HEMOSTASIS & COAGULATION CHANGES IN AIRLINE PILOTS

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Introduction Exposure to low frequency noise (LFN) (≤ 500 Hz, including infrasound) and the development of vibroacoustic disease (VAD) involves an abnormal proliferation of extra-cellular matrices [1]. VAD patients employed as aircraft technicians exhibit hypercoagulability, characterized by a large increase in platelet aggregation, and a dramatic decrease of euglobulin lysis time (ELT) and von Willebrandt factor (vWF) [2]. Studies of hemostasis and coagulation were subsequently conducted on two populations of military pilots: fighter pilots (LFN + G-forces), and P3-Orion aircraft crews (long-term flight + LFN). Controls were not occupationally exposed to LFN nor other types of aviation stress, and on the day of blood collection, were submitted to the same flight pattern of both fighter and P3 crews. Blood was collected immediately after flight. In all groups, platelet aggregation was increased. Fighter pilots had significant changes in PAI-1, while in controls significant changes were observed in the vWF, tPA and APTT. Control group differences were more pronounced after the shorter and more stressful flight than in the P3-Orion long-term flight [3]. To date, studies have focused on the immediate result of flight stress. Considering that airline cockpits are rich in LFN [4], this report investigates whether residual effects of cumulative flight fatigue are reflected in hemostasis and coagulation parameters, in commercial airline pilots.

Methods

Population. Thirty-one male airline pilots (ave. age 44.3 $\pm$ 9.6 yrs, range: 30-59) participated in this study with informed consent. Selection was based on individual availability and absence of any diagnosed pathology. All were on active duty and had received their periodic medical examination within the last 6 months. Blood was collected 3-5 days after flight, while the subject was at rest. Controls were 20 male office workers (ave. age: 38.8 $\pm$ 10 yrs, range: 19-60), with no signs of pathology, and not occupationally exposed to LFN.

Blood sampling and processing. Blood samples were taken by trained nurses through venipuncture, collected into tubes containing 3.2% trisodium citrate as anticoagulant. The ratio of anticoagulant to blood was 1/9 (vol./vol.). Tubes were immediately centrifuged at 3,000 g for 15 min at 4ºC, and plasmas were either tested immediately or frozen in aliquots at –70ºC until use.

Laboratory methods. Fibrinogen was measured by the method of Clauss, using STA Fibrinogen (Diagnostica Stago, Asniéres, France) as reagent, in a STA analyser. Asserachrom D-dimer (Diagnostica Stago, Asniéres, France) is an ELISA assay for the quantitative determination of D-dimer. This assay employs an anti-human D-dimer Mab (2F7) and a polyclonal anti-FDP-D. The upper limit of the reference range is 0.5 mg/L FEU. TintElize PAI-1 (biopool, Ventura, USA) is an ELISA assay for the quantitative determination of human plasminogen activator inhibitor type 1 (PAI-1). This test is based on a double antibody principle, employing a mouse anti-PAI-1 monoclonal antibody. Asserachrom vWF (Diagnostica Stago, Asniéres, France) is an ELISA assay based on the sandwich principle, using two antibodies that react against diferent antigenic determinants on the vWF molecule. This test allows a quantitative

determination of vWF. Euglobulin lysis time (ELT) - plasma was diluted and acidified, the precipitate (euglobulin) formed contained plasminogen activator (mostly t-PA), plasminogen and fibrinogen, most of the inhibitors remain in the solution. This precipitate was redisssolved and fibrinogen clotted with thrombin, and the time for clot lysis was measured. Statistical analysis was conducted using the SPSS package.

Results. Comparison among pilots and controls only yielded a statistically significant (s.s.) difference in PAI-1 (control: 12.16 $\pm$ 5.7 vs. pilots: 19.5100 $\pm$ 10.75, F=7.7877, level of significance=0.0075). Pilots were separated into two subgroups: by accumulated number of flight hours (< 9000 hrs and ≥ 9000 hrs), and by age (< 40 and ≥ 40 yrs of age). See Table I. By accumulated number of flight hours, a s.s. difference was detected in fibrinogen, D-dimer, PAI-1, and ELT. These were highly significant

Table 1. Average values of hemostasis and coagulation parameters for both pilot subgroups and statistical data. (* indicates a s.s. difference; ** indicates a highly s.s. difference.)

	< 40 yrs	**≥ 40 yrs**	**F**	**< 9000 hrs**	**≥ 9000 hrs**	**F**
	(Ave $\pm$ SD)			**(Ave $\pm$ SD)**		
Fibrinogen (mg/dL)	238.4 38.2	299.0* 53.6	12.9070 0.0012	231.23 35.82	297.50** 50.61	16.3052 0.0004
V.Will.Factor: ag (%)	98.46 25.09	106.7 24.1	0.8772 0.3567	97.00 26.63	106.88 22.80	1.2335 0.2758
Ddimer (ng/mL)	99.35 35.02	200.40** 91.67	14.9415 0.0006	93.83 34.54	192.41* 88.75	13.2620 0.0011
PAI 1: ag (ng/mL)	13.45 9.27	24.81* 9.20	11.2942 0.0023	11.06 7.46	25.13** 8.79	20.7056 0.0001
Euglob Lysis Time (min)	148.0 58.9	177.1 36.7	2.7265 0.1064	133.06 49.20	184.16* 40.08	9.8332 0.0039
Platelets	243615.38 20724.37	219466.66 42676.30	2.9830 0.0960	239090.90 26901.50	225235.29 43975.17	0.8732 0.3587
Hematocrit (%)	45.33 2.25	44.72 2.32	0.4758 0.4967	45.10 2.39	44.95 2.25	0.0308 0.8621

for fibrinogen and PAI-1. By age, a s.s. difference was detected in fibrinogen, D-dimer, and PAI-values, but not ELT. Despite the existence of s.s. differences among some parameters, most values were within the normal range with the exception of PAI-1, where normal is considered 18 $\pm$ 10 ng/mL. No s.s. differences were detected among any of the parameters when the pilots were divided by smoking habits or flight profile.

Discussion. The number of accumulated flight hours is a more powerful discriminator than age. Airline pilots appear to have a situation of fibrinolysis for which PAI-1 seems to be a good indicator. The values of other parameters, such as fibrinogen, D-dimer, and ELT increased with accumulated flight time. These values are an aggravating factor for decreased flow within the vessels, already thickened due to extra-cellular matrix proliferation caused by occupational exposure to LFN. The implications of the results herein concerning after flight, deep-venous thrombosis ("economy-class syndrome") seem non-trivial.

Keywords: low frequency noise, vibroacoustic disease, PAI-1, deep-venous thrombosis

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