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高速投射物伤合并休克脂质过氧化反应与细胞损伤的关系

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提 要 本文观察了狗软组织高速投射物伤后伤部及远位肌肉组织中脂质过氧化物（Lipid Peroxides, LPO）和超氧化物歧化酶（Superoxide Dismutase, SOD）的变化。伤后伤部肌肉匀浆、线粒体悬液和血浆LPO含量明显升高，远位组织则无变化。合并休克后伤部及远位组织LPO含量均明显升高，结果提示，脂质过氧化反应在高速投射物伤及合并休克后的细胞损伤过程中可能起重要作用。

关键词 肌；创伤和损伤；休克，出血性；过氧化脂质；超氧化物歧化酶

很多研究表明，自由基诱发的脂质过氧化反应参与创伤过程，是导致细胞损伤的重要途径之一，其作用在缺血及缺血再灌流，烧伤，大手术和机械性创伤等过程中得到了广泛的证实[1-6]。火器伤的这方面研究未见报道。

材 料 与 方 法

雄性狗16条，体重11～14kg，分为两组，每组8条。实验前禁食12h，自由饮水。实验时以3%戊巴比妥钠静脉麻醉，于室内靶道致伤，动物仰卧，将其一后肢垂直悬吊于固定架上。以五三式滑膛枪，1.03g钢球，6m射距射击股后部肌肉丰富处，避开股骨和大血管。碰击速度约1500m/s，传递能量约450J。伤道和创部以纱布压迫止血。高速钢球弹伤组伤后不做其它处理。合并休克组伤后即于股动脉快速放血使血压降至5.33kPa，并在此水平维持2h，然后于股静脉快速输入两倍于最大失血量的复方氯化钠溶液，并输回收集的失血。

于伤前及伤后不同时间以手术切取肌肉标本，标本均取自三个区，A区：距原发伤道边缘0.5～1.5cm，肌肉外观褐色，收缩力弱。B区：距伤道边缘2～3cm，外观正常，收缩力好。C区：健肢相应部位。肌肉标本制成匀浆，分离线粒体并制成悬液。按TBA荧光法测LPO[7][8]，按黄嘌呤氧化酶化学发光法测SOD[9]，按一般生化方法测肌酸磷酸激酶（CPK）、酸性磷酸酶（ACP）和组织蛋白酶（Cath-D）。结果以均数±标准差表示。差异显著性依Student t检验，进行相关分析检验。

结 果

高速钢球弹伤后伤情平稳，血压略降，体温略升，呼吸稍加快，心率、血球比积和血浆蛋白无变化。合并休克组体温下降，呼吸增快，心率无变化，复苏使血压回升至接近伤前水平，但5h后又明显降低，复苏后血球比积和血浆蛋白明显降低。伤后LPO和SOD变化见表1～4。两组血浆各酶活性均明显升高，合并休克者更剧。

相关分析表明，两组伤部LPO含量的升高与血浆酶活性的升高显著相关（两组分别$r=0.91$，0.98，$P<0.05$）。合并休克组伤部SOD活性降低程度与血浆酶活性升高显著相关（$r=-0.96$，$P<0.05$）。

