

Methods of diagnosis and treatment of postpartum uterine infection adopted by Algerian veterinarians

Hamza RAHAB^{1,2,*} , Alessandro RICCI³ , Ahmed KASSAH-LAOUAR⁴ , Christian HANZEN⁵ 

¹High National Veterinary School, Algiers, Algeria

²Research Center in Biotechnology, Constantine, Algeria

³Department of Veterinary Science, University of Torino, Torino, Italy

⁴Bacteriology Laboratory, National Anti-Cancer Centre, Batna, Algeria

⁵Department of Theriogenology of Production Animals, Faculty of Veterinary Medicine, Liege University, Liege, Belgium

Received: 21.05.2018 • Accepted/Published Online: 16.03.2019 • Final Version: 00.00.2019

Abstract: The present study aimed to monitor the practices of Algerian veterinarians in the diagnosis and treatment of puerperal metritis (PM) and clinical endometritis (CE) in cattle. For this purpose, a questionnaire was established and distributed to collect the information concerning veterinarian profiles and practices related to the diagnosis and treatment of PM and CE. The results showed that examinations of the uterus (rectal palpation), vaginal discharge, and rectal temperature were the most practiced methods for PM (71%, 68%, and 83%, respectively) and CE (86%, 60%, and 65%, respectively) diagnosis. Tetracycline was the antibiotic of choice for intrauterine treatment of PM (54%) and CE (57%), whereas penicillin was the preferred parenteral antibiotic against PM (68%) and CE (64%). In addition, molecules combined with antibiotic treatment were PGF₂α (PM: 71%, CE: 79%), vitamins (PM: 73%, CE: 60.5%), and nonsteroidal antiinflammatory drugs (PM: 68.2%, CE: 58%). Inseminators were more likely to use IU cephalosporins to treat PM and CE (OR = 3.5, P < 0.05 and OR = 5.1, P < 0.01, respectively). Veterinarians with more than 10 years of experience were more likely to use IU cephalosporins to treat PM (OR = 3.8, P = 0.03). Moreover, bovine practitioners were less likely to observe hyperthermia in cases of CE (OR = 0.29, P = 0.02).

Key words: Puerperal metritis, clinical endometritis, survey

1. Introduction

Postpartum uterine infections (PPUIs) are considered as one of the main pathologies causing infertility of the cow and its culling [1–5]. They are the outcome of the combination of a determining factor, pathogens (bacteria), and predisposing factors (e.g., retained placenta and hypocalcemia) [6,7].

Clinically, PPUIs were divided into four forms [8]. First, puerperal metritis (PM), with a prevalence of 15%–20% [9], occurs within 21 days postpartum and can be diagnosed based on an abnormal distension of the uterus combined with a fetid watery red-brown uterine discharge and systemic symptoms. When the systemic symptoms are absent, this form of PPUI is called clinical metritis [8]. Second, clinical endometritis (CE) is observed more than 21 days postpartum and can be diagnosed by the presence in the vagina of mucopurulent or purulent uterine discharge [8,10], with a prevalence between 5% and 26% [11]. Third, subclinical endometritis is characterized by the absence of clinical symptoms, cytology analyses being

the only tool for its diagnosis [8]. Fourth, pyometra, a rare condition comprising fewer than 5% of cases of PPUI [7], is defined by the accumulation of purulent material within the uterine lumen with a closed cervix [8]. With a high prevalence, the possibility of clinical diagnosis, and important economic losses, PM and CE are the PPUIs most often confronted and treated by veterinarians in the field.

A large variety of therapeutic agents have been proposed for the treatment of PM and CE. These treatments are based on the intrauterine administration of antibiotics (tetracycline, cephalosporins) [12,13] and antiseptics (iodine solutions) [14] and the parenteral administration of antibiotics (penicillin, ampicillin, ceftiofur) [15–18], hormones (prostaglandin F₂α) [18,19], and supportive therapy (nonsteroidal antiinflammatory drugs and sera) [20,21]. Due to the diversity of molecules proposed to treat PM and CE and the absence of conventional treatment, different treatment approaches may exist in the field. However, little is known about the state of PM and CE and

* Correspondence: h.rahab@gmail.com

their management in field conditions. To our knowledge, the study of Hehenberger et al. [22] in Switzerland was the only survey that was carried out to determine practices of veterinarians in the field in dealing with PM and CE.

In this respect, the practices of veterinarians in Algeria toward PM and CE remain unknown. Thus, the objective of the current work was to study the practices of Algerian veterinarians regarding diagnosis and treatment of PM and CE in field conditions, including the influence of veterinarian experience, practice of artificial insemination, and number of bovine farms managed on those practices.

2. Materials and methods

2.1. Questionnaire

Collection of information on the practices of veterinarians toward PM and CE was carried out using a questionnaire-based survey. The questionnaire was divided into three sections. The first section was designed to collect information about veterinarians and their activities, including sex, years of experience, main activity, number of bovine farms visited, average number of cows per farm, and whether the veterinarian practices artificial insemination. The second and third sections included multiple-choice questions about diagnosis and treatment of PM and CE. For each choice, veterinarians were invited to indicate the frequency of application on a Likert scale (very frequently (more than 80% of cases), frequently (40% to 80% of cases), sometimes (10% to 40% of cases), rarely (1% to 20% of cases), or never (<1% of cases)). The questionnaire was formatted using Google forms and submitted to five practicing veterinarians for assessment. The questionnaire was then distributed as electronic or paper copies to 600 veterinarians. The electronic copies were sent by e-mail to veterinarians affiliated with the National Center for Artificial Insemination and Genetic Improvement (CNIAAG) and the Algerian Veterinary Technical Group (GTVA), whereas the paper copies were distributed by hand on the occasion of professional veterinary meetings.

2.2. Data analysis

The recovered data were loaded into a statistical package (IBM SPSS 20; IBM Corp., Armonk, NY, USA) for statistical analysis.

For descriptive statistics, the frequencies of application of diagnosis and treatment of PM and CE were presented as ordinal variables on a scale from 1 (never) to 5 (very frequently).

