The effect of monensin in the control of transmissible gastroenteritis (TGE) of pigs

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Summary— *Monensin sodium, an ionophore polyether antibiotic, has shown efficacy in controlling certain viral infections. We investigated the effect of monensin sodium in moderating the losses of an epidemic outbreak of transmissible gastroenteritis virus (TGEV) in an immunologically naive swine herd. An epidemic of TGEV occurred on a continuous-far-rowing, large industrial pig farm that had no previous exposure to TGEV. Monensin at the dosage of 100 ppm was used in creep feed and weanling pig diets until 2 months of age and in the gestation and lactation diets. Preweaning mortality in pigs <1 week of age was reduced for litters of the sows that received monensin (20.0%) compared to the control group (57.2%), and total piglet mortality up to the age of 60 days was lower for the monensin group (24.8%) compared to the control group (73.9%). We conclude that monensin was very effective in reducing preweaning mortality during this TGE epidemic.*

Transmissible gastroenteritis (TGE) is a contagious enteric disease that usually results in severe diarrhea, vomiting, dehydration, and high neonatal mortality. Although pigs of all ages are susceptible to this viral infection, mortality is generally much lower in postweaning pigs. Epidemic TGE in non-immune herds can result in serious economic losses.[1-3] In 1946, major epidemics of TGE occurred in the United States and, in early 1960, in many areas of Europe and other parts of the world. The disease seems to reappear at 5-year intervals, perhaps because older, immune sows are being replaced by susceptible gilts, leaving the bulk of the swine population non-immune.[3,4] The epidemiologic picture appears to have changed in recent years as TGE has become endemic, because sows that are naturally infected with TGE virus (TGEV) build up an active immunity and effectively protect their litters.

TGE is caused by a virus that belongs to the genus *Coronavirus* of the Coronaviridae family. At present, the swine industry lacks a completely efficacious vaccine. There are also no effective methods to control and/or treat the disease to reduce losses during a new epidemic in non-immune herds. At present, producers and practitioners attempt to mitigate the negative effects of TGEV by:

- deliberately infecting pregnant sows, at least 3 weeks before they farrow, by exposing them to virulent virus in the viscera of infected piglets;
- improving housing conditions by providing suckling piglets with a warm, dry, draft-free, clean, and disinfected environment with easy access to water and/or milk replacer;
- vaccination programs using either live-attenuated or inactivated TGEV vaccines for the pregnant sows and the neonatal piglets;
- providing electrolyte supportive therapy for piglets with diarrhea; and
- using broad-spectrum antibacterials for possible bacterial complications.

These methods, however, have not been very successful in controlling the preweaning mortality associated with TGEV.[1-3]

Greece was one of the very few countries, at least in Europe, in which epidemic TGE was not reported until the winter of 1989–90. Greece remained free of TGEV even during 1975–85, when the pig industry intensified, including integrator units of 500–3000 sows and when producers were importing breeding stock from countries with TGE problems. In 1985, for the first time, a few herds in the most intensively pig-populated areas were seropositive to TGEV, as was shown by serological investigation. No clinical problems were noted, however. Later, in 1986–87, porcine respiratory coronavirus (PRCV) was detected in Greek swine herds. This virus is antigenically similar to TGEV, and the two viruses have been differentiated only recently.[5,6] The presence of PRCV has made it difficult to interpret the results of tests of breeding animals being introduced from other countries.[7] During the winter of 1989–90, there was a severe epidemic of TGE in large industrial pig herds in Greece, which were totally susceptible.[7]

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Monensin sodium (Elancoban/Rumensin, Eli Lilly and Company) is a polyether ionophore antibiotic, used to control coccidiosis in poultry and in other species[8] and to promote growth in beef cattle and small ruminants.[9,10] In swine, it promotes growth when administered at doses ranging from 25 to 100 ppm,[9,10] and has therapeutic properties that control and treat:

- coccidiosis;[12,13]
- post-weaning diarrhea syndrome;[14]
- swine dysentery;[15]
- porcine intestinal adenomatosis;[16] and
- porcine hemorrhagic enteropathy.[17]

(The maximum dose in all above experiments was 100 ppm.)

Monensin also has been reported to moderate TGE viral infection in sows. When monensin was orally administered at rates of 2.5–10 g/100 lb of feed, neonatal piglet mortality was reduced.[18] In vitro, monensin interferes with glycoprotein transport within the Golgi apparatus.[19] Glycoprotein processing is important in virus assembly, so disrupting the glycosylation pathways could interfere with the production and release of virus particles from infected cells.[20] There is also evidence that significantly less progeny virus is released from infected cells in the presence of monensin for certain enveloped viruses.[21-23] In vitro studies have documented that monensin also prevents replication of DNA in human cytomegalovirus,[24] and in recent experimental work appears to be a potential anti-pseudorabies virus drug.[20]

