

COMPARATIVE STUDY OF THE ANTIPYRETIC
ACTION OF AMINOPYRINE AND SODIUM SALICYLATE
WHEN GIVEN BY THE INTRAVENTRICULAR AND
INTRACISTERNAL ROUTE

N. A. Kalinina

UDC 615.212.3.032.81

The antipyretic action of aminopyrine and sodium salicylate when administered by different methods to rabbits with fever were studied. After systemic administration of these antipyretics in equal doses, aminopyrine was more effective at reducing fever, but when injected into the brain, on the contrary, aminopyrine had a weaker action. Comparison of the action of pyrogens and antipyretics when injected into different parts of the cerebrospinal fluid system shows that the points of application of pyrogenic and antipyretic stimuli for their central action do not coincide exactly.

KEY WORDS: salicylates; methods of administration; fever.

Experiments have shown [4-7] that the injection of sodium salicylate into the lateral ventricles of the brain of febrile animals and also into structures sensitive to pyrogens produces an antipyretic effect. There is no information in the literature on the effect of intracerebral injection of other aromatic antipyretics.

This paper describes a study of the action of two members of this group (sodium salicylate and aminopyrine) when injected intracisternally and into the lateral ventricles of rabbits with fever.

EXPERIMENTAL

Experiments were carried out on 52 rabbits weighing 2.8-3 kg. Fever was induced by the injection of pyrogenal either into a lateral ventricle (0.1 μ g) or intravenously (1 μ g/kg). Aminopyrine and sodium salicylate (2 mg in a volume of 0.1 ml) were injected into the lateral ventricle through previously implanted cannulas [2] or into the cisterna magna through a needle after infiltration of the soft tissues with procaine.

RESULTS

After injection of pyrogenal into the lateral ventricle the rabbits developed a marked febrile reaction that reached a maximum after 4-5 h (Fig. 1, curve 1). Aminopyrine, injected in the third hour of this fever into the lateral ventricle, did not significantly lower the body temperature (Fig. 1, curve 2), whereas sodium salicylate had a distinct antipyretic action (Fig. 1, curve 3).

After intravenous injection of pyrogenal the fever was much shorter in duration and reached a maximum after 3 h (Fig. 2, A and B, curves 1). In this period of the febrile reaction both the antipyretics used lowered the body temperature whether injected into the lateral ventricle or into the cisterna magna; aminopyrine had a somewhat less marked and shorter action than sodium salicylate.

Febrile reactions developing both after intracerebral and after systemic injection of pyrogens are known to have common basic pathogenetic mechanisms, but do differ sharply in the duration of their course. For instance, after intraventricular injection of pyrogens the fever lasts up to 24 h, whereas after their

Laboratory of General Pathophysiology, Division of General Pathology, Institute of Experimental Medicine, Academy of the Medical Sciences of the USSR, Leningrad. (Presented by Academician of the Academy of Medical Sciences of the USSR P. N. Veselkin.) Translated from *Byulleten' Éksperimental'noi Biologii i Meditsiny*, Vol. 78, No. 12, pp. 45-47, December, 1974. Original article submitted January 21, 1974.

© 1975 Plenum Publishing Corporation, 227 West 17th Street, New York, N.Y. 10011. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, microfilming, recording or otherwise, without written permission of the publisher. A copy of this article is available from the publisher for \$15.00.

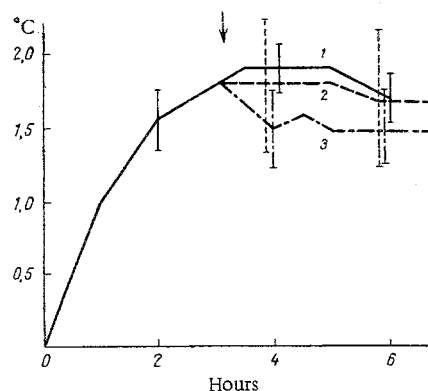


Fig. 1. Effect of aminopyrine and sodium salicylate given by intraventricular injection on the course of centrogenic fever: 1) temperature curve after intraventricular injection of pyrogenal; 2) the same after additional injection of aminopyrine; 3) the same after additional injection of sodium salicylate. Arrow marks injection of aminopyrine or sodium salicylate. Vertical lines represent confidence limits. Abscissa, time after injection of pyrogenal (in h); ordinate, rise of temperature (in deg).

