39. Associations between vaccination and antimicrobial consumption in Danish pig herds, 2013

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Abstract

Antimicrobial agents are being used in modern swine production worldwide, generating concern in regards to the development of antimicrobial resistance. Identifying efficient alternatives has therefore become a subject of interest. The aim of this study was to explore the impact of routinely used vaccination as an alternative to antimicrobial consumption in weaner pig herds. The hypothesis was that herds with increased use of vaccination would have a lower antimicrobial consumption. Data were obtained from the Danish VetStat database in which prescriptions of medication for livestock are recorded as well as the Danish Central Husbandry Register. All Danish one-site pig herds, active in year 2013, with >50 sows and >200 weaners were selected for the study. Initially, data were analysed using a univariable model, and secondly a multivariable linear regression model was applied. The analyses included use of three different vaccines against Porcine Circovirus Type 2 (PCV2), Mycoplasma hyopneumoniae (M_HYO) and Lawsonia intracellularis (LAW), respectively, as well as annual production measured as number of weaners produced in a year. The outcome was the average antimicrobial consumption measured in animal daily does (ADD) per weaner pig. Out of the 1,513 herds selected for the study, 1,415 herds had antimicrobials prescribed for gastrointestinal disorders, and 836 for respiratory disorders. PCV2 vaccine was used in 880 herds, M_HYO vaccine in 787 and LAW vaccine was the least used, with 115 herds using it. The results suggested that antimicrobials to some extent were being used for other disease categories than those officially prescribed by the veterinarians. On average, herds using the different combinations of vaccines had higher use of antimicrobials than herds not using the vaccines – probably as a result of health problems in the herds existing prior to the initiation of vaccine use. Information about vaccination protocols, health status, biosecurity, and management practices was not available limiting the ability to assess causality.

Introduction

In the European Union (EU), antimicrobials (AM) are used extensively in veterinary medicine for therapeutic purposes, as metaphylactic treatment, or as prophylaxis to prevent disease (Aarestrup et al., 2008; Barton, 2014). This has led to concerns about the potential risk of the development of antimicrobial resistance (AR) in animals and the transfer of resistance factors from animals to humans, through zoonotic bacteria or consumption of animal products (Aarestrup et al., 2008; Allen et al., 2013; Seal et al., 2013). In Denmark, there has been political and public focus on this issue since the 1990s (Bager, 2000). As a result, a series of events emerged: phasing out of the use of AM as growth promoters; limited veterinary profit from sales of AM to 5-10% and development of guidelines for prudent use of AM. Moreover, in 2010 the Danish veterinary authorities adopted the Yellow Card initiative, a scheme that sets threshold limits to AM use in swine farms (Alban et al., 2013). That same year, an industry ban was implemented to stop the use of cephalosporins (Alban et al., 2013; Jensen & Hayes, 2014). The measures listed above reflect the increasing political pressure that is forcing Danish pig producers to reduce the usage of AM in their farms. Therefore, efficient alternatives to routinely applied AM have become crucial. Vaccines are being considered as means to decrease the burden of animal diseases and also to reduce the need of AM for therapeutic purposes (Allen et al., 2013). However, the extent of using vaccination as an alternative to AM will depend on its cost, effectiveness and ease of use (Allen et al., 2013).
To explore the impact of further use of vaccination as an alternative to AM, the present study was carried out using data from Danish pig herds covering the year 2013. The aim was to investigate overall associations between vaccination against PCV2, M_HYO and LAW and antimicrobial consumption (AC). The hypothesis was that herds with increased use of vaccination would have a lower AC.

Material and Methods

The data used in this study were obtained from VetStat and the Danish Central Husbandry Register. All Danish one-site pig herds, active in the year 2013, with >50 sows and >200 weaners were selected for the study (N=1,513 herds). In VetStat, the AC is divided into three age groups: sows with piglets, weaners (7 – 30 kg), and finisher pigs. Moreover, the indication the AM were prescribed for is recorded. Only the AC for the weaners was taken into account in the present analysis. In Denmark there are 8 weeks between batches in the nursery. This implies that 52/8 = 6.5 weaners can be produced per year per pen place. Therefore, a conversion factor of 6.5 was used to go from the number of pen places to the number of weaners produced per pen place per year.

For each of the 1,513 herds, a variable was created to reflect the AC per weaner produced per year (2013). This variable was calculated using the total administered animal daily doses (ADD) in weaners in 2013, for each herd, divided by the number of pen places for weaners, multiplied by 6.5. Also, to be able to assess if the production level had an influence on the AC in weaners, the annual production (AP) of weaners was estimated for each herd by using the number of pen places for weaners multiplied by 6.5.

