保温中形成的3个poly-SM组分究竟是SM的几聚体，有待研究。

虽然目前还没见SM能形成聚合物的报道，但SM分子既有氨基，又有醛基，在酸催化条件下，醛基和氨基易发生亲核加成反应。Aronson等也曾认为SM在溶液中可以以其醛基和*N*-甲基葡萄糖胺上的仲氨基分子内缩合[7]。提示SM分子间通过醛基和氨基缩合是可能的。实验中我们通过柠檬酸-乙酸酐反应证明聚合反应和SM分子上的氨基有关。Poly-SM的确切聚合机理及聚合后的结构，有待研究

从商品SM中分离到的主要致敏性杂质"高杂1"在320 nm附近有紫外吸收峰[2]，poly-SM在320 nm附近也有紫外吸收峰。通过对SM生产工艺的了解得知，生产中为除去发酵液中的蛋白质需将发酵液用草酸酸化至pH 3左右，并通蒸气至70℃。在此条件下，SM的聚合反应是可能发生的。Poly-SM一旦形成，现有的主要精制手段都不能将其全部除净(未发表资料)，因此生产过程中产生poly-SM并带到商品SM中是完全可能的。

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全胃肠外营养对丁胺卡那霉素药物动力学的影响

蔡卫民、于广华[1]、陈　刚　(南京军区南京总医院药理科，南京　210002，中国)

Influence of total parenteral nutrition on amikacin pharmacokinetics

CAI Wei-Min, YU Guang-Hua, CHEN Gang

(General Hospital of Nanjing Armed Forces, Nanjing 210002, China)

ABSTRACT Six patients under total parenteral nutrition (TPN) and eight control patients received 200 mg of amikacin by iv infusion in 0.5 h. Amikacin concentrations of serum and urine were determined by fluorescence polarization immunoassay. At 6 h after the beginning of administration.

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[1] Graduate student of *China Pharmaceutical University, Nanjing 210009, China*

the amikacin level in serum of TPN group (2.3±0.8 μg/ml) was significantly higher than control (1.3±0.8 μg/ml). There was no significant difference between the 24-h urine output of 2 groups. Pharmacokinetic calculations were based on a two-compartment open-system model. The $T_{t\beta}$ and apparent volumes of distribution (V_c, $V_{d_{ss}}$, V_2) of TPN group were significantly greater than those of control group. The body clearance of amikacin in TPN group was slower than control. It is suggested that serum amikacin concentrations should be monitored in clinical TPN patients to prevent toxic reactions.

KEY WORDS parenteral hyperalimentation; amikacin; pharmacokinetics; fluorescence polarization; immunoassay

提要 用荧光偏振免疫法测定了6例全胃肠外营养(TPN)病人和8例对照病人静滴200 mg丁胺卡那霉素后血清和尿中药物浓度。TPN组的C_{max}低于对照组，而末端相6 h时血浓度却明显高于后者。两组病人24 h肾排出率无差异。药物动力学呈二室开放型。TPN组的V_c，V_{ss}，V_2和$T_{t\beta}$增大，K_{10}显著减小。实验提示丁胺卡那霉素在TPN病人体内消除减慢。

关键词 胃肠外高营养；丁胺卡那霉素；药物动力学；荧光偏振；免疫测定

营养对药物动力学的影响近年引起重视。如已发现茶碱代谢因饮食高蛋白物质而加速[1]；庆大霉素的消除因过量摄入蛋白质而加快[2]。全胃肠外营养(total parenteral nutrition，TPN)系指非胃肠道输入的一种高能营养剂，临床用于严重肠道疾患病人的营养支持与治疗[3]。TPN能否改变合用药物的代谢、消除，进而影响疗效和毒性，值得探讨。丁胺卡那霉素具有耳、肾毒性，且后者与体内药物浓度密切相关[4]。为此我们选择临床应用TPN并合用丁胺卡那霉素抗感染的病人，用荧光偏振免疫法测定其血清和尿中药物浓度，初步探讨了TPN对丁胺卡那霉素药物动力学的影响。