Logistic regression was performed to show the influence of factors (veterinarians' characteristics) on outcome variables (frequency of using diagnostic and therapeutic approaches towards PM and CE). The outcome variables were regrouped into 2 categories: (i) frequent use (regrouping the modalities of frequently and

very frequently) and (ii) infrequent use (sometimes, rarely, and never). Factors were regrouped as follow: years of experience (<10 years, >10 years), main practice (bovine vs. other species), number of bovine farms managed (>50 farms vs. <50 farms), and practice of artificial insemination (yes vs. no).

For univariate regression, chi-square analyses were performed between each predictor and each outcome variable. When $P < 0.05$, a univariate regression was considered and calculation of the odds ratio (OR) and 95% confidence interval (CI) was carried out.

For multivariate regressions, the variables with a P-value of <0.2 from the univariate regression were included in a series of backward stepwise logistic regressions to obtain a minimal model containing only significant variables ($P < 0.05$) and the OR and 95% CI were calculated to assess the strength of the relationship between two or more factors and one outcome variable.

3. Results

One hundred and sixteen questionnaires were completed, representing 18.2% of the total surveyed veterinarians.

3.1. General characteristics of the veterinarians

The results revealed that 58.6% (68/116) of veterinarians had more than 10 years of experience. The percentages of veterinarians practicing bovine medicine and artificial insemination were 65.1% (69/106) and 57.4% (66/115), respectively. In addition, 53% (61/115) of veterinarians monitored 50 or more bovine herds.

3.2. Descriptive results

3.2.1. Diagnosis of PM

The results on diagnosis showed that 83.5% (81/97) of veterinarians measure, frequently or very frequently, body temperature. Moreover, 71.8% (74/103) of the veterinarians perform transrectal examination by hand, frequently or very frequently, to diagnose PM, while only 17.1% (13/76) do it by echography. A fetid discharge and fever were observed, frequently or very frequently, by 91.0% (101/111) and 83.5% (86/103) of surveyed veterinarians, respectively. More than 60% of veterinarians observe, frequently or very frequently, an appetite loss (74.5%, 70/94), a decrease in milk production (69.4%, 68/98), or a distended uterus at rectal examination (64.0%, 57/89) (Figure 1).

3.2.2. Treatment of PM

The results of PM treatment are given in Tables 1 and 2. They revealed that intrauterine (IU) treatment, mainly antibiotics, was applied, frequently or very frequently, by 76.4% (55/72) of veterinarians. Tetracyclines are used, frequently or very frequently, by 72.2% (70/97) of veterinarians. Penicillin-streptomycin association is, frequently or very frequently, selected by 53.4% (47/88) of surveyed veterinarians. Cephalosporins are used by 32.5%

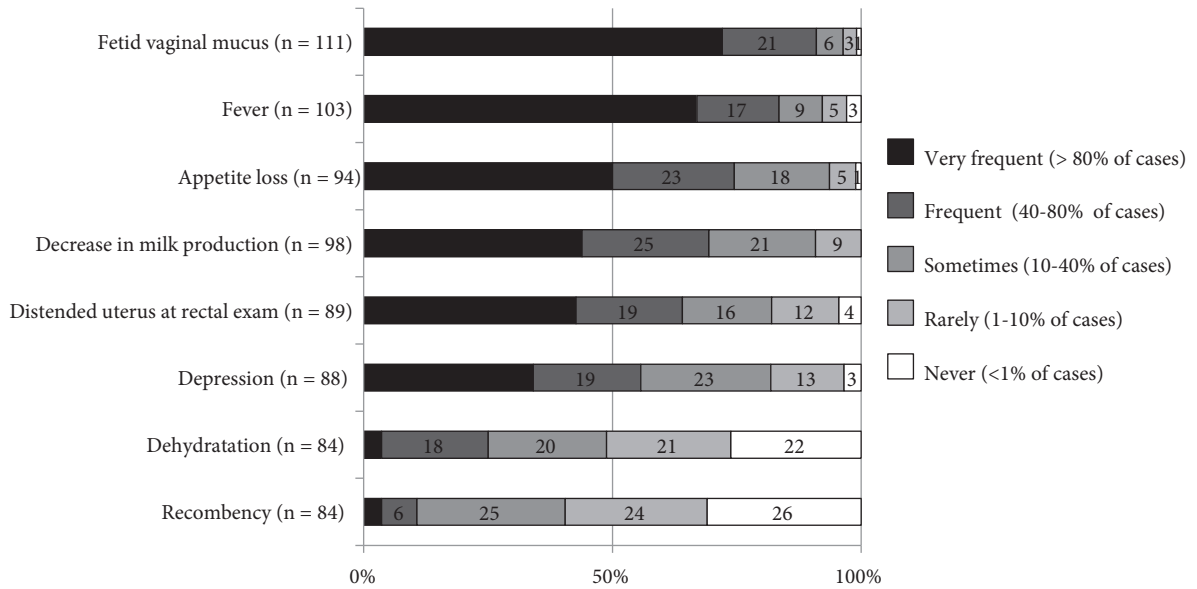


Figure 1. Frequency distribution of the symptoms of PM from the perspective of the responding veterinarians, n = number of responses.

Table 1. Frequencies of the intrauterine drugs used in cows with PM.

Treatment	Very frequent (>80% of cases)	Frequent (40%–80% of cases)	Sometimes (10%–40% of cases)	Rarely (1%–10% of cases)	Never (<1% of cases)	Number of respondents
Tetracycline	53.6%	18.6%	12.4%	8.2%	7.2%	97
Penicillin-streptomycin	38.6%	14.8%	5.7%	13.6%	27.3%	88
Uterine lavage	20.0%	15.3%	16.5%	14.1%	34.1%	85
Cephalosporin	20.5%	12.0%	19.3%	8.4%	39.8%	83
Potassium permanganate	14.8%	7.4%	17.3%	14.8%	45.7%	81
Penicillin	13.2%	15.8%	14.5%	11.8%	44.7%	76
Iodine solution	7.5%	7.5%	11.3%	17.5%	56.3%	83
Aminoglycoside	2.9%	7.2%	7.2%	8.7%	73.9%	69
Rifaximin	00.0%	4.4%	7.4%	82.4%	5.9%	68

Table 2. Frequencies of parenteral antibiotics used by veterinarians in cases of PM.

