

Evaluation of the occurrence of arthritis in nursing piglets, strategically treated shortly after birth with an injection of amoxicillin or by topical application of chlortetracycline on the navel, and in untreated controls.

Fagdyrlæge opgave
Af
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Summary

The effects of parenteral and topical antimicrobial treatment on the navel area against arthritis were compared to a non treated control group. The objective of the trial was to investigate whether the two treatments were equally effective.

The trial was conducted in two farrowing herds including approximately 1500 piglets from each herd. The piglets were divided into 3 groups within each litter, two treatment groups and one non-treated control group. As parenteral treatment an injection with prolonged amoxicillin (Curamox[®] Prolongatum Vet) was used and as topical treatment chlortetracycline in a spray formulation (Cyclo Spray Vet) was used. All treatments were performed on the day of birth.

Effect of the treatments was evaluated on the occurrence of arthritis in the suckling period. A significant ($p < 0.05$) lower occurrence of arthritis in the treated groups compared to the non-treated group was considered as effect of the treatments.

There was no difference in effect between treated and non-treated groups in either of the two herds, but when results from the two herds were added (= 3000 approx. piglets) to avoid herd effect there was a significant difference ($p = 0.01$) between the parenterally treated group and the non-treated control group. Thus the conclusion of the trial is that the two treatments were not equally effective.

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1. Introduction

1.1 Objective

The objective of the trial was to investigate whether the effect on arthritis in the suckling period of treatment with chlortetracycline on the navel shortly after birth was equal to the effect of long-acting amoxicillin shortly after birth, and whether the effect of these two treatments were different from no treatment.

1.2 Justification

Arthritis in the suckling period is a common disease in piglets. It leads to reduced animal welfare and higher mortality as the disease is painful and often not curable. Arthritis can be caused by a long range of different microorganisms with *Streptococcus* spp. and *Staphylococcus* spp. as dominants (>50%) (1). The prevalence of the disease has been reported in the range of 3.3 and 12% (1, 2) and depend on the health status of the sow, intake of colostrum, season and hygiene. Navel infection is known as an infection leading to dissemination of bacteria to blood and joints (3). Navel infection is also described as a reason for umbilical hernia in growers (4) as the infection causes poor closure of the abdominal wall at the navel site. Strategic treatment of piglets with an antibiotic shortly after birth has become common use in Danish herds in order to prevent navel infection and thereby arthritis in the suckling period and umbilical hernia in growers and finishers. This treatment is usually carried out by the parenteral route with a broad-spectrum antibiotic but a topical application of an antibiotic on the navel area might be a good alternative to the parenteral treatment.

2. Material and methods

2.1 Description of herds

The trial was carried out in two Danish herds:

Herd 1:

1300 sows. About 50 sows farrowed every week. All pigs were sold after weaning at 4 weeks. The health status was high with *Mycoplasma hyopneumonia* (Myc) present but not *Actinobacillus pleuropneumonia* (Ap) or PRRS.

Investigator: Kirsten Jensen

Herd 2:

600 sows. About 25 sows farrowed every week. Piglets were weaned at 4 weeks and most of the pigs were sold at 30 kg. Myc., Ap types 2 and 6 and the US and EU strain of PRRS were present in the herd.

Investigator: Thomas Hansen

The herds were included in the trial because of previous problems with arthritis in suckling pigs with a prevalence of >10%.

Both herds were well-run with good standards of management and hygiene. The staff was well educated and experienced.

All farrowing pens in both herds had 2/3 of concrete floor and 1/3 of bars. The pig caves were covered and had heated floors.

2.2 Study design

The study was a non-blinded randomized case-control study with 3 groups, two treated groups and one non-treated control group within the litter. The study unit was the piglet and each group contained approximately 500 piglets. There was no difference in the groups regarding sex, age of sow and type of floor.

2.3 Statistics

Fisher's Exact probability test was performed for the statistical comparison between control and treated groups.