For this study, the AC in weaners is presented by treatment indication. This allows for investigation of biologically meaningful correlations of the AC in weaners and the different vaccinations applied. Three different outcomes were analysed: (1) total AC (TAC) covering all diagnostic groups as applied in VetStat: a) reproduction, urogenital system; b) udder; c) gastrointestinal system; d) respiratory system; e) joints, limbs, hooves, central nervous system, skin and f) metabolism, digestion, circulation); (2) AC with gastrointestinal indication only (ACGI) and (3) AC with respiratory indication only (ACRI). All analyses were carried out in R (version 3.1.2). Univariable analyses were performed for TAC, ACGI, and ACRI, respectively. A t-test was conducted for each of the three types of vaccination comparing herds using the vaccine versus herds which did not use the vaccine. Subsequently, multivariable analyses were performed for 1) TAC, 2) ACGI, and 3) ACRI as three individual outcomes. The explanatory variables were AP and vaccine use. The latter variable had eight levels which reflected all combinations between the three different vaccines. It was tested whether AP was significantly associated with the response and whether it acted as a confounder by being associated with the vaccine use. A P-value < 0.05 was used as threshold for statistical significance.

Results

Out of the 1,513 herds selected for the study, all of them had AM prescribed for the total of diagnostic groups, 1,415 had AM prescribed for gastrointestinal disorders, and 836 for respiratory disorders. Concerning the different vaccines, 880 herds used the PCV2 vaccine, whereas M_HYO vaccination was used in 787 herds, and LAW vaccination was the least used vaccine, with just 115 herds using it. In the following the mean ADD per weaner per year will be reported as ADD.

Univariable analysis

Concerning TAC, herds using PCV2 vaccination (TAC=103.9 ADD, p<0.0001) or M_HYO vaccination (TAC=106.4 ADD, p<0.0001) had a higher mean of AC per weaner than herds not using each of these vaccines (TAC=86.3 ADD and TAC=85.9 ADD, respectively) whereas herds using LAW vaccination had a lower mean of AC (TAC=85.6 ADD, p=0.04) than the ones not using it (TAC=97.4 ADD). The AP explained 0.5% of the variance in TAC (R²=0.005, F=8.6, p=0.004).

Regarding ACGI: herds using PCV2 vaccine (ACGI=72.2 ADD, p=0.01) had a notably higher mean of AC than those not using it (ACGI=64.6 ADD). The AP had no influence on the ACGI (p=0.5).

Regarding ACRI: herds using M_HYO vaccination (ACRI=48.2 ADD, p=0.0006) had a substantially higher mean ACRI than herds not using the vaccine (ACRI=34.0 ADD). On the contrary, herds using LAW vaccination (ACRI=22.2 ADD, p<0.0001) had only half mean ACRI compared to those not using the vaccine (ACRI=44.5 ADD). AP had no influence on ACRI (p=0.6).

Multivariable analysis

Regarding TAC, the results revealed that a model containing AP and different combinations of vaccines explained a total of 3% of the variance in the AC (R²=0.03, F=7.2, p<0.001). The output of the model also showed that, when the AP increases by 1000 weaners, the ADD per weaner per year (TAC), increases by 4 ADD. The use of M_HYO vaccination alone (N=221) or together with PCV2 vaccination (N=507) was associated with a statistically higher TAC than group 0 representing use of none of the three vaccines (N=380): TAC was 19.9 and 31.8 ADD higher per weaner compared with group 0, respectively. The use of only PCV2 vaccination (N=290) was associated with 15.3 ADD per weaner more when compared to group 0. The rest of the groups, reflecting the remaining vaccine combinations, were not associated with statistically different levels of TAC (p>0.05).

Regarding ACGI, PCV2 vaccination was the only significant variable and explained 0.4% of the variance in the ACGI (R²=0.004, F=6.1, p=0.01). Herds using PCV2 vaccination (N=830) were associated with a statistically higher (7.6 ADD) ACGI, than herds not using this vaccination (N=585).

