Achievement of an efficacious human and companion animal’s therapy in Pasteurella multocida infections

Received for publication, June 20, 2009
Accepted, January 15, 2010

SIMONA IVANA1, FILEA I. IVANA4, CHIURCIU CONSTANTIN5, GHEORGHE CÂMPEANU3, ALEXANDRU T. BOGDAN2, IOlITA LUCIAN5, IPATE IUDITH2, ALEXANDRU NICOLAE POPESCU2, BOGDAN GEORGESCU1, CARMEN IONITA1
1Faculty of Veterinary Medicine, University of Agronomical Science and Veterinary medicine Bucharest, 105, Splaiul Independentei, 050097, Bucharest, Romania.
2Center of Study and Research for Biodiversity from Animal Genetic Resources Academy David Davidescu Romanian Academy, 13 Calea 13 Septembrie, 050711, Bucharest Romania
Corresponding author: Simona Ivana, Faculty of Veterinary Medicine, 105, Splaiul Independentei, 050097, Bucharest, Romania, email: simonaivana@yahoo.com
3Faculty of Biotechnologies, University of Agronomical Science and Veterinary medicine Bucharest, 59, Mărășești Bd., cod: 011464, Bucharest, Romania
4“Asclepius” Biotechnological Researches Center, Bucharest, Romania
5Romvac Co., Voluntari, Romania

Abstract

The zoonosis according to The Health World Organization, are defined as being “diseases or infections which are naturally transmitted between the vertebrate animal and man” but this definition is still submissive of some wide debates. The close cohabitation of people with their animals in large areas of the world, often in inadequate conditions, continues to favor the zoonotic infections. The dogs and cats population as pets increased in the whole world. The danger of this kind of zoonotic diseases is increasing, but national and local settlements have been promulgated to establish the places where animals can be accepted and to prevent the environment pollution.

Keywords: treatment, zoonosis, Pasteurella multocida, antibiotic, epidemiology

Introduction

Currently, the research in zoonosis area is in process with separate teams/communities with medical or veterinary profile [18, 21, 41]. The World Organization of Animal Health (OIE) as well as Directorate-General for Health and Consumer Protection (European Commission) often abbreviated as "SANCO" or "DG-SANCO", recently presented documents by which The National Competent Authorities responsible for animal health and food safety are encouraged to use proportioned schemes to get comparative and representative data concerning the evaluation of the sources tendencies of the zoonosis and zoonotic agents. Also, another important document is represented by The Common Order of the Romanian Ministry of the Agriculture and Alimentation, No. 25/1993 and Romanian Health Ministry Order No. 474/1993, concerning the preventive health jobs, ensured by sanitary-veterinary organs and human-sanitary ones for the prevention and struggle of the diseases from the animals to man kind. Pasteurella spp. may induce in pets some diseases. The human infections arise after bites, scratches or by direct contact with the saliva of the infected animals, taking into account that 90% of the feline population is Pasteurella carrier. Pasteurella multocida subspecies multocida and septica were isolated from severe or systemic infections caused by the bite or licking the wounds by dogs and cats. Also lots of cats and dogs carry the germ in the saliva but the risk of infections in man is decreasing in the absence of the bites or scratches [35]. Yet they pointed out cases of infection to immunocompromised human subjects.
*Pasteurella multocida* develops in usual mediums with pH 7.8, in aerobiosis at 37°C. It may be bipolar coloured, especially in fresh isolates, by the Giemsa, Wright or Romanowsky staining methods. The cultures and different variants of colonies selected can be kept on: BBL-soy-trypticase, Difco-tryptose-starch-Gibco-dextrosis or other similar mediums with or without serum addition.

The precocious diagnosis is important especially in young and elder people as well as in the immunosuppressed patients including the pregnant woman [24, 22]. We must search a historian of contact with the animals. Recently, with good results in the identification of the species of *Pasteurella* was used the API system.

The serological tests to detect the specific antibodies aren’t used frequently in the aim of diagnosis. The higher titration (from 1/160 up to 1/1280 or higher ones) obtained through an immunohemagglutination reaction can give indications for a recent exposure. The patients with food-borne diseases have a clinical view with explosive disturbance syndrome at digestive tract level, it having a short incubation period, produced by microbial agents or its metabolites, represented by microbial toxins [1].

Above 250 food-borne diseases have been described, and usual these have bacterial or viral etiology. These diseases have many different symptoms, so there is no one "syndrome" that is food-borne illness [2].

