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RECENT ADVANCES IN DOPING ANALYSIS (11)

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EXCRETION STUDIES WITH HYDROXYETHYL STARCH

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Introduction

Hydroxyethyl starch (HES) was included in the Olympic Movement Anti-Doping Code List of Prohibited Substances [1] in January 2000, and since Thevis et al. introduced screening [2] and confirmation methods [3] for the analysis of HES in urine, the analysis has been implemented for routine doping control samples. The aim of this work was to study several aspects of the administration of HES, performance enhancing capacity, effects on haematological parameters and excretion time.

Experimental

Seven healthy male volunteers were administered HES (500 ml Haes-Steril 100 mg/ml, Fresenius Kabi, Norway) and placebo (500 ml NaCl 9 mg/ml, Pharmacia & Upjohn, Norway) in a randomised, double blind, cross-over study. The volunteers were moderately to well-trained amateurs.

The possible performance enhancing capacity of volume loading with either HES or NaCl was examined by measuring maximal aerobic capacity (VO_2max) before and 4 hours after the administration of HES and NaCl, respectively.

Blood samples were collected before and 2 hours after the administration to evaluate the effects of the administration of HES and NaCl on the following haematological parameters: haemoglobin (Hb), haematocrit (Hct), total protein, albumin, EPO, and soluble transferrin receptor (sTfR).

Urine samples were collected every day for the first 7 days after administration and then every second or third day for up to 18 days after the administration. The amount of HES in the samples was measured by a semi-quantitative approach applying the screening method previously published by Thevis et al. [2]

Results and conclusion

In Figure 1 the change in VO_2max after administration of HES and NaCl respectively is presented. No significant difference in performance enhancing capacity after administration of HES (Students T-test, p=0.142) or NaCl (Students T-test p=0.199) could be demonstrated in this study and VO_2max remained unchanged after the administration of both HES and NaCl. The results are in agreement with the results from Warburton et al.[4] and references therein, who found that in well-trained endurance athletes, plasma volume expansion did not result in any further improvements of VO_2max.

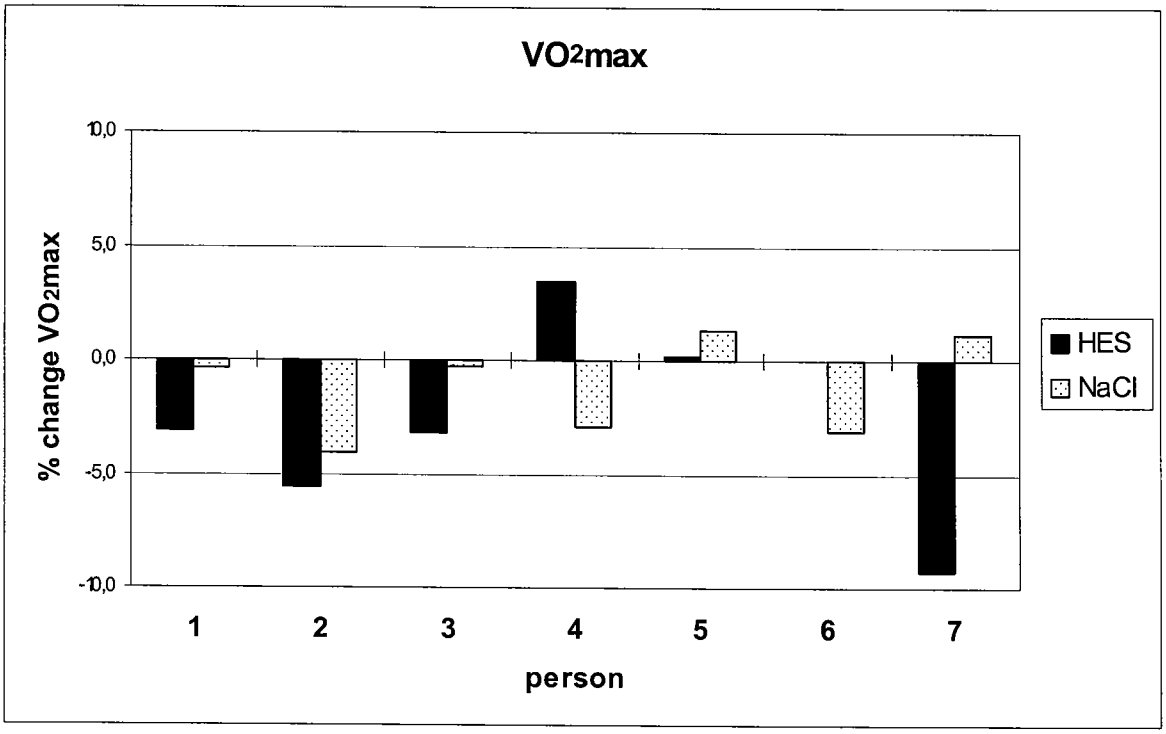

Figure 1. Change in maximal aerobic capacity (VO_2max) after administration of HES and NaCl respectively.

In Table 1 haematological parameters before and after the administration of HES and NaCl are presented. The concentration of Hb, total protein and albumin were significantly decreased following administration of HES. Hct, sTfR and EPO remained unchanged or the

change was not significant after HES administration. None of the haematological parameters changed significantly after administration of NaCl.

Table 1. Haematological parameters before and after the administration of HES and NaCl (mean values from the 7 volunteers).