MATERIALS AND METHODS

硫酸丁胺卡那霉素(amikacin sulphate)注射液(天津和平制药厂)；TPN：由本院腹部外科配液室按医嘱配制；荧光偏振免疫分析仪(TDx)及其专用丁胺卡那霉素测定试剂盒(批号950802 AZ)由美国Abbott公司提供[5]。

实验对象和给药方案 受试者均为本院腹部外科住院病人。其中TPN组6例(♂)肠瘘患者，年龄43±SD 23 yr (20-70 yr)，体重46±6 kg (39-52 kg)，等热量、氮量TPN全量3 d后给药；对照组8人(3 M，5 F)，其中1人患肠瘘，2人胆囊炎，5人胆石症，年龄46±13 yr (27－64 yr)，体重60±10 kg (48－72 kg)。受试者血清肌酐、尿素氮、血钾、血糖等用药前、后各测定1次，均正常。控制饮水，均无合并用药。两组病人每日3次每次恒速静滴200 mg丁胺卡那霉素0.5 h，给药间隔为8 h。

血、尿药浓测定和数据处理 两组病人于首次给药后0.5，1，2，3和6 h分别取上肢静脉血1 ml，分离血清；收集24 h内混合尿液并记录尿量，尿液用PB缓冲液(pH 7.8)稀释。用荧光偏振免疫法[5]测定血清和尿中丁胺卡那霉素浓度。

血清药物动力学按二室模型分析[6]，模型表达式为$C = Ae^{-\alpha t} + Be^{-\beta t}$；用"PKBP-N 1"程序[6]在微型计算机上对原始数据进行拟合，估算模型参数。部分动力学参数$V_{d_{ss}}$，V_2和CL系根据文献计算公式[7-9]求得。TPN组与对照组血清、尿药浓度及动力学参数的比较用t检验分析。

RESULTS

荧光偏振免疫法测得TPN组和对照组平均血清浓度及显著性检验结果见Tab 1。

丁胺卡那霉素200 mg静脉滴注开始后0.5 h，TPN组与对照组血清浓度均达高峰，分别为14.2±3.3和20.4±4.7 μg/ml，TPN组略低于对照组；至6 h分别降至2.3±0.8和1.3±0.8 μg/ml，此时TPN组的血清药浓度明显高于对照组药浓度($P<0.05$)。血清药浓度变

Tab 1. Serum amikacin concentration (μg/ml) after iv infusion of 200 mg in 6 total parenteral nutrition (TPN) and 8 control patients. $\bar{x}\pm SD$. *$P>0.05$, **$P<0.05$.

Time (h)	Control	TPN
0.5	20.4±4.7	14.2±3.3**
1.0	10.8±2.4	10.0±3.8*
2.0	5.8±1.4	6.0±2.1*
3.0	3.7±1.0	4.3±1.4*
6.0	1.3±0.8	2.3±0.8**

化的方程式分别为：

TPN 组 $C=21.89e^{-2.06t}+12.79e^{-0.24t}$

对照组 $C=54.79e^{-3.03t}+10.81e^{-0.35t}$

TPN 组 24 h 内尿量、尿药浓度、肾排出量和%与对照组比较均无显著性差异。

TPN 组与对照组药物动力学参数比较见 Tab 2。与对照组相比，TPN 组的中央室分布容积(V_c)和稳态分布容积(V_{dss})显著增大($P<0.01$)，周边室分布容积(V_2)也明显增大($P<0.05$)。而中央室消除速率常数(K_{10})显著减小($P<0.01$)。TPN 组丁胺卡那霉素的消除相半衰期($T_{\frac{1}{2}\beta}$)为 3.20±1.23 h，明显高于对照组值 2.11±0.50 h ($P<0.05$)和文献报道正常值(1.90±0.28 h)[7]。

Tab 2. Pharmacokinetic parameters of amikacin after iv infusion of 200 mg in 6 total parenteral nutrition (TPN) and 8 control patients. $\bar{x}\pm SD$. *$P>0.05$, **$P<0.05$, ***$P<001$.