A food-borne infection is suspected if some suspect signs are reported in association with several epidemiological data [3]:

a) it is affecting one or more person that eat the same food;
b) it has an acute start based on initial health of the subject;
c) they have a super acute or acute evolution to a rapid recovery or death;
d) they are not transmissible;
e) the symptoms are very well defined, being specific for evolution of food-borne infections represented by:
   • superior digestive syndrome (nausea, vomiting);
   • inferior digestive syndrome (gastroenteritis, coloenteritis);
   • neurological syndrome (paralysis, neuromotor disturbances).

Following a statistical analysis of epidemiological data food-borne infections commonly recognized are bacteria *Campylobacter, Salmonella*, and *E. coli* O157:H7, and by a group of viruses called calcivirus, also known as the Norwalk and Norwalk-like viruses [2], but in alimentary industry or chattering the most bacteria organisms incriminated in food-borne pathology are *Staphylococcus aureus, Clostridium perfringens, Clostridium botulinum* and *Salmonella spp.* [3].

**Transmission to man**

It is mainly caused by bites or scratches of dogs and cats. Other transmission ways have been described, like contact of mucous or cutaneous lesions with their saliva [15, 17]. The meningitis and otics infection cases with *Pasteurella multocida* were associated with the licking of the face and ears by cats and dogs and a endocarditis case was associated with the licking of some ulcers of the owner legs by his dog. Also, the man can be infected on respiratory path through aerosols, causing tonsillitis, sinusites, epiglotitis, undermandible cellulitis (Ludwig’s angina).

Most infections underwent local treatments with or without systemic antibiotherapy. *Pasteurella* is very sensitive to penicillin and ampicillin. Antibiotics treatment is used in subjects with low resistance (for instance: steroids treatment, lesions of the face and hands, immunocompromised or diabetic patients).

**Prognostic**

The disease is auto limited but toxemia or other severe complications can appear. The studies presented in this paper were performed from January 2007 to may 2008 as part as the Institute of Comparative Medicine in Bucharest, the Faculty of Veterinary Medicine Bucharest, The Cantacuzino Institute and the Biodiversity Center as part as the Romanian Academy.
Achievement of an efficacious human and companion animal’s therapy in Pasteurella multocida infections

Materials and methods

The aim of the experiment: the human and companion animals therapy of Pasteurella multocida infections.

Experimental groups:

1st experimental group: 20 cats, which from saliva was sampled for bacteriological test. The tests were performed at the Faculty of Veterinary Medicine Bucharest. The laboratory test consisted in the isolation of the germs on Media Blood Agar 5% as well as their identification.

2nd experimental group: 13 dogs who bit their owners. Bacteriological tests were made in order to isolate the etiologic agents.

The new element of the research was the administration of a sulphadimidine sodium injectable solution, which was given in a dose of 2-4 ml/kg, intramuscular (in 3 dogs) every day, until fever remission. The results were excellent, all animals being cured. Good results were also obtained by association of ampicillin with amoxicillin by oral administration every 8 hours for 7-10 days in a dose of 10 mg/kg. Before and after therapy were taken samples in order to perform bacteriological test, and blood with EDTA for determining the leukocytic formula as well as integral blood for the serological test. All samples were processed and investigated at the Institute of Comparative Medicine in Bucharest and Center of Study and Research for Biodiversity.

3rd experimental group: 10 persons bitted or scratched by companion animals (cats or dogs). Pasteurella multocida was isolated in the laboratory and the respective treatment was performed, according to the stage of the disease. The tests were performed at the Cantacuzino Institute and the Institute of Comparative Medicine. The drug therapy was performed with ampicillin + amoxicillin or ampicillin + clavulanate. The local treatment was performed with a saline Ringer solution and with a 1% solution of iodated povidone.

Experiment course: The epidemiological and microbiological monitoring circuit in veterinary and human investigation was performed is presented in follows diagram.

Results and discussions

The results of the clinical examination before the therapy were following:

- In human patients were observed abrasions, avulsions, lacerations after an aggression caused by dogs and cats, mainly by bites or scratches; in more serious cases were detected lesions of ligaments and tissue necrosis;
- Most lesions caused by cats through scratches, stings and bites were produced at the level of fingers, arms, legs, feet, face and neck
- As regards the dogs, there are various kinds of aggression: dominant aggression, possession aggression, aggression determined by fear, aggression to protect the territory, aggression induced by punishment, aggression induced by pain [21, 28, 36, 47]
The causes of aggression produced by cats are: fear, play, the syndrome of bites through caressing, as well as repeated aggressions by the owner.

1st group: 20 cats from the following breeds: Burmese (4), Siamese (2), Persian (1) and commune (13). 50% exhibited variable clinical manifestations (abscesses, toxemia or sepsis), 20% of cats was carriers, and 30% of cats was with inapparently evolution (see Chart no. 1).