Treatment	Very frequent (>80% of cases)	Frequent (40%–80% of cases)	Sometimes (10%–40% of cases)	Rarely (1%–10% of cases)	Never (<1% of cases)	Number of respondents
Penicillins	42.9%	25.0%	20.2%	3.6%	8.3%	84
Tetracyclines	10.3%	7.4%	4.4%	7.4%	70.6%	80
Cephalosporin	36.4%	14.3%	6.5%	6.5%	36.4%	77
Macrolides	27.5%	20.0%	17.5%	8.8%	26.3%	80
Sulfamides	15.5%	12.7%	23.9%	15.5%	32.4%	71
Aminoglycosides	6.2%	13.8%	13.8%	12.3%	53.8%	65
Quinolones	4.7%	7.8%	12.5%	12.5%	62.5%	64
Phenicol	0%	3.0%	6.1%	9.1%	81.8%	66

(27/83) of veterinarians frequently or very frequently. In addition, 48.2% (41/85) of responding veterinarians perform uterine lavage rarely or never to treat PM. Iodine solution, aminoglycosides, and penicillins are rarely or never used.

Concerning parenteral administration of drugs, 80% of veterinarians perform, frequently or very frequently, parenteral antibiotherapy. Penicillins, tetracyclines, and cephalosporins are, frequently or very frequently, used by more than 50% of veterinarians (Table 1). Macrolides are also injected, frequently or very frequently, by 47.5% (38/80) of veterinarians. Quinolones and phenicols are rarely or never used. Veterinarians included supporting therapy frequently or very frequently, particularly vitamins (73.1%, 68/93), PGF2α (61.4%, 75/105), and nonsteroidal antiinflammatory drugs (68.2%, 60/88).

3.2.3. Diagnosis of CE

Visual examination of vulvar discharge and rectal palpation are performed to diagnose CE frequently or very frequently by the majority of the veterinarians (91.3%, 94/103 and 86.7%, 85/98, respectively). Moreover, monitoring body temperature and vaginal examination by gloved hand are performed frequently or very frequently by 65.1% (54/83) and 60.9% (56/92) of veterinarians, respectively.

The results revealed that most veterinarians do not use a vaginoscope or a speculum frequently or very frequently (29.8% and 17.5%, respectively). Furthermore, 97% of veterinarians never use a laboratory.

Pus flakes and mucopurulent vaginal discharge are observed frequently or very frequently by 76.7% (79/103) and 75.8% (75/99) of veterinarians, respectively. Half of veterinarians observe general symptoms and a distended uterus in rectal examination (60.2% (56/93), 55.1% (49/89), respectively) (Figure 2).

3.2.4. Treatment of CE

In the case of CE presenting with mucopurulent or purulent discharge, an association between general and intrauterine treatments was frequently or very frequently established by 64.1% (66/103) and 71.3% (72/101) of veterinarians, respectively.

PGF2α is used by 78.6% (77/98) of veterinarians frequently or very frequently to treat CE and it is used even in the absence of a corpus luteum by 56.5% (61/108) of veterinarians.

Intrauterine administration of antibiotics is carried out by 87% of veterinarians. Tetracycline and penicillin-streptomycin association are used frequently or very frequently by 57% (49/86) and 58% (51/88) of veterinarians, respectively. Cephalosporins are used frequently or very frequently by 40.5% (32/79) of veterinarians (Table 3).

The systemic administration of antibiotics is used systematically by 53.3% of veterinarians to treat CE. Parenteral penicillins were systemically applied frequently or very frequently by 64.4% (58/90) of veterinarians, whereas macrolides and cephalosporins were frequently or very frequently injected by 49.4% (40/83) and 48.2% (40/83) of practitioners, respectively (Table 4).

3.3. Univariate analysis

The results of univariate analysis are presented in Tables 5 and 6.

3.3.1. Puerperal metritis

Compared to veterinarians whose main activity was not bovine medicine, bovine practitioners (main activity was bovine medicine) were 3 times more likely to practice palpation of the uterus (83.6% vs. 61.8%, P = 0.022) and 4.8 times less likely to observe an elevation of temperature (75.8% vs. 93.5%, P = 0.037) for diagnosis of PM. They were also 4.5 times less likely to use IU tetracycline (61.4% vs.

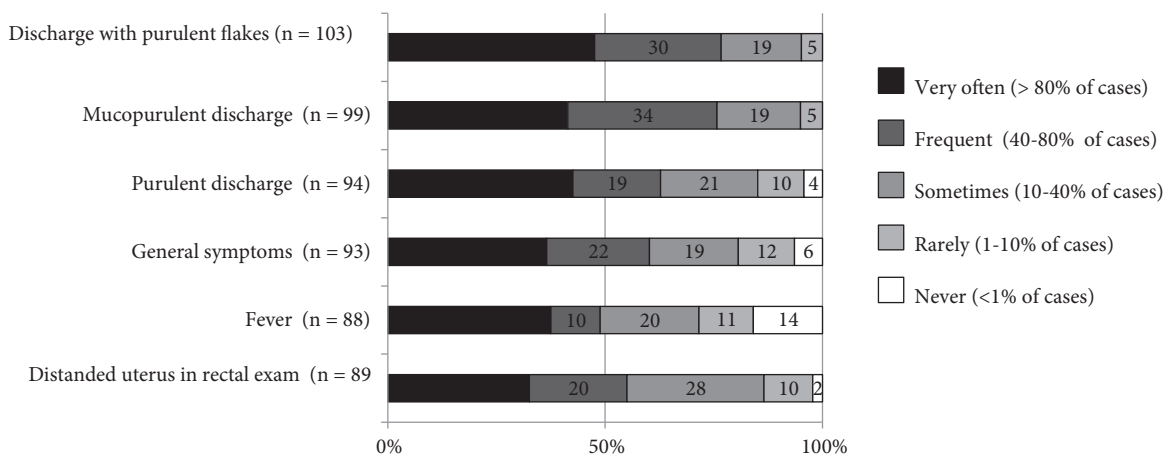


Figure 2. Frequency distribution of the symptoms of CE from the perspective of the responding veterinarians, n = number of responses.

Table 3. Frequencies of the intrauterine drugs used in cows with CE.

