In Table 2 the functional parameters of cardiac output at a moderate LV filling pressure of 10 cm H_2O are presented. Coronary flow and cardiac output were estimated to reach 44 and 55% of the pre-ischemia level, respectively, in 45 min after the reperfusion. Mean aortic pressure was shown to recover to 51%, while experimental cardiac output reached only 33% of the initial level.

The functional parameters of the hearts subjected to ischemia in BDM-containing cardioplegic solution were higher as compared to the controls. The restoration of minute volume as well as of external cardiac output increased by 19%. Mean aortic pressure and coronary flow exceeded the control level by 18 and 25%. Better restoration of minute volume and external cardiac output was detected in the entire range of volume loadings (see Fig.1)

Cardioplegic solution is known to arrest contractile function before ischemia and, therefore, to reduce the outlay of energy significantly. Nevertheless, BDM addition has an additional protective effect possibly due to its ability to inhibit ATPase activity. At least the degree of the reduction of ATPase activity of the normal heart under the influence on BDM (29%) is similar to the degree of the enhancement of pump heart function (19%).

Based on these facts, the addition of BDM to cardioplegic solution seems to reduce the disintegration rate of adenine nucleotides during ischemia.

LITERATURE CITED

1. E.M.Blanchard, L.A.Mulieri, and N.R.Alpert, *Biophys.J.*, **45**, 48a (1984).
2. E.M.Blanchard, G.L.Smith, D.G.Allen *et al.*, *Pflugers Arch.* **416**, p. 219-221 (1990).
3. M.W.Fruer, I.R.Neering, and D.G.Stephenson, *J.Physiol.*, **407**, 53-75 (1988).
4. S.E.Harding, G.Vescovo, M.Kirby, *et al.*, *J.Molec.Cell Cardiol.*, **20**, 635-647 (1988).
5. E.J.Hartree, *Analyt.Biochem.*, **48**, 422-427 (1972).
6. K.Horiuti, H.Higuchi, Y.Umazume, et al., *J.Musc.Res.Cell.Motility*, **9**, 156-164 (1988).
7. T.Li, N.Sperelakis, R.E.Teneick, *et al.*, *J.Pharmacol.Exp.Ther.*, **232**, 688-695 (1985).
8. H.E.Morgan, B.H.L.Chua, E.O.Fuller, *et al.*, *Amer.J.Physiol.*, **238**, E431-E442 (1980).
9. H.E.Morgan, Y.Kira, and E.E.Gordon, *Europ.Heart J.*, **4**, 141-146 (1984).
10. W.G.Nayler, J.S.Elz, and D.J.Buckley, *Amer.J.Phisiol.*, **254**, H678-H685 (1988).
11. V.A.Saks, R.Ventura-Clapier, Z.A.Huchua, *et al.*, *Biochim.Biophys.Acta*, **803**, 254-264 (1984).

0007-4888/93/0001-0052$12.50 ©1993 Plenum Publishing Corporation

Solcoseryl: Ulcerostatic Effect and Its Possible Mechanisms

M. M. Rasulov, I. G. Kuznetsov, L. I. Slutskii, A. G. Zabozlaev, and M. G. Voronkov

UDC 616.832-004.2-07:616.153.96-097-078.33

Translated from *Byulleten' Experimental'noi Biologii i Meditsiny*, Vol. 115, No. 1, pp. 49-51, January, 1993
Original article submitted July 5, 1992

Key Words: *solcoseryl; collagen; noncollagen proteins; stomach ulcer; repair*

Currently solcoseryl, a Swiss-Yugoslav preparation, has become a widespread agent to treat wounds of various origin. However, the mechanism of its action remains obscure.

It has been established that ulcer progression is determined by the state of the connective tissue and its components [2, 3, 7]. The balance of the latter at various stages of ulcer formation and during treatment with therapeutic agents characterizes intimate aspects of ulcerogenesis and the mechanisms of action of ulcerostatic preparations. The aim of the present study was to elucidate the dynamics of the connective tissue components in the formation of stomach ulcer and to analyze the effect of solcoseryl under experimental conditions.

MATERIAL AND METHODS

All experiments were carried out on albino laboratory rats of body weight 150-180 g. Stomach ulcer was induced by the acetate method [8]. Starting from the first day of the experiment the animals received solcoseryl intraperitoneally (2 mg/kg x 24 h). Euthanasia of the groups (n=10) was performed after 7, 14, and 28 days. The stomach was excised and the ulcer area was measures. The ulcerated tissue

Research Institute of the Meat Industry, Russian Academy of Agricultural Sciences, Moscow; Irkutsk Institute of Organic Chemistry, Siberian Department of Russian Academy of Sciences, Irkutsk (Presented by Academician D. S. Sarkisov, of the Russian Academy of Medical Sciences)