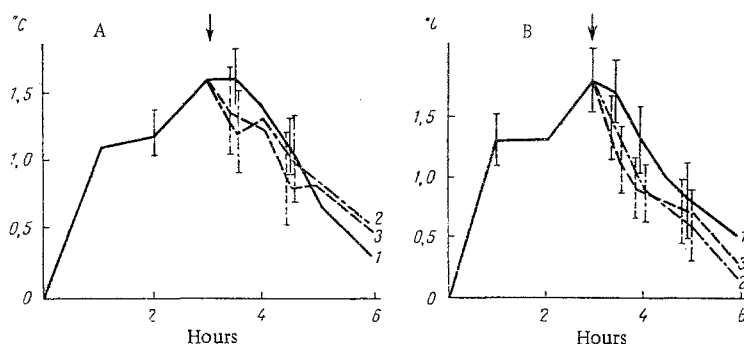


Fig. 2. Effect of intraventricular and intracisternal injection of aminopyrine (A) and sodium salicylate (B) on the course of fever induced by intravenous injection of pyrogenal: 1) temperature curves after intravenous injection of pyrogenal; 2) the same after additional intracisternal injection of aminopyrine (A) or sodium salicylate (B); 3) the same after additional intraventricular injection of aminopyrine (A) or sodium salicylate (B). Remainder of legend as in Fig. 1.

intravenous injection it lasts only for up to 6 h. Naturally, all phases of fever are of longer duration after intraventricular injection of pyrogens. The sensitivity to antipyretics varies in the different phases of fever: it was much lower during the period when the body temperature was rising than when it was falling [1]. In these experiments injection of the antipyretics in the third hour of centrogenic fever coincided with the rising phase of the body temperature, i.e., the phase of low sensitivity to antipyretics. This could be why the antipyretic action of aminopyrine could not be demonstrated in these experiments.

During the period of falling body temperature (in the third hour of fever induced by intravenous injection of pyrogenal) aminopyrine was effective.

Both antipyretics thus caused the body temperature to fall when injected by the intracerebral route, but under these conditions aminopyrine had a weaker action than sodium salicylate. When given by subcutaneous injection, on the other hand, aminopyrine was more effective; a roughly equal antipyretic effect in febrile rabbits was produced by aminopyrine in a dose of 20 mg/kg and sodium salicylate in a dose of 100 mg/kg.

These two antipyretics evidently differ considerably in the character of their metabolism in the body; other differences in the mechanisms of action of these substances may also exist.

Data in the literature [3] and the writer's own experiments shows that a more intensive febrile reaction develops after the injection of pyrogens into the ventricles of the brain than into the cisterna magna. The antipyretic action of aminopyrine and sodium salicylate, however, was equal in intensity when given by the two methods. This fact contradicts the view that the points of application of the central action of pyrogenic and antipyretic stimuli are completely identical.

LITERATURE CITED

1. L. N. Bystrova, in: *Physiological Mechanisms of the Febrile Response* [in Russian], Leningrad (1957), p. 197.
2. I. S. Repin and A. V. Sorokin, *Pat. Fiziol.* No. 4, 47 (1965).
3. M. D. Khudaiberdiev, A. I. Anisimov, and E. M. Belyavskii, *Pat. Fiziol.*, No. 1, 78 (1970).
4. W. G. Clark and M. T. Alderdice, *Proc. Soc. Exp. Biol. (New York)*, 140, 399 (1972).
5. W. J. Cranston, M. D. Rawlins, and C. Rosendorff, *J. Physiol. (London)*, 206, 19 (1970).
6. W. J. Cranston and M. D. Rawlins, *J. Physiol. (London)*, 215, 27 (1971).
7. W. J. Cranston and M. D. Rawlins, *J. Physiol. (London)*, 222, 256 (1972).