Treatment	Very frequent (>80% of cases)	Frequent (40%–80% of cases)	Sometimes (10%–40% of cases)	Rarely (1%–10% of cases)	Never (<1% of cases)	Number of respondents
Tetracycline	43.0%	14.0%	11.6%	10.5%	20.9%	86
Penicillin-streptomycin	39.8%	18.2%	13.6%	3.4%	25.0%	88
Cephalosporin	34.2%	6.3%	19.0%	5.1%	35.4%	79
Uterine lavage	20.0%	15.0%	12.5%	15.0%	37.5%	80
Potassium permanganate	18.4%	11.8%	13.2%	11.8%	44.7%	76
Penicillin	16.2%	21.6%	14.9%	8.1%	39.2%	74
Other	6.2%	7.7%	9.2%	12.3%	64.6%	65
Diluted betadine	4.1%	13.7%	16.4%	13.7%	52.1%	73
Aminoglycosides	5.8%	8.7%	13.0%	5.8%	66.7%	69
Rifaximin	0%	1.4%	5.8%	15.9%	76.8%	69

Table 4. Frequencies of parenteral antibiotic therapy used in cows with CE.

Treatment	Very frequent (>80% of cases)	Frequent (40%–80% of cases)	Sometimes (10%–40% of cases)	Rarely (1%–10% of cases)	Never (<1% of cases)	Number of respondents
Penicillins	38.9%	25.6%	13.3%	7.8%	14.4%	90
Tetracycline	33.3%	27.3%	9.1%	6.1%	24.2%	33
Cephalosporin	32.5%	15.7%	8.4%	12.0%	31.3%	83
Association	31.9%	18.1%	20.8%	9.7%	19.4%	72
Macrolides	25.9%	23.5%	14.8%	9.9%	25.9%	81
Sulfamides	13.2%	11.8%	23.7%	9.2%	42.1%	76
Aminoglycosides	7.2%	14.5%	15.9%	15.9%	46.4%	69
Quinolones	5.9%	8.8%	11.8%	13.2%	60.3%	68
Phenicol	1.5%	3.0%	6.1%	7.6%	81.8%	66

87.5%, $P = 0.009$), 3.4 times more likely to use parenteral cephalosporins (64.4% vs. 34.8%, $P = 0.02$), and 3.1 times less likely to use vitamins to treat PM (65.5% vs. 85.4%, $P = 0.05$).

Veterinarians with more than 10 years of experience were 2.7 times less likely to use intrauterine tetracyclines (64.9% vs. 83.3%, $P = 0.042$) and 5.4 times more likely to use IU cephalosporins (43.4% vs. 12.5%, $P = 0.003$) compared to veterinarians with less than 10 years of experience.

Inseminators were 4.3 times less likely than those not practicing insemination to take body temperatures (75.5% vs. 93.0%, $P = 0.019$) and to observe fever (76.8% vs. 93.5%, $P = 0.021$). Inseminators were also 4.7 times more likely to use IU cephalosporins (44% vs. 14.3%, $P = 0.004$), 5.6 times more likely to not use systemic treatment (27% vs. 6.25%, $P = 0.023$), 4.3 times less likely to use systemic penicillin (52.3% vs. 82.9%, $P = 0.003$), and 2.5 times more

likely to use systemic cephalosporins (60.1% vs. 38.9%, $P = 0.053$).

In comparison with those monitoring fewer than 50 bovine farms, veterinarians monitoring more than 50 farms were 3.1 times less likely to use IU tetracycline (62% vs. 83.7%, $P = 0.015$), and 3.8 times more likely to use IU cephalosporin (42.6% vs. 16.2%, $P = 0.01$). They were also 2.6 times less likely to use parenteral macrolides (35.6% vs. 61.1%, $P = 0.022$).

3.3.2. Clinical endometritis

When compared to noninseminators, inseminators were 4.7 times more likely to use echography (37.0% vs. 11.1%, $P = 0.008$) and 2.9 times more likely to use a vaginoscope (37.5% vs. 17.1%, $P = 0.043$) to diagnose CE. They were also 2.5 times less likely to observe fever (38.3% vs. 61%, $P = 0.034$) and 2.5 times less likely to observe an alteration of the general state of the cow (50.0% vs. 72.5%, $P = 0.029$).

Table 5. Summary of the results of a univariate logistic regression with statements

Parameter	Bovines as main activity	P	>10 years of experience	P
Palpation of the uterus	3.03 (1.15–8.00)	0.022		
Fever	0.21 (0.046–1.01)	0.037		
Intrauterine tetracycline	0.22 (0.07–0.73)	0.009	0.37 (0.14–0.98)	0.042
Intrauterine cephalosporin			5.37 (1.65–17.47)	0.003
Parenteral cephalosporin	3.40 (1.19–9.74)	0.02		
Parenteral macrolide				
Vitamins	0.32 (0.1–1.04)	0.05		
	Practice of AI	P	>50 herds	P
Palpation of the uterus				
Taking rectal temperature	0.23 (0.06–0.85)	0.019		
Fever	0.23 (0.06–0.86)	0.021		
No parenteral antibiotics	5.55 (1.12–27.65)			
Intrauterine tetracycline			0.32 (0.12–0.82)	0.015
Parenteral tetracycline	0.4 (0.16–0.97)	0.042		
Intrauterine cephalosporin	4.71 (1.57–14.15)	0.004	3.84 (1.34–10.91)	0.01
Parenteral cephalosporin	2.46 (0.98–6.15)	0.053		
Parenteral penicillins	0.23 (0.082–0.62)	0.003		
Parenteral macrolides			0.35 (0.14–0.87)	0.022

Table 6. Summary of the results of the univariate logistic regression model for statements regarding the diagnosis and treatment of CE.

Parameter	Bovines as main activity	P	>10 years of experience	P
Rectal temperature	0.29 (0.1–0.84)	0.019		
Fever	0.23 (0.09–0.61)	0.003	0.44 (0.18–1.03)	0.056
Distended uterus			2.52 (1.06–5.97)	0.034
Intrauterine tetracycline	0.30 (0.11–0.80)	0.014		
Intrauterine cephalosporin	4.17 (1.41–12.34)	0.008	3.16 (1.21–8.28)	0.017
Parenteral antibiotics systematically	0.40 (0.17–0.96)	0.037		
PGF2α without corpus luteum			2.33 (1.06–5.10)	0.033
	Practice of AI	P	>50 herds	P
Echography	4.69 (1.41–15.56)	0.008		
Vaginoscopy	2.90 (1.01–8.33)	0.043		
Fever	0.4 (0.17–0.94)	0.034	0.28 (0.12–0.67)	0.004
Alteration of the general state	0.38 (0.16–0.92)	0.029	0.30 (0.13–0.74)	0.007
Intrauterine tetracycline			0.34 (0.14–0.83)	0.017
Intrauterine cephalosporin	8.70 (2.84–26.69)	<0.001	2.60 (1.01–6.70)	0.046
Parenteral antibiotics systematically	0.31 (0.14–0.70)	0.004	0.35 (0.16–0.79)	0.01
Parenteral macrolides			0.38 (0.15–0.94)	0.034
Parenteral vitamins			0.2 (0.08–0.52)	0.001

Furthermore, inseminators were 3.2 times less likely to use parenteral antibiotics systematically (40.7% vs. 68.9%, $P = 0.004$) and 8.7 times more likely to use IU cephalosporin for CE treatment (60.0% vs. 14.7%, $P < 0.001$).