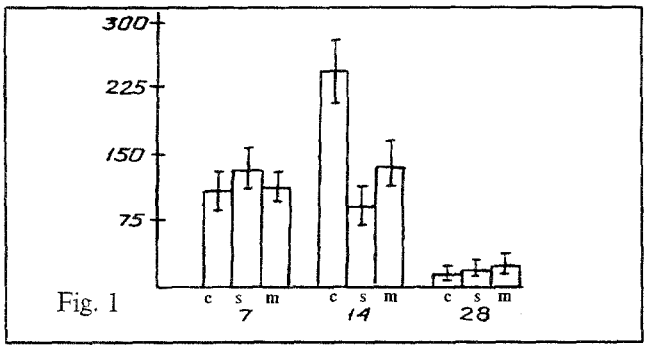

Fig. 1

Fig. 1. Change in the area of induced acetate stomach ulcer in rats. Abscissa: healing period of ulcer injury (in days); ordinate: area of ulcer injury (mm^2). C: ulcer area in control animals; S: ulcer area in animals treated with solcoseryl; M: ulcer area in animals treated with methyluracil.

was excised and placed in liquid nitrogen to prepare for the assay of connective tissue components.

The level of DNA. RNA, hydroxyproline, hydroxylysine, tyrosine, arginine, hexoses, hexosamines, hexuronic acids in the stomach sections was determined in each group by a quantitative method by us in detail earlier [4-6].

The effect of solcoseryl was compared with that of methyluracil, which was applied *per os* in a dose of 500 μg/kg x 24 h daily starting from the first day of the experiment [1].

Similar experiments on untreated animals served as the control. Investigations on intact rats served as a reference. Statistical analysis of the data was performed according to Student's test.

TABLE 1. Dynamics of Biochemical Indexes of Tissue from Induced Untreated (Control) Stomach Ulcer (g/100 g Dry Fat-Free Tissue, M±m)

Index	Days			
	Reference	7	14	28
DNA	4.25±0.11	4.35±0.07	4.39±0.06	4.01±0.00
RNA	0.98±0.05	1.11±0.01	1.07±0.07	1.50±0.05
Hydroxyproline	1.51±0.02	1.44±0.04	1.93±0.02	1.65±0.02
Hydroxylysine	0.32±0.01	0.32±0.01	0.32±0.01	0.25±0.01
Tyrosine	2.64±0.05	2.41±0.03	2.55±0.02	2.48±0.02
Arginine	3.88±0.21	3.55±0.02	4.45±0.14	4.25±0.24
Hexosamines	1.28±0.03	1.37±0.01	1.42±0.03	1.61±0.05
Hexoses	3.58±0.04	3.79±0.05	3.73±0.09	4.21±0.05
Hexuronic acids	0.73±0.02	0.75±0.01	0.66±0.02	0.73±0.01
0.4 M	0.49	0.42	0.32	0.41
1.2 M	0.19	0.24	0.28	0.24
2.1 M	0.05	0.09	0.06	0.08
Sialic acids	0.39±0.01	0.70±0.04	0.59±0.01	0.52±0.01

Note: GAG: mg of hexuronic acids/100 g tissue.

TABLE 2. Dynamics of Biochemical Indexes of Tissue from Induced Stomach Ulcer under Solcoseryl Effect (g/100 g Dry, Fat-Free Tissue, M±m)

Index	Days		
	7	14	28
DNA	3.90±0.09*	4.55±0.06	3.85±0.05*
RNA	0.89±0.05*	0.09±0.04	1.05±0.04*
Hydroxyproline	1.44±0.02	1.76±0.02*	1.48±0.04*
Hydroxylysine	0.35±0.01	0.32±0.00	0.23±0.02
Tyrosine	2.30±0.06	2.42±0.46	2.34±0.05*
Arginine	3.52±0.13	4.10±0.17	4.44±0.16
Hexosamines	1.18±0.03*	1.48±0.05	1.31±0.01*
Hexoses	3.88±0.07	3.68±0.07	4.08±0.07
Hexuronic acids	0.82±0.02*	0.68±0.01	0.75±0.02
GAG fractions:			
"0.4 M"	0.46	0.33	0.45
"1.2 M"	0.26	0.28	0.21
"2.1 M"	0.10	0.07	0.09
Sialic acids	0.58±0.01*	0.66±0.01	0.51±0.01

Note: Asterisk indicates values $p<0.05$ as compared with the control.

RESULTS

Morphometric analyses revealed that solcoseryl considerably altered the progression of induced acetate ulcer of the stomach (see Fig. 1). A juvenile granulation tissue was found to be formed in the ulcer tissue of the control group 7 days after the operation, and fibrous tissue with hyalinosis was observed to appear by the end of a chronic ulcer. Methyluracil and solcoseryl application accelerated healing of the induced ulcer and prevented it from becoming chronic.

The biochemical indexes of ulcerogenesis were as follows. the content of hexuronic acids in the ulcerated tissue of the control animals in the final stages of the study was closest to the reference (Table 1). By the end of the observations the level of hexuronic acids, as well as of the GAG fractions, was close to the reference in the group of animals that received solcoseryl (Table 2).