The level of significance tests is $\alpha = 95\%$; tests will be performed two-sided. Fisher's Exact test is performed with SAS[®] procedure freq. (proc. FREQ). (5)

2.4 Strength

With an assumed prevalence of arthritis in the non-treated group of 2% and 0% in the treated groups the strength is 88%

With an assumed prevalence of arthritis in the non-treated group of 3% and 0.5% in the treated groups the strength is 85%

With an assumed prevalence of arthritis in the non-treated group of 12.5% and 7% in the treated groups the strength is 84%

2.5 Groups

Table 1.

Group	Treatment	Time of treatment	Marking
1	Curamox [®] Prolongatum	Day 1	One cut top right ear
2	Cyclo Spray	Day 1	One cut top left ear
3	Control (No treatment)	Day 1	One cut bottom right ear

The newborn pigs were randomized within the litters, allocated into 3 groups, treated according to group and put back into the farrowing pens. This procedure was performed once a day in the morning between 8:00 and 12:00. All piglets were treated within the first 24 hours after birth.

2.6 Randomization procedure

On day one, just before treatment, the pigs were given a temporary number from one to the amount of pigs in the litter. This number was written on the skin of the pig with a pen. The number was only used during allocation into the 3 groups which was carried out immediately after. It was controlled that this procedure resulted in an even distribution of sexes in the groups.

2.7 Inclusion criteria

All pigs born in each herd without congenital deformity and a birth weight above 800 grams were included.

2.8 Exclusion criteria

- Pigs in group 2 and 3 treated parenterally on day one for any reason were excluded
- If there was any doubt about the marking, the pig was to be excluded.

2.9 Investigational Veterinary Products

Curamox[®] Prolongatum vet, (150 mg amoxicillin/ml in oil suspension) from Boehringer Ingelheim was used as parenteral antibiotic. The recommended dose is 15 mg/kg body weight, 1 ml/10 kg. Withdrawal time: 30 days.

For topical application of chlortetracycline (CTC) Cyclo Spray vet, (3,210 g CTC/can) from Novartis AH, Nordic was used.

Withdrawal time: 0 days.

2.10 Treatment

Group 1:

All pigs in the group were injected in the neck-muscle with Clamoxyl[®] Prolongatum with an automatic syringe and needles size 19 G. The dose used in the trial was 0.5 ml pr. piglet (30-60 mg/kg body weight).

Group 2:

The pigs in the group were sprayed on the umbilical cord with Cyclo Spray at the connection to the skin until the site was colored evenly blue all around. The jet on the spray-can was replaced with a smaller jet to focus the application and reduce amount of drug. Dosage depended on how long and how hard the jet was pressed during application. In herd 1 one can pr. 120 pigs was used as in herd 2 one can was enough for treatment of 300 pigs. The dose of CTC / cm² of the treated site was 3-6 mg.

Group 3:

No treatment on day one.

All treatments and markings were performed at the same time within a litter. The navel cords were cut to a length of 5-8 cm if they were very long. In herd 2 the tails were docked at the same time as the treatment and the pigs were castrated on day 3-4. In herd 1 the tail docking and castration was performed on day 3-4. In herd 2 the carnivores were polished. There was no treatment of the carnivores in herd 1.

2.11 Marking

The pigs were marked according to group by U-shaped cuts in the rim of the ear (see table 1). Excluded pigs received a round hole in the middle of the ear. When pigs were treated for any reason after day 1 they got round plastic ear tags (Allflex Small tag, white) with consecutive numbers to ensure that arthritis in a pig was only recorded once.

Apart from the treatment on the day of farrowing there were no changes in the husbandry practice on the trial farms.

3 Assessment of effect

3.1 Definition of effect

A statistically significant difference ($p < 0.05$) in occurrence of arthritis in the suckling period between the non-treated group (group 3) and groups 1 and 2 was interpreted as an effect of parenteral and topical treatment.

3.2 Diagnosing and registration

The diagnosing of arthritis and other diseases on a daily basis was performed by the herd staff under supervision of the investigators and registered on special forms. Diseases were treated according to the normal husbandry practice on the trial farms and the ear tag number given to the pig was recorded along with the diagnosis. Dead pigs were recorded by group together with the assumed course of death.

Diagnosing of the umbilical hernia was performed by the investigators when the pigs weighed about 30 kg.