Bovine practitioners were 3.4 times less likely to measure body temperature (51.1% vs. 78.6%, $P = 0.019$) and 4.3 times less likely to observe fever (32.7% vs. 67.9%, $P = 0.003$). They were also 3.3 times less likely to use IU tetracycline (41.3% vs. 70.0%, $P = 0.014$), 2.5 times less likely to use parenteral antibiotics systematically (41.3% vs. 63.6%, $P = 0.037$), and 4 times more likely to use IU cephalosporins (55.6% vs. 23.1%, $P = 0.008$) for CE treatment.

Veterinarians with more than 10 years of experience were 2 times less likely to observe fever (40% vs. 60.5%, $P = 0.056$) and 3 times more likely to note a distended uterus (64.7% vs. 41.7%, $P = 0.034$). They were 3 times more likely to use IU cephalosporins (52.3% vs. 25.7%, $P = 0.017$) and 2 times more likely to use PGF2 α in the absence of a corpus luteum (65.1% vs. 44.4%, $P = 0.033$).

Veterinarians monitoring more than 50 bovine farms were 3.6 times less likely to observe fever (33.3% vs. 64.3%, $P = 0.004$) and 3.3 times less likely to observe alteration of the general state of the cow (46.9% vs. 74.4%, $P = 0.007$). They were also 2.9 times less likely to use tetracyclines (44.2% vs. 69.8%, $P = 0.017$) and 2.6 times more likely to use IU cephalosporins (50.0% vs. 27.8%, $P = 0.046$). In addition, they were 2.9 times less likely to use parenteral antibiotics systematically (48.9% vs. 66.0%, $P = 0.01$), 2.6 times less likely to use systemic macrolides (39.1% vs. 62.9%, $P = 0.034$), and 5 times less likely to use vitamins (43.5% vs. 79.5%, $P = 0.001$).

3.4. Multivariate analysis

Inseminators were 4 times more likely to use IU cephalosporins to treat PM and 5 times more likely to treat CE. Likewise, veterinarians with more than 10 years of experience were 4 times more likely to use IU cephalosporins to treat PM. Moreover, bovine practitioners were 3 times less likely to observe hyperthermia in cases of CE (Table 7).

4. Discussion

The present survey was undertaken to investigate practices of Algerian veterinarians in the diagnosis and treatment of PM and CE. We hypothesize that factors related to the experience of the veterinarians, their practice of AI, main activity, and number of farms monitored may influence their practices towards the uterine infections.

It was reported that clinical diagnosis of PM is based on the presence of general and local signs including purulent vaginal discharge, fever, appetite loss, decrease in milk production, and distended uterus [8,10,23]. In our survey, these signs were adopted by most veterinarians for PM diagnosis. Moreover, the surveyed veterinarians indicated that signs of intoxication are rarely present, which may be related to early diagnosis before intensification of the animal's state and the appearance of signs of intoxication. A similar survey conducted with Swiss veterinarians reported the same results for PM diagnosis [22].

The use of systemic antibiotics is the conventional treatment of PM [17,24]. In our study, the majority of Algerians veterinarians used systemic antibiotics for PM. A similar result was observed for Swiss practitioners [22]. In the current survey, practitioners used penicillins most often, followed by tetracyclines, cephalosporins, and aminoglycosides. Likewise, in a study in Sweden, PM was treated principally with penicillins and secondarily with tetracyclines. In the same study, cephalosporins were not used by veterinarians [25]. In this study, the choice of the treatment was based on the recommendations of the Swedish policy recommending penicillin as the first choice antibiotic for PM [25]. Tetracyclines, however, were the principal antibiotics reported by Swiss veterinarians for PM treatment [13]. Different studies were conducted to reveal the optimum antibiotics for PM. In this respect, the efficiency of tetracycline and penicillins requires their use at high concentrations, which enhances their withdrawal periods in meat and milk [26]. Cephalosporin is efficient at recommended doses. Furthermore, at the recommended dose, high concentrations of cephalosporin were observed in the serum, endometrium, caruncles, cotyledons, and lochia with no withdrawal periods [26–

Table 7. Summary of the results of a series of multivariable logistic regression models for statements regarding the diagnosis and treatment of PM and CE.

Parameter for PM			>10 years of experience	P	Practice of AI	P
Intrauterine cephalosporin			3.8(1.13–13.36)	0.031	3.5 (1.02–12.23)	0.046
Parameter for CE	Bovines as main activity	P	>10 years of experience	P	Practice of AI	P
Hyperthermia	0.29 (0.11–0.83)	0.02	0.26 (0.18–1.34)	0.16		
Intrauterine cephalosporin			2.8 (0.91–8.76)	0.072	5.1 (1.58–16.84)	0.007

28]. In order to show the antibiotics of choice for PM, Smith et al. compared penicillin G and cephalosporin. No difference in terms of cure was observed between the two tested antibiotics [13]. Thus, cephalosporin seems more appropriate for systemic treatment of PM. The lack of use of cephalosporin in our study may be attributed to its price and its relatively recent introduction to the field compared to penicillins and tetracyclines. In our survey, bovine practitioners and inseminators more frequently used cephalosporins, which may be due to their more frequent dealings with bovine pathologies including PM, allowing the adoption of the appropriate treatment.