	HES		NaCl	
	Before	After	Before	After
Hb (g/dL)	14.8 ± 0.63.7	13.9 ± 0.9*	14.6 ± 0.7	14.3 ± 0.7
Hct	0.4 ± 0.1	0.4 ± 0.1	0.4 ± 0.1	0.4 ± 0.1
Total protein (g/L)	74 ± 3.2	67 ± 2.2*	76 ± 2.0	75 ± 2.5
Albumin (g/L)	44 ± 2.5	40 ± 2.0*	45 ± 1.9	44 ± 2.4
sTfR (mg/L)	2.4 ± 0.8	2.1 ± 0.4	2.4 ± 0.6	2.2 ± 0.6
EPO (IU/L)	8.7 ± 3.3	8.5 ± 2.1	10.8 ± 3.7	10.8 ± 4.0

*Significant change ($p<0.05$)

Analysis of the urine samples revealed that the excretion of HES varied strongly from one subject to the other, both with regard to maximum concentration and detection time. The detection time of HES varied from 8 to at least 18 days and the maximum concentration in urine ranged from 1 to 75 mg/ml in the different volunteers. Excretion study curves are presented in Figure 2. The limit of detection for the most abundant hydrolysis product, α-2-Hydroxyethylglucose (2-HEG), in urine was 0.1 mg/ml.

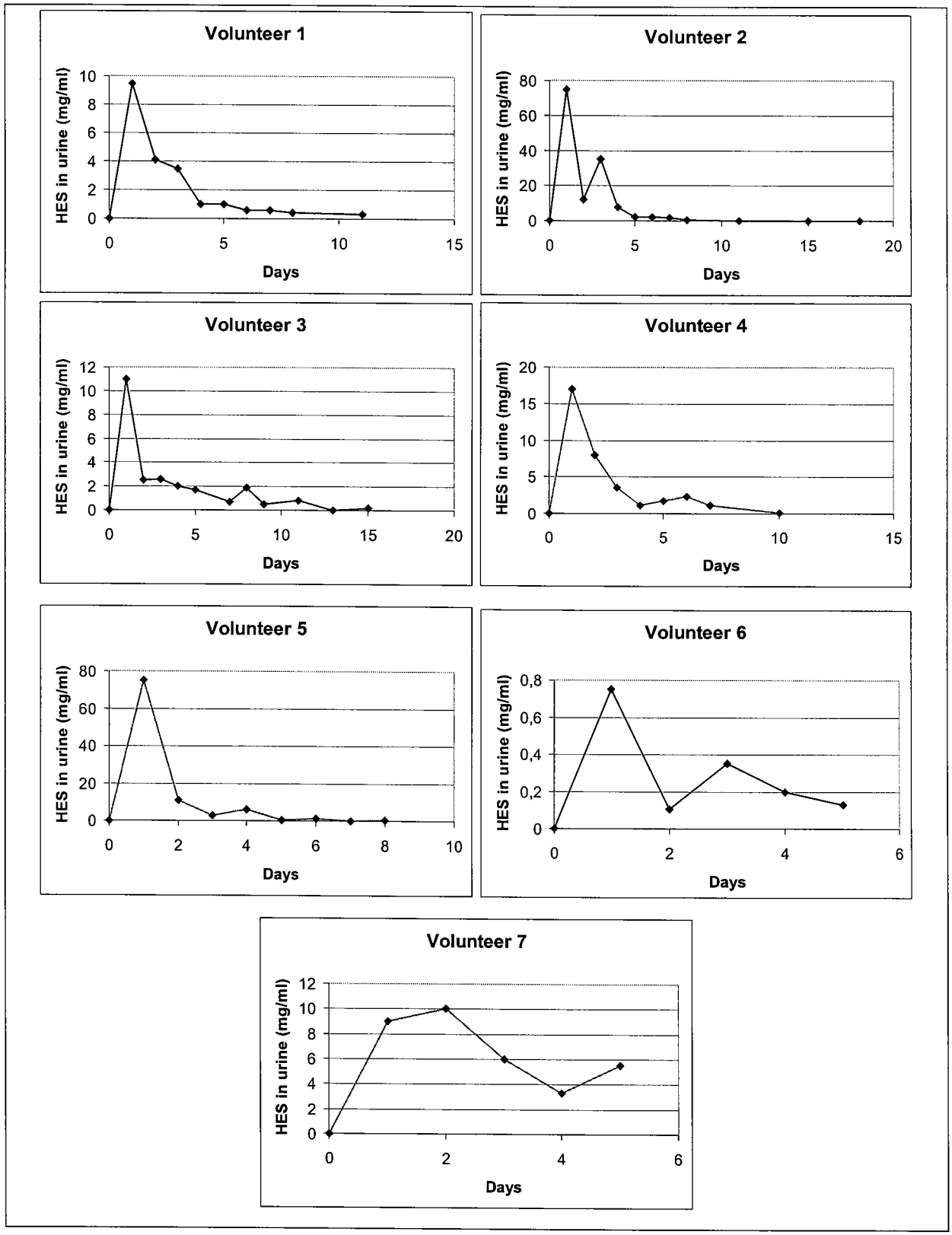

Figure 2. Excretion study curves from 7 volunteers after administration of 500 ml of a 100 mg/ml HES- solution. The ion trace of *m/z* 261 from α-2-HEG (2-Hydroxyethyl-glucose-penatkis-TMS) was used for determination of HES-concentration.

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