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表1 高速钢球弹伤后LPO含量的变化（n = 8）

		伤前	伤后 (h)			
			0.5	2	7	12
肌肉匀浆 (nmolMDA/mg prot)	A区	0.93±0.27	1.06±0.33	1.33±0.43$^{\Delta\Delta ac}_{\Delta\Delta ac}$	1.29±0.44$^{\Delta\Delta ac}_{\Delta\Delta ac}$	1.37±0.32$^{\Delta\Delta ab}_{\Delta\Delta ab}$
	B区	〃	0.99±0.31	1.20±0.48$^{\Delta bc}_{\Delta bc}$	1.08±0.34	1.13±0.40*
	C区	〃	1.06±0.28	0.93±0.24	0.93±0.44	1.21±0.53*
线粒体悬液 (nmolMDA/mg prot)	A区	2.71±0.58	3.51±0.88$^{\Delta\Delta ac}_{\Delta\Delta ac}$	3.59±1.39$^{\Delta\Delta ac}_{\Delta\Delta ac}$	3.50±0.93$^{\Delta\Delta ac}_{\Delta\Delta ac}$	3.57±0.97$^{\Delta\Delta ac}_{\Delta\Delta ac}$
	B区	〃	3.40±0.99$^{\Delta\Delta bc}_{\Delta\Delta bc}$	3.45±0.93$^{\Delta\Delta bc}_{\Delta\Delta bc}$	3.13±1.08	3.48±1.04$^{\Delta\Delta bc}_{\Delta\Delta bc}$
	C区	〃	2.71±0.97	2.71±0.74	2.50±0.54	2.69±0.91
血浆(nmolMDA/ml)		4.02±0.89	5.36±2.29*	4.77±0.88	5.27±1.80*	5.25±1.37*

注：与伤前比较：*：$P<0.05$；**：$P<0.01$。各区间比较：$^{\Delta}$：$P<0.05$；$^{\Delta\Delta}$：$P<0.01$。表中a、b、c指A、B、C区。下同。

表2 高速钢球弹伤合并失血性休克后LPO含量的变化（n = 8）

		伤前	休克 (h)	复苏 (h)	
			2	2	5
肌肉匀浆 (nmolMDA/mg prot)	A区	0.37±0.13	0.97±0.26*	0.84±0.17	0.97±0.31*
	B区	〃	1.07±0.30**	0.99±0.17**	0.94±0.19*
	C区	〃	1.02±0.29**	1.05±0.23**	0.95±0.19**
线粒体悬液 (nmolMDA/mg prot)	A区	3.75±0.83	5.34±0.22**	4.68±1.11**	5.36±1.45**
	B区	〃	5.37±1.86**	4.74±1.17**	5.21±2.46*
	C区	〃	4.68±1.55*	5.08±1.89*	5.82±2.04**
血浆 (nmolMDA/ml)		4.05±0.61	3.13±0.53**	2.71±1.08**	1.96±0.65**

表3 高速钢球弹伤后SOD活性的变化（n = 8）

		伤前	伤后 (h)			
			0.5	2	7	12
肌肉匀浆 (u/mg prot)	A区	53.36±10.72	47.67±16.63$^{\Delta\Delta ab}_{\Delta ac}$	52.85±17.83$^{\Delta ac}$	59.42±21.06	59.95±25.80$^{\Delta ab}$
	B区	〃	61.32±12.44**	61.85±23.68	62.74±21.12	69.45±20.51*
	C区	〃	63.18±19.54*	63.62±21.61*	67.36±23.34*	70.37±23.14*
全血(u/μl)		11.01±2.46	10.43±2.66	10.49±1.76	11.00±2.79	10.72±2.40

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表4。高速钢球弹伤合并失血性休克后SOD活性的变化（n=8）

		伤前	休克(h)	复苏(h)	
			2	2	5
肌肉匀浆 (u/mg prot)	A区	54.31±12.69	39.76±14.48$^{**}_{\Delta ac}$	44.36±14.27**	45.94±11.87*
	B区	〃	40.06±15.59**	45.47±19.18	46.26±11.38*
	C区	〃	50.18±10.10	47.42±10.45	49.19±12.79*
全血(u/ul)		10.11±2.21	9.55±2.65	8.32±3.27*	5.04±2.97**

讨　论

枪弹伤由于能够准确地确定并控制能量传递，并能较好地复制，而被认为是较好的创伤模型[9]。但伤后失血较难控制，为此我们参考Wiggers失血性休克模型[11]，在伤后定量放血以造成休克，从而使伤情定量化。枪弹伤后组织细胞损伤明显，局部损伤已有较多描述[12]，全身效应表现为巨大的应激反应，伤后血浆CPK和两种溶酶体酶活性的升高是细胞损伤的标志。休克使伤情加重，细胞损伤更加明显，尤其是远离伤道的部位。