In the present survey, almost 80% of surveyed veterinarians performed intrauterine treatment for PM with tetracycline and to a lesser extent with penicillin-streptomycin and cephalosporin, respectively. Inseminators and veterinarians monitoring more than 50 bovine farms used more IU cephalosporin. In a similar survey in Switzerland [22], the results revealed that more than 90% of veterinarians performed intrauterine therapy using tetracycline and cephalosporin, but not penicillin-streptomycin. Many studies showed beneficial effects of IU use of oxytetracycline at high doses [9], but other studies reported the noneffectiveness [13]. In addition it is irritating to the endometrium and alters local immunity. However, our survey, like that in Switzerland, revealed that tetracyclines are still used by veterinarians for PM treatment.

In association with antibiotics, several molecules are used to reinforce the treatment for uterine infections. Among these molecules, PGF_{2α} and nonsteroid antiinflammatory drugs are the most often implicated in PM treatment. Regarding PGF_{2α}, it is used for its luteolytic effect, uterotonic nature, and leukocyte stimulation. However, many studies reported no effect of PGF_{2α} when used to treat uterine infection. In our survey and that in Switzerland, PGF_{2α} was used systematically despite the contradictory results concerning its effect. In cases of PM, one study evaluated the use of PGF_{2α} as a complementary treatment to cephalosporin. It was concluded that 2 doses of PGF_{2α} were beneficial for primiparous cows having PM but not for multiparous cows [29].

Concerning nonsteroid antiinflammatory drugs, the Algerian veterinarians, like those of Switzerland [22], frequently use them in association with antibiotics. The use of nonsteroid antiinflammatory drugs in cases of PM may be explained by the presence of fever. However, there is a contradiction regarding the benefits of nonsteroid antiinflammatory drugs in PM. Amiridis et al. showed a more rapid uterine involution and onset of ovarian activity in animals having PM treated by nonsteroid antiinflammatory drugs (flunixin meglumine) in addition to systematic antimicrobials [30]. On the contrary, other

studies found no superior effect when these drugs were used in combination with antibiotics [31,32]. Further studies are required to provide evidence-based medicine with the proof about the use of nonsteroid antiinflammatory drugs to treat PM.

Clinical endometritis is a uterine infection occurring after 21 days postpartum, characterized by the presence of purulent material in the vagina [8]. In the present study, the surveyed veterinarians observed CE between 22 and 30 days postpartum. Furthermore, they frequently observed local symptoms by visual exam of the vulvar discharge and rectal palpation. Likewise, the survey in Switzerland revealed that CE was diagnosed between 21 and 35 days postpartum by local symptoms. Moreover, in this study, rectal palpation and vaginal examination were the diagnostic tools used [22]. Previous clinical studies reported that efficient tools for CE diagnosis are detection of purulent material in the vagina by gloved hand or vaginoscope and rectal palpation of the uterus combined with external inspection of vulvar discharge [11]. In the current survey, Algerian veterinarians used rectal palpation of the uterus and external inspection of vulvar discharge to diagnosis CE. Concerning Swiss veterinarians, diagnosis is based on rectal palpation and detection of purulent material in the vagina by gloved hand. CE diagnosis tools adopted by Algerian and Swiss veterinarians could be justified by their efficiency and practicability, not requiring an instrument (vaginoscope).

In our survey as well as in the survey performed in Switzerland [22], PGF_{2α} is used by the majority of veterinarians for treating CE. Previous studies showed that PGF_{2α} is efficient in the treatment of CE when a corpus luteum exists. Thus, the purpose of inclusion of PGF_{2α} in CE treatment is to provoke luteolysis, the apparition of estrus, and subsequent uterine contractility. These processes lead to clearance of the uterine cavity. Moreover, PGF_{2α} improves the local immunity of the uterus and the recovery of the physiologic uterine state [33,34]. In addition, PGF_{2α} was reported to be preferred to antibiotics due to its null withdrawal period and its lack of implication in the emergence of resistant bacteria [35]. In cases of CE with absence of a corpus luteum, several clinical trials showed conflicting results about the efficiency of PGF_{2α} [12,36,37]. In our survey, an important part of the veterinarians used PGF_{2α} in the absence of a corpus luteum. Even in the absence of a corpus luteum, PGF_{2α} increases leukotriene B₄ secretion by the uterus, which supports chemotaxis, cell-mediated cytotoxicity, phagocytosis, and lymphocyte function [34]. This may justify its use by the surveyed Algerian veterinarians.

Intrauterine administration of antibiotics is considered as the best approach for CE. This is because infection is limited to the endometrium. In our study, tetracycline

is used by most surveyed veterinarians. However, Swiss veterinarians mainly used IU cephalosporin for CE [22]. The selection of tetracycline by Algerian veterinarians may be attributed to its high endometrial concentration and its poor absorption after intrauterine administration [38]. However, bacteriological studies showed that a large part of bacteria causing uterine infection are resistant to tetracycline [39–44]. Cephapirin is reported as the most appropriate antibiotic for treatment of CE and the effectiveness of cephalosporin against uterine pathogens was proven *in vitro* [39–44]. In addition, it has no withdrawal period in milk and meat. In our study, the multivariate analysis indicated that inseminators, whatever their experience, used IU cephalosporin more frequently to treat CE. This may indicate that inseminators are more concerned about uterine health, which is a determinant factor for the success of AI.

Systemic antibiotics are also used by Algerian veterinarians (more than half) to treat CE. In the Swiss survey, most of the veterinarians did not use systemic antibiotics. It was reported that administration of

antibiotics within the uterus is efficient to treat CE without a need for further systemic antibiotics. Furthermore, the use of systemic antibiotics is costly and requires long withdrawal period in milk. Thus, the parenteral use of antibiotics in cases of CE by Algerian veterinarians is not justified.

Finally, we conclude that the diagnoses of PM and CE by surveyed veterinarians are close to the reported criteria. However, a contradiction in the treatment for CE and PM is observed, particularly in the use of IU antibiotics in PM and PGF2 in the absence of a corpus luteum in CE. Moreover, some antibiotics used are not reported in the literature, like macrolides and penicillin-streptomycin association. Inseminators seem more interested in looking for recent advances about treatment of uterine infection and updating their treatment approaches accordingly.

Acknowledgments

The authors are grateful to all the veterinarians who responded to the survey. The help of Dr Samir Souames and Dr Karim Benhenia is gratefully acknowledged.

