any relapse during the time of observation. In a subgroup of patients with chronic obstructive lung disease and acute cardio-respiratory insufficiency the high loading dose of parenteral augmentin was a keystone to improve the overall situation of the patients by suppressing the exacerbation of the chronic infection of the respiratory tract.

References

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