Diagnoses recorded in the suckling period:

- Limping and swelling of a joint was diagnosed as “Arthritis”
- Limping and swelling of the hooves was diagnosed as “Hoof- abscess”.
- Pigs with impairment of the motion function that did not fit the diagnoses above were diagnosed as “Trauma”.
- Pigs with red swelling around the navels were diagnosed as “Navel infection”.
- Pigs with diarrhea were diagnosed “Diarrhea”.
- Pigs with meningitis were diagnosed “Meningitis”.
- Pigs with dyspnoe were diagnosed “Pneumonia”
- Badly performing pigs with rough hair coat were diagnosed “Weakling”

Umbilical hernia at 30 kg:

All pigs with a swelling at the navel area were examined for content of the swelling deriving from the abdomen, and the size of the navel ring was determined.

Swellings with abdominal content and with a detectable navel ring were diagnosed as “Umbilical hernia”.

It was not expected to find a significant difference in umbilical hernia between treated and untreated groups in this trial as the sample sizes were much too low. Yet the diagnosis was included because a numerical difference might give a hint of effect.

3.3 Autopsies

Most pigs that died or were euthanized later than 3 days after birth were submitted to autopsy on the farm by the investigators. Pigs that die within 3 days after birth usually die because of hunger, low birth weight or because the sow lies on them, and it was considered irrelevant to this study to perform autopsy on these pigs.

3.4 Laboratory investigation

Pigs from each herd with typical signs of arthritis were sent to laboratory (Danish Meat Association Laboratory, Kjellerup) for a bacterial diagnosis.

4. Results

4.1 Diagnoses and deaths

In table 2 and 3 the number of pigs in the 3 groups, deaths, pigs with arthritis, poorly performing pigs (“Weaklings”) and umbilical hernia are listed. The diagnosed numbers of hoof-abscesses, trauma, navel infection, meningitis and pneumonia were added under “Other diseases”.

Table 2.

Herd 1	Group 1 Amoxicillin	Group 2 CTC local	Group 3 Non-treated	p-value*
Number of pigs	644	632	620	
Dead	57 (8.9 %)	42 (6.6 %)	40 (6.5 %)	0.2000
Arthritis	26 (4.0%)	38 (6.0%)	41 (6.6%)	0.1022
“Weaklings”	10 (1.6 %)	24 (3.8 %)	19 (3.1 %)	
Other disease	4 (0.6 %)	8 (1.3 %)	7 (1.1 %)	
Number of pigs at weaning	587	590	580	
Umbilical hernia (30 kg)	2 (0.34 %)	0	1 (0.17 %)	0.4407

* : p-value: Fisher's Exact, two-tailed

Table 3.

Herd 2	Group 1 Amoxicillin	Group 2 CTC local	Group 3 Non treated	p-value*
Number of pigs	537	536	551	
Dead	38 (7.1%)	35 (6.5%)	53 (9.6%)	0.1373
Arthritis	19 (3.5 %)	25 (4.7 %)	30 (5.4 %)	0.3108
“Weaklings”	25 (4.7 %)	19 (3.5 %)	19 (3.5 %)	
Other disease	8 (2.6 %)	9 (2.9 %)	10 (3.1 %)	
Number of pigs at weaning	347	365	380	
Umbilical hernia (30 kg)	4 (1.2%)	4 (1.1%)	7 (1.8%)	0.6827

* : p-value: Fisher's Exact, two-tailed

Table 4.

Herd 1+2	Group 1 Amoxicillin	Group 2 CTC local	Group 3 Non treated	p-value*
Number of pigs	1181	1168	1171	
Dead	95	77	93	0.3266
Arthritis	45	63	71	0.0346

* : p-value: Fisher's Exact, two-tailed

There was no significant difference in the number of arthritis and deaths between the two treated groups and the untreated control group in either of the two herds when they were analyzed separately (Table 2 and 3).

When the results from the two herds were added (Table 4) there was a significant difference ($p = 0.0346$) between the treated groups and the non-treated control group. The differences between group 1 and 2 and between group 2 and 3 were not of significance, $p = 0.0760$ and $p = 0.5336$, respectively. The difference between group 1 and 3 was of significance, $p = 0.0131$.

