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CORRESPONDENCE

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Imipenem/cilastin dosage during acute renal failure and hemofiltration

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Building on data published by MC Vos and colleagues in 1992 on imipenem/cilastatin and CAVHD [1] we investigated imipenem/cilastatin in 16 patients with (n = 10, group 1) and without (n = 6, group 2) renal insufficiency; both groups received continuous, volume-constant hemofiltration (CVHF). The indications for hemofiltration were oliguric renal dysfunction and increases in urea and creatinine of 8 mmol/day and 50 μmol/day, respectively. CVHF was performed as a postdilution technique with a polysulfone high-flux filter and an blood pump. The blood flow ranged from 100 to 200 ml/min and was adjusted to Qb = 20–30 ml/min. The filter was discharged when transmembrane pressure reached 200 mmHg of when the volumes of filtrate dropped to 50% of the initial filtration rate. Anticoagulation was maintained with up to 1000 IU heparin/h to keep PTT at about 40 s. Arterial blood and ultrafiltrate samples were collected 10, 20 and 30 min and every hour from 1 to 12 h after the beginning of imipenem/cilastatin infusion. Pharmacokinetics were calculated under the condition of steady-state application. Curve approximation according to serum and cumulative ultrafiltrate levels was calculated by a least-square iteration process with the TOPFIT pharmacokinetic program. A predictive algorithm for drug dosage during HF was developed to obtain a sufficient dosage without measuring blood levels. It was based on Dettli's equation for renal insufficiency [2]: D = Dm

(Qa + Qf × S/Clf), where Qa = individual extracorporeal elimination fraction; Qf = filtration flow (ml/min); S = drug sieving (= 1-protein binding), and Clf of imipenem was taken from our control group. For imipenem, we presume only a low influence of Qs on dosage because the normal Qs (= Qs) was 0.3.

Continuous, volume-constant hemofiltration is becoming recognized as the best treatment for ARF. This method replaced arteriovenous hemofiltration and dialysis because of its fewer side effects: CAVH depends on a sufficient blood pressure for Qb, and dialysis sometimes affects patients' circulation. Peak levels of imipenem were lower than those reported in the literature [3, 4]. Imipenem has a marked metabolic degradation, and therefore half-lives were only doubled compared to normals (group 1: 2.21 ± 0.59 h, group 2: 1.38 ± 0.41 h, normals: 1.0 h). This is the reason for the low calculated initial concentration and the lower area under the curve (AUC). The extrapolated initial concentration C0 has a mean of 30.7 μg/l, which, however, is still comparable to results of other authors [1, 3]. Sieving coefficient was calculated from the area under the curve of serum and ultrafiltrate because this method resulted in smaller standard deviations with respect to predictive values than from single data. Qa of group 1 was always greater than the normal elimination. The dosage reduction factor was 0.4. Dosage corrections following CVHF are small compared to non-renal elimination. This would imply that the CVHF correction is comparable to untreated end-stage renal disease. Cilastatin has no antibiotic effect and accumulates during renal dysfunction. In patients with no kidney function, cilastatin is not indicated. The results confirmed the prediction for ARF patients: the dose of imipenem/cilastatin has to be reduced from 4 g/day to 1.5–3.0 g/day in patients with ARF during CVHF.

References


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Primary laryngospasm in a patient with Parkinson's disease: treatment with CPAP via minitracheostomy following intubation

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Sir: We would like to report on a primary laryngospasm in a patient with Parkinson's disease and its treatment with CPAP (continuous positive airway pressure) via minitracheostomy. A 60-year-old man with about a 10-year history of Parkinson's disease treated with Sinemet (carbidopa and levodopa) was admitted to the hospital with a life-threatening upper airway obstruction. He was intubated, and mechanical ventilation was initiated. Chest X-ray revealed bilateral basal consolidations. After 3 days, the condition had improved, blood gases were normal and the patient could be extubated. Stridor immediately resumed, however. On fiberoptic bronchoscopy, the vocal cords appeared to be almost completely adducted without edema or signs of inflammation. A minitracheostomy was performed and treatment with continuous-flow CPAP connected to the minitracheostomy was started. This resulted in a marked reduction of the stridor, with adequate ventilation. The patient was successfully weaned from this CPAP arrangement without recurrent laryngospasms and was transferred to the ward after 5 days with minitracheostomy in situ. Additional investigation with body-plethysmography breathing showed a marked increase in inspiratory resistance, with almost normal expiratory resistance, pattern in accordance with extrathoracic, variable airflow obstruction, e.g. vocal cord dysfunction. Episodes of severe stridor recurred after 2 weeks. On direct laryngoscopy, the vocal cords were still adducted. A permanent tracheostomy was performed to avoid further ICU admission and interventions.

In Parkinson's disease, dopamine depletion leads to diminished inhibition of the extrapyramidal motor system. This may lead to severe laryngospasm. Respiratory problems are well known, and aspiration pneumonia is one of the most common causes of death among such patients [1].
Dysfunction of the upper airways has only recently been recognized in patients with Parkinson's disease [2]. In most cases, this leads to impairment of static and dynamic pulmonary function. In some patients, laryngeal involvement was the main reason for airway obstruction [2]. In our patient, the most likely diagnosis is primary laryngospasm associated with Parkinson's disease.

Treatment by minitracheostomy connected to a continuous flow CPAP resulted in a clinically relevant relief of stridor. The mechanism of this effect might be the slight positive airway pressure of 2-4 cmH2O in combination with a 4-mm free artificial airway. However, the latter cannot be the only explanation for the clinical relief of stridor, since the stridor increased while the patient was breathing through an open minitracheostomy without CPAP connection. Although minitracheostomy is most frequently used in the treatment of sputum retention, it allows an artificial airway to be combined with several other arrangements [3, 4].

In conclusion, laryngospasm caused by dysfunction of recurrent laryngeal nerves may be associated with Parkinson's disease. CPAP via minitracheostomy proved to be temporarily successful in the management of this problem. Tracheostomy may be inevitable in cases of persistent relapses.

References