Perioperative in vivo pharmacokinetics of succinylated gelatins: a pilot study.

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Background and Goal of Study:

Gelatins are colloids used for volume expansion [1]. There is no information available on the volume expansion and the excretion of gelatins in inflammatory conditions such as surgery. Among the increased proinflammatory cytokines, matrix metalloproteinases (MMPs) have gelatins as ideal substrate [2]. Aim of our study is to evaluate if the pharmacokinetics of succinylated gelatins is influenced by inflammation during surgery.

Materials and Methods:

Observational study conducted on ten patients undergoing major abdominal surgery in the University Hospital “S. Anna” in Ferrara from October to December 2015. Exclusion criteria: age < 18 years, emergency surgery, NYHA III or IV, Hb < 6.2 mmol/L, Creatinine >220 µmol/L, treatment with corticosteroids or NSAIDs, allergy to gelatins. The elimination half-life and urinary excretion was determined after the administration of 1000 ml IV of succinylated gelatin. Five blood and urine samples were collected: after the surgical incision, at the end of the infusion (T0) and one (T1), two (T2), three (T3) and four (T4) hours after the end of infusion. We assayed the gelatin in the serum and urine by evaluating the amount of hydroxyproline after acid hydrolysis with concentrated HCl. The active form of MMP9 and MMP2 were measured using an activity assay system (Table 1).

Results and Discussion:

Population: Male n 7, Female n 3, Age 64.4 (±8.4), BMI 26.6 (±2.8). We observed a time dependent decrease in the gelatin serum concentration, with a maximum at the end of the infusion (Figure 1, panel A, 0 hours), mirrored by the increase of gelatin in the urine (Figure 1, panel B). The plasmatic half-life was 3.6 (±1.2) hours. We observed a significant positive correlation between the sum of concentration of active MMP9 and active MMP2 (p< 0.05) and the rate of elimination.

	Hours after the infusion					
	before	0	1	2	3	4
MMP-9 (ng/ml)	5.4 (4.5-6.4)	5.1 (4.4-5.9)	4.8 (4.0-5.0)	4.6 (4.4-6.2)	4.5 (3.8-6.2)	4.9 (4.1-6.0)
MMP-2 (ng/ml)	9.4 (4.6-10.3)	4.1 (3.7-9.8)	4.5 (4.2-8.3)	4.8 (4.4-9.4)	5.2 (3.9-9.2)	6.6 (4.0-8.9)
MMP-9 + MMP-2 (ng/ml)	14.9 (9.2-16.6)	9.4 (8.3-16.7)	9.4 (8.5-13.2)	10.6 (8.7-14.0)	10.3 (8.1-14.8)	11.1 (8.3-13.4)

Table 1. Concentrations of active MMP-9 and active MMP-2 and their sum. Mean (max – min value).

Conclusion:

Our preliminary results suggest that the pharmacocinetic of gelatins is influenced by the expression of matrix metalloproteas.

References:

1. Niemi TT et al. J Anesth 2010; 24: 913925
2. Volta CA et al. Anesthesiology 2007; 106:8591.