After the therapy an improvement of the symptoms and general state was observed, with the exception of 2 cases which did not respond to the treatment.

Table 1. Results of clinical exam, bacteriological diagnosis, and therapy in 6 cases of feline pasteurellosis

<table>
<thead>
<tr>
<th>Index number of feline cases</th>
<th>Clinical signs</th>
<th>Pasteurella sp. isolated</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>Bitten ulcer, bad general state, anorexia</td>
<td>P. multocida</td>
<td>Ampicillin</td>
</tr>
<tr>
<td>4</td>
<td>Multiple bitten ulcers, moody appetite, septic state</td>
<td>P. multocida</td>
<td>Chloramphenicol</td>
</tr>
<tr>
<td>10</td>
<td>Abrasions, sad face, anorexia</td>
<td>P. septica</td>
<td>Ampicillin</td>
</tr>
<tr>
<td>13</td>
<td>Abscesses, anorexia, bad general state</td>
<td>P. multocida</td>
<td>Ampicillin</td>
</tr>
<tr>
<td>15</td>
<td>Bitten ulcers, sad face, anorexia</td>
<td>P. multocida</td>
<td>Chloramphenicol</td>
</tr>
<tr>
<td>18</td>
<td>Septic state, anorexia, moody appetite</td>
<td>P. septica</td>
<td>Ampicillin</td>
</tr>
</tbody>
</table>

The treatment administration was made depending on the age and average weight. The treatment with antibiotics was made by oral administration every 8 hours for 3-7 days in dose of 10mg/kg. After the treatment we remarked the improvement of general state in most of the cases. An exception was case 18 (Table 1).
Achievement of an efficacious human and companion animal’s therapy in Pasteurella multocida infections

The administration of Sodic sulphamidine injectable solution in dogs was made depending on age and weight of the animals in doses of 4 ml in 5 cases; 6ml in 3 cases and 8ml in 2 cases. After the therapy an improvement of the symptoms and general state was observed in most of the cases treated with Sodic sulphamidine injectable solution [9, 14, 38]. We didn’t notice any modification to the inoculation place in the case of hypodermic administration.

**Table 2. The administration of the treatment with Sodic sulphamidine injectable solution in dogs**

<table>
<thead>
<tr>
<th>Index Number of Dog Cases</th>
<th>Age (years)</th>
<th>Dose (ml)</th>
<th>Administration Path</th>
<th>Period of Time (hours)</th>
<th>Duration (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5</td>
<td>6</td>
<td>I.M.</td>
<td>24</td>
<td>5</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>8</td>
<td>S.C.</td>
<td>24</td>
<td>4</td>
</tr>
<tr>
<td>6</td>
<td>3</td>
<td>6</td>
<td>S.C.</td>
<td>24</td>
<td>3</td>
</tr>
<tr>
<td>7</td>
<td>5</td>
<td>8</td>
<td>I.M.</td>
<td>24</td>
<td>4</td>
</tr>
<tr>
<td>9</td>
<td>5</td>
<td>2</td>
<td>I.M.</td>
<td>24</td>
<td>5</td>
</tr>
<tr>
<td>11</td>
<td>5</td>
<td>4</td>
<td>I.M.</td>
<td>24</td>
<td>4</td>
</tr>
<tr>
<td>12</td>
<td>4</td>
<td>4</td>
<td>I.M.</td>
<td>24</td>
<td>6</td>
</tr>
</tbody>
</table>

The clinical and paraclinical evaluation of the dogs was made to establish or confirm the diagnosis and for the appreciation of curative efficiency of the treatment. The antibiogram was made through the comparison of the results in the case of the dogs treated with Sodic sulphamidine injectable solution and of those treated with ampicillin + amoxicillin. Investigations of the biochemical profile of dog were made for the identification and evaluation of the hematological and renal dysfunctions, before and after the therapy. In the table below values of the total number of leucocytes and leukocyte formula are marked in the case of the dogs treated with Sodic sulphamidine injectable solution [29].

**Chart no. 3. The result of the Sodic sulphamidine injectable solution therapy in dogs**

**Chart no. 4. The result of the Ampicillin + Amoxicillin therapy in dogs**
A diminution of the average number of leucocytes is observed. A substantial diminution of monocytes number from the average value of 9.8 to 4.6 is noticed after the therapy and Eosinophil granulocytes from an average value of 10.4 before therapy to 4.6 after the therapy. The ultrasound exam was done before and after therapy to a dog with hepatic abscess.