Parameter	Control	TPN
$T_{\frac{1}{2}\alpha}$ (h)	0.26±0.11	0.39±0.12*
$T_{\frac{1}{2}\beta}$ (h)	2.11±0.50	3.20±1.23**
V_c (L/kg)	0.11±0.02	0.25±0.11***
V_{dss} (L/kg)	0.23±0.05	0.43±0.14***
V_2 (L/kg)	0.18±0.04	0.24±0.05**
K_{21} (h^{-1})	1.22±0.60	1.00±0.38*
K_{12} (h^{-1})	1.29±0.54	0.81±0.55*
K_{10} (h^{-1})	0.88±0.16	0.50±0.21***
CL (L/h)	5.81±1.65	5.16±1.71*

DISCUSSION

TPN 主要含葡萄糖(约 20%)、水解蛋白、脂肪乳剂、电解质和维生素等，而丁胺卡那霉素又是主要从肾脏排泄的药物。因此，我们原先推测病人应用 TPN 后可能会因血中高糖而引起高渗性利尿，进而增加丁胺卡那霉素的尿排泄。但从实验数据看，TPN 病人无论从尿量，还是药物肾排出率等与对照组比较，均无明显差异。这可能是因为 TPN 中含有一定量的胰岛素，或者高糖促使病人内源性胰岛素分泌增加，使 TPN 病人血糖下降，这可以从临床测定 TPN 病人血糖值均正常(<135 mg%)来加以说明。

TPN 病人静滴 200 mg 丁胺卡那霉素后，峰浓度略低于对照组，但给药 6 h 后的末端相浓度却明显高于后者。这可能是因为 TPN 病人输入大容量的高能营养剂后，造成药物体内分布容积 V_c、V_{dss} 和 V_2 明显增大，加上中央室消除速度 K_{10} 显著减小，因而使 TPN 病人的血药浓度下降比较缓慢。由于丁胺卡那霉素的耳、肾毒性与药物的分布、排泄关系密切，因此 TPN 病人药物动力学的改变有可能造成药物在上述组织中的蓄积，导致毒性反应。所以，TPN 病人尤其是肾功能下降的病人长期使用丁胺卡那霉素，应定期监测其血药浓度，以指导临床合理用药。

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薄层色谱扫描测定蒿甲醚在大鼠体内的吸收与分布[1]

姜纪荣、邹崇达[2]、束汉麟、曾衍霖 （中国科学院上海药物研究所，上海 200031，中国）

Assessment of absorption and distribution of artemether in rats using a thin layer chromatography scanning technique[1]

JIANG Ji-Rong, ZOU Chong-Da, SHU Han-Lin, ZENG Yan-Lin
(*Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai 200031, China*)

ABSTRACT TLC scanning technique was fonnd to have good specificity for studying the absorption and distribution of artemether in rats. Plasma or tissue homogenates 0.2-1.0 ml were placed in glass extraction tubes and water was added to make 1.0 ml. Each sample was extracted 3 times with 4 ml mixed organic solvent (*n*-pentane: dichloromethane = 1:1, vol:vol). The organic layers of 3 extractions were combined and evaporated. The residue was dissolved in 100-300 μl of ethylacetate and spotted on TLC plates. The chromatogram was developed in solvent system consisting of petroleum ether: chloroform: ethylacetate (4:2:1). The color developing agent was 0.25 g p-dimethylaminobenzaldehyde dissolved in a mixture of 2.25 ml 85% phosphoric acid, 47.6 ml of acetic acid and 20 ml of water.

Artemether fat emulsion was given intravenously at the dosage of 80 mg/kg. Groups of 5 rats were killed at 15, 30, 60 and 120 min after iv. The results showed that the peak tissue levels were obtained within 15 min, the drug disappeared from the blood very rapidly, and only 0.34 μg/ml was found in the plasma after 120 min. The higest level was found in brain which attained about 13.9 μg/g wet tissue 15 min after iv injection, moderate in heart, lung and skeletal muscle, whereas the levels in liver and kidney were low.

At 15, 30 and 60 min, the plasma drug concentrations were 18.5, 6.9 and 2.3 μg/ml, and the brain drug concentrations were 14.0, 8.8 and 3.4 μg/g wet tissue, respectively.

In vivo and *in vitro* experiments (Tab 2) indicated that artemether entered blood cells less than 15 min after iv injection. The ratio of blood cell/plasma artemether concentration was low, but gradually increased with time. Although the quantities of artemether trasported into the

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[1] Project supported by the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases
[2] 华东化工学院毕业实习生