At high dosages, however, monensin can cause problems. Cases of poisoning were reported when monensin, at the dose of 100 ppm, was included in feed simultaneously with tiamulin (at the therapeutic level of 200 ppm).[2,25] Growing pigs fed 500 ppm monensin for 111 days demonstrated:

- severe cardiac and skeletal muscle degenerative myopathy;
- mortality up to 40%;
- reduced daily gain; and
- reduced feed intake.[26,27]

In general, however, pigs readily accept feed that contains 300 ppm monensin.[27] Continuously feeding growing pigs 120–240 ppm monensin did not alter their growth performance, health status, and biochemical profile.[2,15,29] Finally, liver and kidney tissues collected from pigs that were fed 100 ppm monensin for 100 days were found to contain no detectable monensin residues at the test sensitivity of <0.05 ppm for lean and <0.025 ppm for fat (the test sensitivity was defined as the lowest recovery sample registering a zone of inhibition on the bioautographic plate).[30]

Case Report

We investigated the effect of monensin on a naturally occurring epidemic of TGE in a large, non-immune swine herd. This new herd was located in the most densely pig-populated area in Greece. The herd was separated into six subunits, each of which contained the following facilities:

- a service area for artificial insemination (AI);
- a dry sow area; and
- a farrowing house.

At weaning (23 ±2 days), the piglets from all six subunits are moved into a common flat deck facility. Piglets remain in the flat deck facility until they are 60 days old.

All pigs were from the same genetic source. Housing and nutritional methods used in this study were the same for both the treatment and the control groups, although the sub-unit used for the control group was the newest (built 1 year before the TGE outbreak) and had almost ideal housing conditions (better ventilation and more modern equipment).

The TGE outbreak
The TGE outbreak occurred during the winter months of 1989-1990. The virus rapidly spread to most animals of all ages. Diagnosis was based on epidemiological evidence, clinical signs, and macroscopic and histologic findings typical of TGE (viral antigen in the enterocytes of small intestine of the neonatal piglets). We confirmed the diagnosis by isolating TGEV from the contents of the small intestine of affected neonatal piglets. Finally, by using electron microscopy, we were able to observe the corona-like particles of TGEV ultrastructurally within the macrophages of the mesenteric lymph nodes of the neonatal piglets.

Experimental use of monensin
A week after the first symptoms of TGE, monensin at 100 ppm was administered in the feed in five of the six sub-units to:

- all gilts (n = 350) and boars (n = 31);
- all gestating, lactating, and dry sows (n = 2583) with 1640 farrowings;
- suckling piglets (in the creep feed) (n = 16,700); and
- weaners until 2 months of age.

In the negative control sub-unit, there were 651 sows. During the study period, there were 374 farrowings with a total of 3,860 piglets.

Records
Piglet mortality was recorded for the following periods:

- from birth to 7 days of age;
- 8–14 days old;
- 15 days old to weaning (23±2 days);
- weaning to 60 days old; and
- total mortality from birth to 60 days old.

We compared the treatment and control groups and also compared piglet mortality during the study to the average mortality that occurred in the herd during the 6 months previous
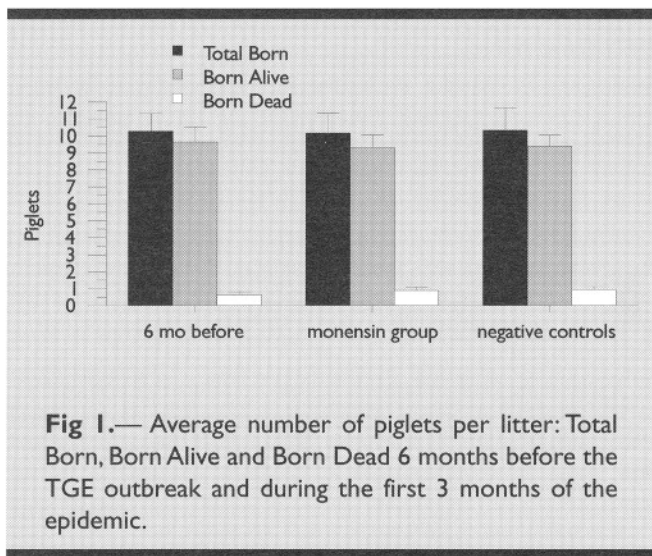
Fig 1.— Average number of piglets per litter: Total Born, Born Alive and Born Dead 6 months before the TGE outbreak and during the first 3 months of the epidemic.

to the TGE outbreak. The observation period began a week after the onset of TGE and lasted for 3 months.