4.2 Autopsies

In herd 1 18 dead or euthanized pigs were autopsied. They were diagnosed with arthritis (3), pericarditis (1), pleuritis/pericarditis (1), pneumonia (5), enteritis (2) and hunger (6).

4.3 Laboratory tests

One pig with typical signs of arthritis from herd 1 was sent to laboratory for bacteriologic diagnosis. *Stafylococcus hyicus* was isolated from the joint.

Several arthritic pigs from herd 2 have been sent to the laboratory for bacterial isolation, but it has not been possible to isolate any infectious agents.

5. Discussion

There was a significant effect of the parenteral treatment with amoxicillin compared to no treatment in the added results from the two herds, but not in the herds separately. The local treatment on the navel area did not have a significant effect in either of the analyses. Thus there was a difference in the effect of the two treatments.

In herd 1 the canine teeth were not polished, resulting in fighting and scarring of the piglets' faces during the first week. These facial wounds could have been entrance for the infection that led to arthritis. This was supported by the retrieval of *Stafylococcus hyicus* from the joint of an arthritic pig. In this instance treatment on day one is not expected to have effect on arthritis.

The recommended dose of amoxicillin is 15 mg/kg. The relatively large dose of 30-60 mg/kg used in this trial was chosen because 0.5 ml of prolonged amoxicillin / piglet is widely used in Denmark for this purpose.

Because of the difference in nature of the two treatments it was not possible to design the study as a blinded trial. This was not considered a problem because the diagnosis of arthritis was so obvious that it was discovered before the ear cut could be noted.

No pigs were excluded from the trial because there was doubt about the marking (ear cut), and the ear cuts remained clear until 30 kg.

The number of pigs included in this trial was not big enough to evaluate an effect on navel hernia and some navel hernia evolves after 30 kg during the finishing period. Therefore this trial was not designed to document an effect of the two treatments on navel hernia but could have been used a hint of an effect if the problem had been bigger.

The occurrence of arthritis in the two herds was not as high as expected, 6.6% and 5.4% in the untreated group. When the herds were chosen for the trial, a rather large number of piglets (10-15%) suffered from arthritis, but the problem had diminished at the time of the trial and was not severe any longer. There might have been significant effect of both treatments if the disease had been due to an aggressive bacteria present in the herd.

6. Litteratur

1. N.C. Nielsen et al. Nord Vet. Med.(1975), **27**: 129-139
2. M. Zoric et al. Vet. Rec.(2003)**153**: 323-328
3. R.S. Windsor. Vet Annu. **18** (1978):134-143
4. Diseases of Swine 9th edition: 1122
5. SASOnlineDocVersion8,Cary,NC:SASInstituteInc.,1999.

Randomisering uge : 3

Antal grise	Gruppe nummer	Antal
1	2	
2	1	
3	3	
4	2	
5	1	
6	3	
7	1	
8	3	
9	2	
10	3	3 3 4
11	2	3 4 4
12	1	4 4 4
13	1	5 4 4
14	3	5 4 5
15	2	5 5 5
16	1	6 5 5
17	3	6 5 6
18	2	6 6 6

STUDY: Cyclo Spray /01/herd 1

Evaluation of the occurrence of arthritis in nursing piglets, strategically treated shortly after birth with an injection of amoxicillin or by topical application of chlortetracycline on the navel, and in untreated controls.

Report on statistical evaluation – final draft version 2

Date: 04.10.2006

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1. Summary and Conclusions

HERD 1:

Groups were compared with respect to dead and arthritis-diarrhea (Yes / No), using a Fisher Exact probability test with SAS® procedure *freq* (SAS Online Doc® Version 8, Cary, NC: SAS Institute Inc., 1999). The group differences in dead and arthritis-diarrhea are not of significance, since $p > 0.10$

Parameter: Dead

Group	Yes/No	Counts	Total	Percent	p-value (*) ₁
1	YES	57	.	8.9	0.2000
1	NO	587	644	91.1	
2	YES	42	.	6.6	
2	NO	590	632	93.4	
3	YES	40	.	6.5	
3	NO	580	620	93.5	