Collagen concentration was the most important index of the development of granulation-fibrosis tissue. It decreased due to collagen destruction at the stage of stomach ulcer formation in the control experiments, and then was followed by collagen accumulation, thus indicating tissue fibrosis. The level of the noncollagen proteins was even higher. As a result, the scar tissue exhibited an excess of collagen and a deficit of noncollagen proteins. The level of hexoses in the stomach remained practically unchanged, which is indirect evidence that secretory activity of the stomach is preserved at a certain level. Thus, ulcer progression

in the control group is accompanied by a stable functioning of the glandular tissue. It can play a negative role at a certain stage of ulcerogenesis, hindering the repair process.

Solkoseryl was found to have an effect on ulcer progression: the level of collagen proteins, as well as DNA and RNA, was more stable, which ultimately had an impact on the healing rate of ulcer injury.

A comparative analysis of the ulcerostatic effects of solcoseryl and methyluracil showed a considerable similarity in the mechanism of action of these preparations. However, solcoseryl is likely to inhibit the secretory function of the stomach much more than methyluracil. Earlier we extensively studied the effect of methyluracil on the biochemical indexes of stomach tissue in induced acetate ulcer [2, 3]. Therefore a comparative analysis was not performed. However it should be noted that the dynamics of stomach ulcer progression under the influence of secret and methyluracil exhibited some distinctions, although a certain similarity was also observed. This allows us to assume that only a certain similarity is observed in the mechanisms of the ulcerostatic effect of the preparations mentioned.

Thus, the dynamics of DNA and RNA, collagen, noncollagen proteins, hexoses, and glycosaminoglycans indicates their role in the pathogenesis of induced acetate ulcer of the stomach and allows one to estimate the various components of the mechanism of ulcerostatic action of solcoseryl.

LITERATURE CITED

1. I.K.Asalyuk and P.P.Zhdan, *Vrach. Delo*, No. 3, 24-28 (1980).
2. I.G.Kuznetsov, M.M.Rasulov, L.I.Slutskii, and M.G.Voronkov, *Izv. Akad. Nauk SSSR, Ser. Biol.*, No. 3, 343-352 (1991).
3. M.M.Rasulov, I.G.Kuznetsov, A.A. Belousov, L.I.Slutskii, M.G.Voronkov, *Dokl. Akad. Nauk SSSR*, **313**, No. 2, 501-505 (1990).
4. L.I.Slutskii, Rheumatism (Cells and Colloids, Correlations and Patterns) [in Russian], Riga (1966), pp. 284-297.
5. L.I.Slutskii, Biochemistry of Connective Tissue [in Russian], Leningrad (1969).
6. L.I.Slutskii, *Izv. Akad. Nauk Latv.SSR*, **408**, No. 7, 94-108 (1981).
7. A.Chocha and J.Chmiel, *Diagn. Lab.*, **7**, No. 4, 65-71 (1971).
8. K.Takagi, S.Okabe, and R.Saziki, Japan J. Pharmacol., No. 19, 899-906 (1969).

0007-4888/93/0001-0054$12.50 ©1993 Plenum Publishing Corporation

Nootropic Drugs Potentiate the Nerve Cell Responses Evoked by Activation of the NMDA-Glutamate Receptors

I.I.Abramets, P.V.Andreev, I.V.Komissarov, I.M.Samoilovich, and A.V.Titievskii

UDC 616.8-018.1-02:615.214.3:547.745]-07

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 115, No. 1, pp. 51-53, January, 1993
Original article submitted June 30, 1992.

Key Words: *nootropic drugs; glutamate receptors; sections of rat brain*

The specific effect of nootropics is determined to a great extent by their influence on nerve cell bioenergetics as well as their membrane-stabilizing action conditioned by lipid peroxidation inhibition, accelerated phosphatide circulation and the suppression of free-radical processes [2]. The Neurotransmitter mechanisms of the antiamnestic effect have been less studied [2], but it has been established that blockade of NMDA-glutamate receptors weakens the behavioral effects of nootropic drugs [8,9], while aniracetam increases the excitatory postsynaptic potentials (EPSP) amplitude in pyramidal neurons of the CA1 field, caused by stimulation of the radial layer of rat huppocampus sections [10]. Since EPSP of these neurons can be a result of activation of both N-methyl-D-aspartate (NDMA) and non-NMDA-receptors [6], it is not clear which kind of glutamate receptors is involved in the aniracetam effect described. In experiments on frog oocytes with expressed excitatory amino acids by injection of rat brain mRNA it was found that aniracetam intensifies the transmembrane currents caused by quisqualate and AMRA [7]. Meanwhile, piracetam strengthens the aspartate and glutamate influence on the spinal motoneurons, affecting

Department of Pharmacology with Clinical Pharmacology, M.Gorky Donetsk Medical Institute
(Presented by Academician D.A.Kharkevitch, of the Russian Academy of Medical Sciences)