Results

In this herd, TGEV did not appear to affect litter size at farrowing. Compared to the 6-month period prior to the outbreak,

- total born piglets per litter;
- piglets born dead per litter; and
- piglets born alive per litter

remained essentially the same for the treatment groups and the control group during the first 3 months of the TGE outbreak (Fig 1). The survival of these piglets over the course of their first 60 days of life was, however, dramatically affected by the TGE outbreak (Fig 2). The number of piglets that survived was lower throughout the outbreak compared to the number of piglets that survived during the pre-outbreak period. The survival rate of the treatment group during the outbreak never achieved the level observed during the pre-outbreak period but was significantly higher than the survival rate of the control group during the outbreak (Fig 2). Both before and during the outbreak, most piglets died during their first week of life (Fig 3). The percent of piglet mortality during the first week dramatically increased during the outbreak, both for the treatment and the control groups (Fig 3). Piglet mortality in the control group remained high during the second week of life compared to pre-outbreak levels and compared to piglets in the treatment group.

Discussion

The very high losses noted in this herd are typical of an epidemic of TGE, although the producer deliberately exposed sows to TGEV at least 3 weeks before farrowing. The piglets
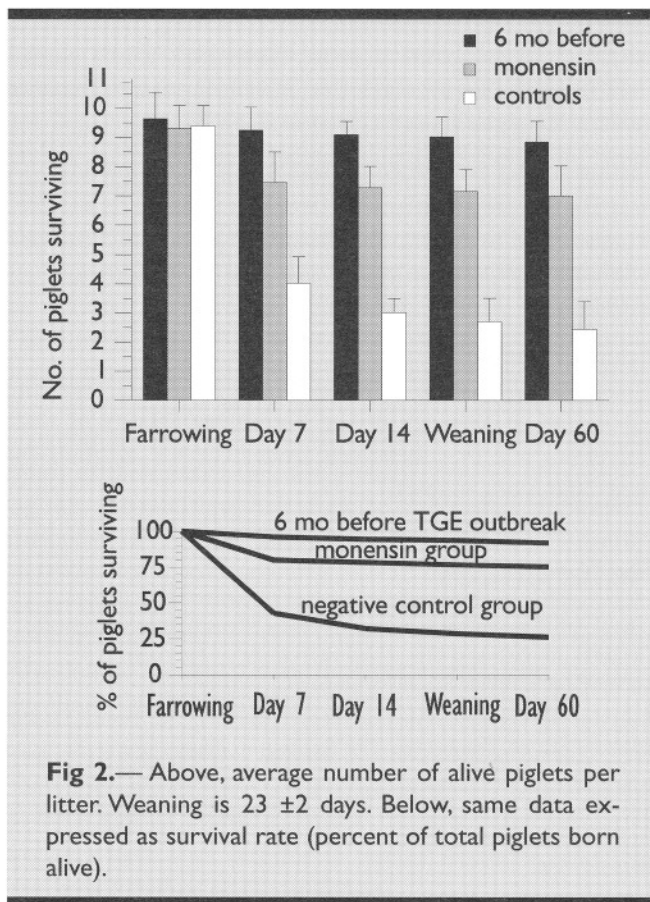

Fig 2.— Above, average number of alive piglets per litter. Weaning is 23 ±2 days. Below, same data expressed as survival rate (percent of total piglets born alive).

had proper housing and nutritional conditions and were given electrolyte supportve therapy in combination with broad spectrum antibacterials. This deliberate exposure could be the reason that the mortality rate dropped precipitously during the second week of life in control pigs (Fig 2), and had virtually returned to pre-outbreak levels by the third week of life. It could be, however, that even without these management techniques, mortality from TGEV infection would have decreased in pigs more than 1 week old.
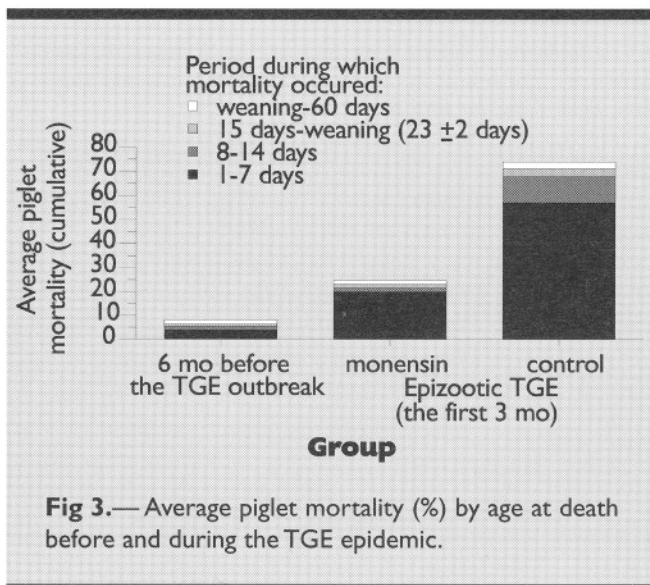

Fig 3.— Average piglet mortality (%) by age at death before and during the TGE epidemic.

Based in part on previous research documenting the detrimental effects of monensin on some viruses and in part on this field research, we conclude that monensin was effective in moderating piglet mortality due to TGEV.

Further studies are needed to establish the optimum dose and to strike the proper balance between its cost and its benefits. We also need to determine what other pathogenic virus infections in animals can be moderated by ionophore polyether antibiotics.

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