References

- Barlett PC, Kirk JH, Wilke MA, Kaneen JB, Mather EC. Metritis complex in Michigan Holstein-Friesian cattle: incidence, descriptive epidemiology and estimated economic impact. *Preventive Veterinary Medicine* 1986; 4: 235-248.
- Dubuc J, Duffield TF, Leslie KE, Walton JS, Leblanc SJ. Effects of postpartum uterine diseases on milk production and culling in dairy cows. *Journal of Dairy Science* 2011; 94 (3): 1339-1346. doi: 10.3168/jds.2010-3758
- Fourichon C, Seegers H, Malher X. Effect of disease on reproduction in the dairy cow: a meta-analysis. *Theriogenology* 2000; 53: 1729-1759.
- Lewis GS. Uterine health and disorders. *Journal of Dairy Science* 1997; 80 (5): 984-994.
- Nakao T, Moriyoshi M, Karata K. The effect of postpartum ovarian dysfunction and endometritis on subsequent reproductive performance in high and medium producing dairy cow. *Theriogenology* 1992; 37 (2): 341-349.
- Pantaleo M, Rizzo A, D'Onghia GG, D'Onghia GG, Roncetti M et al. Immunological aspects of metritis in dairy cows: a review. *Endocrine Metabolic & Immune Disorders - Drug Targets* 2014; 14 (3): 196-205. doi: 10.2174/1871530314666140527142346
- Sheldon IM, Williams EJ, Miller ANA, Nash DM, Herath S. Uterine diseases in cattle after parturition. *Veterinary Journal* 2008; 176 (1): 115-121. doi: 10.1016/j.tvjl.2007.12.031
- Sheldon IM, Lewis GS, LeBlanc S, Gilbert RO. Defining postpartum uterine disease in cattle. *Theriogenology* 2006; 65 (8): 1516-1530. doi: 10.1016/j.theriogenology.2005.08.021
- Gilbert RO. Management of reproductive disease in dairy cows. *Veterinary Clinics of North America: Food Animal Practice* 2016; 32 (2): 387-410. doi: 10.1016/j.cvfa.2016.01.009
- LeBlanc SJ. Postpartum uterine disease and dairy herd reproductive performance: A review. *Veterinary Journal* 2008; 176 (1): 102-114. doi: 10.1016/j.tvjl.2007.12.019
- LeBlanc SJ, Duffield TF, Leslie KE, Bateman KG, Keefe GP et al. Defining and diagnosing postpartum clinical endometritis and its impact on reproductive performance in dairy cows. *Journal of Dairy Science* 2002; 85 (9): 2223-2236. doi: 10.3168/jds.S0022-0302(02)74302-6
- LeBlanc SJ, Duffield TF, Leslie KE, Bateman KG, Keefe GP et al. The effect of treatment of clinical endometritis on reproductive performance in dairy cows. *Journal of Dairy Science* 2002; 85 (9): 2237-2249. doi: 10.3168/jds.S00220302(02)74303-8
- Smith BI, Donovan GA, Risco C, Littell R, Young C et al. Comparison of various antibiotic treatments for cows diagnosed with toxic puerperal metritis. *Journal of Dairy Science* 1998; 81 (6): 1555-1562.
- Nakao T, Moriyoshi M, Kawata K. Effect of post-partum intrauterine treatment with 2% polyvinylpyrrolidone-iodine solution on reproductive efficiency in cows. *Theriogenology* 1988; 30 (6): 1033-1043.
- Sannmann I, Burfeind O, Voigtsberger R, Heuwieser W. Comparison of two monitoring and treatment strategies for cows with acute puerperal metritis. *Theriogenology* 2013; 79 (6): 961-969. doi: 10.1016/j.theriogenology.2013.01.016