(*)₁: p-value: Fisher's Exact, two-tailed

Parameter: Arthritis - Diarrhea

Group	Yes/No	Counts	Total	Percent	p-value (*) ₁
1	YES	26	.	4.0	0.1022
1	NO	618	644	96.0	
2	YES	38	.	6.0	
2	NO	594	632	94.0	
3	YES	41	.	6.6	
3	NO	579	620	93.4	

(*)₁: p-value: Fisher's Exact, two-tailed

Groups were also compared with respect to hernia (Yes / No), using a Fisher Exact probability test. The group differences are not of significance, since $p > 0.4$

Parameter: Hernia

Group	Yes/No	Counts	Total	Percent	p-value (*) ₁
1	YES	2	.	0.3	0.4407
1	NO	587	589	99.7	
2	YES	0	.	0	
2	NO	590	590	100.0	
3	YES	1	.	0.2	
3	NO	580	581	99.8	

(*)₁: p-value: Fisher's Exact, two-tailed

HERD 2:

Groups were compared with respect to dead, arthritis (Yes / No), using a Fisher Exact probability test with SAS[®] procedure *freq* (SAS Online Doc[®] Version 8, Cary, NC: SAS Institute Inc., 1999). The group differences in dead, arthritis are not of significance, since $p > 0.13$

Parameter: Dead

Group	Yes/No	Counts	Total	Percent	p-value (*) ₁
1	YES	38	.	7.1	0.1373
1	NO	499	537	92.9	
2	YES	35	.	6.5	
2	NO	501	536	93.5	
3	YES	53	.	9.6	
3	NO	498	551	90.4	

(*)₁ :p-value: Fisher's Exact, two-tailed

Parameter: Arthritis

Group	Yes/No	Counts	Total	Percent	p-value (*) ₁
1	YES	19	.	3.5	0.3108
1	NO	518	537	96.5	
2	YES	25	.	4.7	
2	NO	511	536	95.3	
3	YES	30	.	5.4	
3	NO	521	551	94.6	

(*)₁ :p-value: Fisher's Exact, two-tailed

Groups were also compared with respect to hernia (Yes / No), using a Fisher Exact probability test. The group differences are not of significance, since $p > 0.6$

Parameter: Hernia

Group	Yes/No	Counts	Total	Percent	p-value (*) ₁
1	YES	4	.	1.2	0.6827
1	NO	343	347	98.8	
2	YES	4	.	1.1	
2	NO	361	365	98.9	
3	YES	7	.	1.8	
3	NO	373	380	98.2	

(*)₁ :p-value: Fisher's Exact, two-tailed

HERD 1 + HERD 2:

Groups were compared with respect to dead, arthritis (Yes / No), using a Fisher Exact probability test with SAS[®] procedure *freq* (SAS Online Doc[®] Version 8, Cary, NC: SAS Institute Inc., 1999). The group differences in dead are not of significance, since $p > 0.32$. Group differences in arthritis are of significance, since $p < 0.035$.

Parameter: Dead

Group	Yes/No	Counts	Total	Percent	p-value (*) ₁
1	YES	95	.	8.0	0.3266
1	NO	1086	1181	92.0	
2	YES	77	.	6.6	
2	NO	1091	1168	93.4	
3	YES	93	.	7.9	
3	NO	1078	1171	92.1	

(*)₁ :p-value: Fisher's Exact, two-tailed

Parameter: Arthritis

Group	Yes/No	Counts	Total	Percent	p-value (*) ₁
1	YES	45	.	3.8	0.0346
1	NO	1136	1181	96.2	
2	YES	63	.	5.4	
2	NO	1105	1168	94.6	
3	YES	71	.	6.1	
3	NO	1100	1171	93.9	

(*)₁ :p-value: Fisher's Exact, two-tailed

Remark: If only two groups were compared for parameter arthritis, we get the following results: The differences between group 1 and 2 and between group 2 and 3 are not of significance, $p = 0.0760$ and $p = 0.5336$, respectively. The difference between group 1 and 3 is of significance, $p = 0.0131$.

All calculations were carried out on the AH Development Biometrics IT infrastructure, PC AHCHBS-W10017, using the software SAS[®], Version 8.2.