本实验中，高速钢球弹伤后局部肌肉组织和血浆LPO含量明显升高，且与血浆酶学升高显著相关，说明两者具有因果关系。结果表明损伤并不局限于外观变色的区域，外观正常的组织也受到一定程度的损伤，这在亚细胞水平表现得更加明确。脂质过氧化反应主要损伤细胞及亚细胞膜上的多不饱和脂肪酸分子，使之裂解成一系列的LPO，LPO又与膜上的酶及其它成份共价结合，导致膜完整性的破坏[13]。线粒体膜的损伤首先造成膜离子运转功能障碍，继之呼吸链受损，能量代谢紊乱。溶酶体膜的损伤导致通透性增加，酶释放，进而造成一系列继发损伤。

合并休克使损伤明显加重，三区LPO含量均显著升高，且与血浆酶活性的变化显著相关。除了钢球弹的损伤外，又加上失血这一因素。缺血缺氧使大量还原型小分子物质聚积，它们在Fe^{2+}催化下发生氧化还原反应，同时黄嘌呤脱氢酶迅速转变为氧化酶，这些都有利于氧自由基的产生。本实验仅测定了肌肉组织LPO的变化情况，有作者[14]证实重度失血性休克时心、肝、肺和胃肠等器官LPO含量明显升高，而SOD活性明显抑制，说明LPO损伤是全身性的，是细胞损伤向不可逆发展的可能机制。

SOD是机体清除氧自由基最有力的一组酶[15][16]，通过歧化反应清除自由基。一般认为创伤早期或程度较轻时SOD活性可代偿性升高，而重度损伤时多明显抑制。本实验在伤后远离伤部的健肢观察到SOD活性升高，而创伤局部则无明显变化。这可能是局部伤情较重，损伤了SOD的生成能力。合并休克后SOD活性明显抑制，这说明机体自由基清除能力的破坏，且SOD活性的下降与LPO含量的升高具有相关性，说明两者之间具有内在联系。本实验表明，脂质过氧化反应可能是创伤后细胞损伤的一个重要机制。

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Relationship between Lipid Peroxidation and Cell Damage after High-velocity Missile Trauma with or without Hemorrhagic Shock

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The relationship between lipid peroxidation and cell damage was studied in 8 dogs after they were inflicted with high-velocity missile trauma to the soft tissues of a leg and in another 8 to whom hemorrhagic shock was induced immediately after missile trauma. It was found that after trauma, the lipid peroxide(LPO) content of the muscle homogenate and mitochondria suspension of the wounded region and in plasma was markedly increased, and it had no tendency to restore to the normal until 12 hours after trauma. The increase of LPO occurred earlier in mitochondria suspension than in muscle homogenate. In addition, the activities of plasma creatine phosphokinase, acid phosphatase and cathepsin-D and of superoxide dismutase(SOD) were also increased, which was in significant correlation with LPO increase. The LPO content of the tissues of the remote regions remained un-

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changed. In the shock group, the LPO content of both the wounded region and the opposite leg was increased, which was in significant correlation with the increase of plasma enzyme activities, but SOD activity was markedly decreased.

The results suggest that lipid peroxidation plays an important role in cell damage after high-velocity missile trauma and hemorrhagic shock. SOD may be activated as a compensatory response, but it is usually inhibited in severe trauma to result in irreversible damages.

Key words: Muscles; Wounds and iujuries; Shock, hemorrhagic; Lipid peroxides; Superoxide dismutase

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and degranulation of WBC were prominent features 24 hours after injury. The basement membrane of the endothelium was broken. Type I pneumocytes became swollen and deteriorated. The lamellar bodies of Type II pneumocytes were evacuated rapidly. 48 to 72 hours after injury, these pathological changes gradually ameliorated.

The pulmonary pathology occurring after bullet-induced fracture observed in this study is similar to that of adult respiratory distress syndrome(ARDS) in character but much milder in intensity. Its prognosis is always fine. Most of the experimental animals showed no symptoms or signs of ARDS. It is concluded that severe limb trauma can induce subclinical ARDS.

Key words: Lung; Femur; Wounds and injuries; Respiratory distress syndrome, adult

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