16. Reppert EJ. Evidence for the use of ceftiofur for treatment of metritis in dairy cattle. *Veterinary Clinics of North America: Food Animal Practice* 2015; 31 (1): 139-149. doi: 10.1016/j.cvfa.2014.11.007
17. Haimerl P, Heuwieser W. Invited review: Antibiotic treatment of metritis in dairy cows: a systematic approach. *Journal of Dairy Science* 2014; 97: 1-13. doi: 10.3168/jds.2014-8462
18. Kaufmann TB, Westermann S, Drillich M, Plöntzke J, Heuwieser W. Systemic antibiotic treatment of clinical endometritis in dairy cows with ceftiofur or two doses of cloprostenol in a 14-d interval. *Animal Reproduction Science* 2010; 121 (1-2): 55-62. doi: 10.1016/j.anireprosci.2010.04.190
19. Paisley LG, Mickelsen WD, Anderson PB. Mechanisms and therapy for retained fetal membranes and uterine infections of cows: a review. *Theriogenology* 1986; 25 (3): 353-381.
20. Szenci O. Recent possibilities for diagnosis and treatment of post parturient uterine diseases in dairy cow. *Journal of Fertilization: In Vitro - IVF-Worldwide, Reproductive Medicine, Genetics & Stem Cell Biol* 2016; 4 (1): 1000170. doi: 10.4172/2375-4508.1000170
21. Pohl A, Bertulat S, Borchardt S, Burfeind O, Heuwieser W. Randomized, controlled clinical trial on the efficacy of nonsteroidal antiinflammatory drugs for the treatment of acute puerperal metritis in dairy cows. *Journal of Dairy Science* 2016; 99: 1-9. doi: 10.3168/jds.2015-10775
22. Hehenberger EM, Doherr MG, Bodmer M, Steiner A, Hirsbrunner G. Diagnosis and therapy of retained fetal membranes, puerperal metritis and clinical endometritis in cattle: Results of the Online-survey among Swiss practitioners. II. Puerperal metritis and clinical endometritis. *Schweizer Archiv für Tierheilkunde* 2015; 157 (9): 503-512 (in German with an abstract in English). doi: 10.17236/sat00033
23. Sheldon IM, Cronin J, Goetze L, Donofrio G, Schubert HJ. Defining postpartum uterine disease and the mechanisms of infection and immunity in the female reproductive tract in cattle. *Biology of Reproduction* 2009; 81 (6): 1025-1032. doi: 10.1095/biolreprod.109.077370
24. Haimerl P, Heuwieser W. Antibiotic treatment of metritis in dairy cows: a meta-analysis. *Journal of Dairy Science* 2017; 97 (11): 6649-6661. doi: 10.3168/jds.2016-11834
25. Ordell A, Unnerstad HE, Nyman A, Gustafsson H, Båge R. A longitudinal cohort study of acute puerperal metritis cases in Swedish dairy cows. *Acta Veterinaria Scandinavica* 2016; 58 (1): 79. doi: 10.1186/s13028-016-0257-9
26. Drillich M, Arlt S, Kersting S, Bergwerff AA, Scherpenisse P et al. Ceftiofur derivatives in serum, uterine tissues, cotyledons, and lochia after fetal membrane retention. *Journal of Dairy Science* 2006; 89 (9): 3431-3438. doi: 10.3168/jds.S0022-0302(06)72380-3
27. von Krueger X, Scherpenisse P, Roiger S, Heuwieser W. Determination of ceftiofur derivatives in serum, endometrial tissue, and lochia in puerperal dairy cows with fever or acute puerperal metritis after subcutaneous administration of ceftiofur crystalline free acid. *Journal of Dairy Science* 2013; 96 (2): 1054-1062. doi: 10.3168/jds.2012-6034
28. Okker H, Schmitt EJ, Vos PLAM, Scherpenisse P, Bergwerff AA et al. Pharmacokinetics of ceftiofur in plasma and uterine secretions and tissues after subcutaneous postpartum administration in lactating dairy cows. *Journal of Veterinary Pharmacology and Therapeutics* 2002; 25 (1): 33-38. doi: 10.1046/j.1365-2885.2002.00372.x
29. Melendez P, McHale J, Bartolome J, Archbald LF, Donovan GA. Uterine involution and fertility of Holstein cows subsequent to early postpartum PGF2 alpha treatment for acute puerperal metritis. *Journal of Dairy Science* 2004; 87 (10): 3238-3246. doi: 10.3168/jds.S0022-0302(04)73460-8
30. Amiridis GS, Leontides L, Tassos E, Kostoulas P, Fthenakis GC. Flunixin meglumine accelerates uterine involution and shortens the calving-to-first-oestrus interval in cows with puerperal metritis. *Journal of Veterinary Pharmacology and Therapeutics*. 200; 24 (5): 365-367. doi: 10.1046/j.1365-2885.2001.00358.x
31. Drillich M, Voigt D, Forderung D, Heuwieser W. Treatment of acute puerperal metritis with flunixin meglumine in addition to antibiotic treatment. *Journal of Dairy Science* 2007; 90 (8): 3758-63. doi: 10.3168/jds.2007-0052
32. Jeremejeva J, Orro T, Waldmann A, Kask K. Treatment of dairy cows with PGF2alpha or NSAID, in combination with antibiotics, in cases of postpartum uterine inflammation. *Acta Veterinaria Scandinavica* 2012; 54 (1): 45. doi: 10.1186/1751-0147-54-45
33. Dubuc J, Duffield TF, Leslie KE, Walton JS, LeBlanc SJ. Randomized clinical trial of antibiotic and prostaglandin treatments for uterine health and reproductive performance in dairy cows. *Journal of Dairy Science* 2011; 94 (3): 1325-1338. doi: 10.3168/jds.2010-3757
34. Lefebvre RC, Stock AE. Therapeutic efficiency of antibiotics and prostaglandin F2a in postpartum dairy cows with clinical endometritis: an evidence-based evaluation. *Veterinary Clinics of North America: Food Animal Practice* 2012; 28 (1): 79-96. doi: 10.1016/j.cvfa.2012.01.002
35. Okawa H, Fujikura A, Wijayagunawardane MMP, Vos PLAM, Taniguchi M et al. Effect of diagnosis and treatment of clinical endometritis based on vaginal discharge score grading system in postpartum Holstein cows. *Journal of Veterinary Medical Science* 2017; 79 (9): 1545-1551. doi: 10.1292/jvms.16-0593
36. Haimerl P, Heuwieser W, Arlt S. Therapy of bovine endometritis with prostaglandin F2a: a meta-analysis. *Journal of Dairy Science* 2013; 96 (5): 2973-2987. doi: 10.3168/jds.2012-6154
37. McDougall S, de Boer M, Compton C, LeBlanc SJ. Clinical trial of treatment programs for purulent vaginal discharge in lactating dairy cattle in New Zealand. *Theriogenology* 2013; 79 (8): 11391145. doi: 10.1016/j.theriogenology.2013.02.002
38. Sheldon IM, Noakes DE. Comparison of three treatments for bovine endometritis. *Veterinary Record* 1998; 142 (21): 575-579. doi: 10.1136/vr.142.21.575
39. Guerin-Fauble V, Flandrois JP, Broye E, Tupin F, Richard Y. *Actinomyces pyogenes*: susceptibility of 103 clinical animal isolates to 22 antimicrobial agents. *Veterinary Research* 1993; 24 (3): 251-259.

40. Yoshimura H, Kojima A, Ishimaru M. Antimicrobial susceptibility of *Arcanobacterium pyogenes* isolated from cattle and pigs. *Antimicrob Agents Chemother* 2000; 47: 139-143.
41. Sheldon IM, Bushnell M, Montgomery J, Rycroft N. Minimum inhibitory concentrations of some antimicrobial drugs against bacteria causing uterine infections in cattle. *Veterinary Record* 2004; 155 (13): 383-387. doi: 10.1136/vr.155.13.383
42. Malinowski E, Lassa H, Markiewicz H, Kaptur M, Nadolny M et al. Sensitivity to antibiotics of *Arcanobacterium pyogenes* and *Escherichia coli* from the uteri of cows with metritis/ endometritis. *Veterinary Journal* 2011; 187 (2): 234-238. doi: 10.1016/j.tvjl.2009.12.010
43. Brodzki P, Bochniarz M, Brodzki A, Wrona Z, Wawron W. *Trueperella pyogenes* and *Escherichia coli* as an etiological factor of endometritis in cows and the susceptibility of these bacteria to selected antibiotics. *Polish Journal of Veterinary Science* 2014; 17 (4): 657-664.
44. de Boer M, Heuer C, Hussein H, McDougall S. Minimum inhibitory concentrations of selected antimicrobials against *Escherichia coli* and *Trueperella pyogenes* of bovine uterine origin. *Journal of Dairy Science* 2015; 98 (7): 4427-4438. doi: 10.3168/jds.2014-8890