CLINICAL EXPERIENCE WITH A NEW THERAPEUTIC PRINCIPLE IN PIGS: THE ß-RECEPTOR BLOCKER CARAZOLOL

W. Bartsch*, K. Vollers, G. Sponer, B. Müller-Beckmann and K. Strein
Med. Forschung, Boehringer Mannheim GmbH and Praemix Wirkstoff GmbH
Sandhofer Straße 116, D-6800 Mannheim 31, Federal Republic of Germany

ß-receptor blocking agents (synonym: ß-sympatholytics) are drugs which have been tested since the 60s for therapeutic and prophylactic use in various cardiovascular diseases in man (e.g. angina pectoris, arrhythmias, and myocardial infarction).

The effective cardioprotective properties of ß-blocking agents in experimental models [4] and in man [10] inspired us in 1977 to use these drugs for the prophylaxis and therapy of various disorders characterized by cardiac overload and metabolic derangement in animals [3]. These disorders are caused by high epinephrine levels in stress situations. This hormone induces - mainly by binding to ß-receptors - rapid glycogenolysis, increased heart and respiratory rates. These stress reactions are extremely critical in pigs. Due to the large muscle volume, the production of lactate by glycolysis is very fast and leads to a decrease of blood pH and to an increase in body temperature. The results are weight-loss and poor meat quality (PSE).

The ratio of systole to diastole in the cardiac cycle in pigs is nearly 1. Increased heart frequencies reduce the duration of diastole, the nutrition phase of the heart muscle. Sudden heart death is a frequent consequence. Conversely a reduction of heart rate prolongs diastole resulting in improved cardiac metabolism.
Thus the prophylatic administration of a ß-blocking agent is able to diminish considerably the economic losses caused by stress reactions.
First investigations in dogs [7], horses [8], and exotic species (not yet published) confirmed the beneficial effects of reduction of cardiac overload.

Carazolol is a ß-blocking agent with an extremely high potency [2, 9 etc.]. The dosage in pigs is 1 mg/100 kg i.m. The metabolism is very rapid and the potency on oral administration only 10 %. Investigations on residues in pigs of the 10 mcg/kg i.m. dose have been published [5].

Carazolol (Suacron^{R})★ has been used in pigs for the following indications.

1. Transport of pigs to the slaughter house in the Netherlands and Belgium

	Number of animals	Dead animals %	Rejected %	Poor meat quality %
Controls	4,849	0.62	1.52	0.91
Carazolol	5,818	0.05 **	0.67 **	0.62 *

significance: * $p < 0.05$
** $p < 0.001$

2. Improvement of meat quality

In separate investigations in Italy [1] and in England, specific studies on meat quality showed that carazolol considerably improved the meat quality of stress-sensitive pigs and reduced the occurrence of PSE [WARRIS and LISTER, not yet published].

★ Trade mark of PRAEMIX Wirkstoff GmbH (Germany)
The drug is available in Belgium, France, Germany, Netherlands, Philipines and Spain.

3. Transport of weaned piglets in Germany

	Number of animals	Death rate %
Controls	1,633	2.2
Carazolol	2,079	0.05 **

4. Boars and sows during mating

Increased heart rates of breeding boars occasionally lead to death during or shortly after mating. In untreated boars (n = 9) the heart rate rose from 119 ± 2 to 180 ± 9 beats/min. Carazolol-treated boars (n = 9) showed only an acceleration from 116 ± 2 to 135 ± 2 beats/min.

5. Sows during farrowing

In sows with overtaxed circulation during farrowing with tachycardia and tychypnoea, carazolol produced a reliable reduction of the cardiac and respiratory rates [6].

n = 21	Heart rate	Respiratory rate
Initial values	122 ± 7	77 ± 4
After carazolol	78 ± 4 **	46 ± 3 **

Particularly striking is the fact that out of 23 almost moribund sows 20 survived. Measurements were not possible in 2 animals, so the results of 21 sows are given in the table.

ACKNOWLEDGEMENTS:
We should like to thank the following Doctors for their assistance, or for providing us with their results: R.Hooper; P.Lexa; D.Dister; W.Schmidt; W.J.H.Verstraaten; D.Wengert; W.Woerner

REFERENCES:

1. BALLARINI,G.; F.GUIZZARDI:
Tierärztl. Umschau 36,3,171-180 (1981)
2. BARTSCH,W.; K.DIETMANN; H.LEINERT; G.SPONER:
Arzn.-Forsch./Drug Res. 27(I),5,1022-1026 (1977)
3. BARTSCH,W.:
Vortrag Baden-Württembergischer Tierärztetag Sindelfingen, 07.05.1977
4. BARTSCH,W.; G.SPONER; K.DIETMANN; M.KOHLER:
Arzn.-Forsch./Drug Res. 31(II),1885-1888 (1981)
5. BARTSCH,W.;K.KOCH;K.VOLLERS;G.SPONER;K.DIETMANN:
Elsevier Scientific Publishing Company, Amsterdam-Oxford-New York, p.322-323 (1980)
6. FIEBIGER,E.u.K.; K.J.NITZ; K.VOLLERS; W.BARTSCH:
Tierärztl. Umschau 33,10,531-536 (1978)
7. GASTAUER,R.:
Tierärztl. Umschau 33,5,259-262 (1978)
8. HEPTNER,B.:
Tierärztl. Umschau 34,5,338-342 (1979)
9. INNIS,R.B.; F.M.A.CORREA; S.H.SNYDER:
Life Sciences 24,2255-2264 (1979)
10. The Norwegian Multicenter Study Group
New Engl.J.Med. 304,801-807 (1981)

For further references or test samples contact
Dr. W. Bartsch, Sandhofer Str.116, Post Box 31 01 20
D-6800 Mannheim 31, Germany