In relation to the ACRI: the results indicated that the variable representing different combinations of vaccines explained 2% of the variance in the ACRI (R²=0.02, F=3.5, p=0.001). This final model suggested that use of M_HYO vaccination alone (N=134) or in combination with PCV2 vaccination (N=349) was associated with a higher ACRI, compared to group 0. M_HYO vaccine alone was associated with 24.7 ADD more per weaner compared to group 0; and M_HYO+PCV2 vaccination with 17.3 ADD more (ACRI) compared to group 0. The changes in ACRI associated with the remaining vaccine combinations were not statistically significant (p>0.05).

Discussion

LAW vaccination is used to prevent proliferative enteropathy (Stege et al., 2000). Thus, it would have been expected that ACGI would have been reduced in herds using the vaccine instead of the ACRI, as shown in our results. This could suggest that – too some extent – AM are being used for other disease categories than those officially prescribed by the veterinarians. Certain AM, such as some doxycyclines, are not registered for treating infections with gastrointestinal indication in Denmark, although they are known to be effective...
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However, the results of the multivariable analyses revealed that when taking into account all three vaccines simultaneously, the differences in AC between the groups that used LAW vaccination and those that did not use it, were no longer statistically significant. This probably because only 62 herds (7.4%) used this vaccine – hence the effect was “diluted” in the large analysis.

Herds using M_HYO vaccination had a higher ACRI than herds not using it. It is likely that these herds had previously detected M_HYO and, subsequently, had had a higher ACRI because of need to control M_HYO infection. Thacker and Minion (2012) point to the predisposition of M_HYO–infected animals to secondary invaders, especially other pulmonary pathogens. Another explanation is that these herds could have been using AM with the aim of preventing respiratory disorders and, after detecting M_HYO, started the vaccination as a complementary tool. This approach makes sense, since pigs treated with AM such as tetracyclines and macrolides have less clinical signs and a lower number of secondary infections (Vicca et al., 2004; Ciprian et al., 2012). Moreover, vaccination is associated with reduced clinical signs, diminished lung lesions and fewer treatment costs (Maes et al., 1999).

Herds using PCV2 vaccination had a higher ACGI than those not using it. PCV2 is associated with enteritis, which may explain the higher ACGI for vaccination and, at the same time higher ACGI weaners. Above all, the weaners as an age group are associated with gastrointestinal inflammation, increased permeability of the gut (Moeser and Blikslager, 2007) and high occurrence of diarrhoea that may lead to high AM use (Oostindjer et al., 2014). These herds could also have initiated routine to PCV2 vaccination with the aim of preventing various other clinical syndromes which PCV2 can be linked to (Tomás et al., 2008). Moreover this vaccination has been associated with decreased mortality rate and increased average daily weight gain (Kristensen et al., 2011).

Herds that used both M_HYO and PCV2 vaccines were associated with a higher ACRI when compared to those not using any of the three vaccines. However, when M_HYO and PCV2 were used together, ACRI were lower than the ones just using M_HYO. This suggests that the use of both vaccines might provide a better immune protection to the animals than the use of M_HYO on its own and therefore, reducing the need for AM. In fact, interaction between both of these agents has been described previously (Harms et al., 2002; Kim et al., 2003). Herds that used both M_HYO and PCV2 vaccines were associated with increased TAC compared to the ones not using any of the three vaccines. In this situation, is possible that presence of M_HYO amplified the persistence of PCV2, that is in agreement with previous studies (Opriessnig et al., 2004). Thus, being the ones with a higher TAC. Another possibility is that these herds have been using AM routinely with the aim of preventing/treating early health problems and, after detection, started vaccination against both of these agents. Results also showed a lower TAC in herds which used PCV2 vaccination alone compared to herds that used both PCV2 and M_HYO vaccines. These findings are in agreement with an experimental study undertaken by Seo et.al (2014), which aimed at determining the effects of both vaccines in disease severity. On the other hand, PCV2 is linked with several disease syndromes. Thus, protection by vaccination may be justified to use less AM for various indications.

The F-statistics for the final models suggest a strong association between the AC and the use of vaccines. However, the adjusted squared correlation coefficient ($R^2$) for all three final models was low, which means that other unknown factors are important to describe the variation in AC. Some of the possible factors are: (1) vaccination protocols, (2) time of vaccination, (3) use of other vaccines, (4) herd health status, (5) internal and external biosecurity, (6) management practices, (7) turnover of animals in each herd and (8) requirement from buyers of weaners. At the time of this study, this information was not available limiting the ability to assess causality.

**Conclusion**

On average, herds using the different combinations of vaccines had higher use of antimicrobials than herds not using the vaccines – probably as a result of health problems in the herds existing prior to the use of vaccination.

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**References**

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