**Table 3.** Total number of leucocytes and differential leucocytes count in lot 2 of dogs (before therapy)

<table>
<thead>
<tr>
<th>Sample no.</th>
<th>Total number of leucocytes (mmc)</th>
<th>Differential white blood cell count (%)</th>
<th>Protein serum concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>N  L   M   E   B</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>14,000</td>
<td>83 10 10 10 0</td>
<td>5.9</td>
</tr>
<tr>
<td>2</td>
<td>16,000</td>
<td>79 11 12 15 0</td>
<td>6.3</td>
</tr>
<tr>
<td>3</td>
<td>14,000</td>
<td>74 14 9 7 0</td>
<td>7.3</td>
</tr>
<tr>
<td>4</td>
<td>15,000</td>
<td>75 13 7 8 0</td>
<td>7.0</td>
</tr>
<tr>
<td>5</td>
<td>14,000</td>
<td>80 15 11 12 0</td>
<td>6.8</td>
</tr>
<tr>
<td>mean</td>
<td>14,000</td>
<td>78.2 12.6 9.8 10.4 0</td>
<td>6.6</td>
</tr>
</tbody>
</table>

* N = neutrophils, L = lymphocytes, M = monocytes, E = eosinophils, B = basophils.

**Table 4.** Total number of leucocytes and differential leucocytes count in lot 2 of dogs (after the treatment)

<table>
<thead>
<tr>
<th>Sample no.</th>
<th>Total number of leucocytes (mmc)</th>
<th>Differential white blood cell count (%)</th>
<th>Protein serum concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>N  L   M   E   B</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>10,000</td>
<td>65 20 5 2 0</td>
<td>6.7</td>
</tr>
<tr>
<td>2</td>
<td>13,000</td>
<td>65 21 5 4 0</td>
<td>7.2</td>
</tr>
<tr>
<td>3</td>
<td>11,000</td>
<td>62 24 5 5 0</td>
<td>6.3</td>
</tr>
<tr>
<td>4</td>
<td>12,000</td>
<td>65 22 4 3 0</td>
<td>6.8</td>
</tr>
<tr>
<td>5</td>
<td>9,000</td>
<td>70 26 4 4 0</td>
<td>7.4</td>
</tr>
<tr>
<td>mean</td>
<td>11,000</td>
<td>66 22.6 4.6 4.6 0</td>
<td>6.8</td>
</tr>
</tbody>
</table>

* N = neutrophils, L = lymphocytes, M = monocytes, E = eosinophils, B = basophils.

**Chart no. 5.** Temperature graph before the treatment (bt) and during the treatment with the Sodic sulphamidine injectable solution at the lot 2 of dogs
Achievement of an efficacious human and companion animal’s therapy in Pasteurella multocida infections

Table 5. Results of bacteriological test and treatment for 3rd lot (10 persons attacked by dogs and cats)

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Age</th>
<th>Sex</th>
<th>Relation with animal</th>
<th>Date of aggression</th>
<th>Wound characteristics</th>
<th>Bact. test</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>25</td>
<td>F</td>
<td>Unknown owner</td>
<td>06 10</td>
<td>Scratch – hand and face</td>
<td>P. multocida</td>
<td>1% solution of iodated povidona</td>
</tr>
<tr>
<td>2</td>
<td>34</td>
<td>F</td>
<td>Owner</td>
<td>07 13</td>
<td>Scratch – fingers</td>
<td>P. multocida</td>
<td>Saline Ringer solution</td>
</tr>
<tr>
<td>3</td>
<td>30</td>
<td>F</td>
<td>Unknown owner</td>
<td>07 12</td>
<td>Scratch – arms</td>
<td>P. multocida</td>
<td>Saline Ringer solution + ampicillin + amoxicillin</td>
</tr>
<tr>
<td>4</td>
<td>28</td>
<td>F</td>
<td>Owner</td>
<td>07 14</td>
<td>Bites – arms</td>
<td>P. multocida</td>
<td>1% solution of iodated povidona + ampicillin + amoxicillin</td>
</tr>
<tr>
<td>5</td>
<td>26</td>
<td>F</td>
<td>Owner</td>
<td>07 11</td>
<td>Scratch – face and neck</td>
<td>P. multocida</td>
<td>Local treatment + amoxicillin + clavulanate</td>
</tr>
<tr>
<td>6</td>
<td>29</td>
<td>M</td>
<td>Unknown owner</td>
<td>08 15</td>
<td>Bite – leg and feet</td>
<td>P. multocida</td>
<td>1% solution of iodated povidona + amoxicillin + clavulanate</td>
</tr>
<tr>
<td>7</td>
<td>6</td>
<td>M</td>
<td>Owner</td>
<td>08 22</td>
<td>Bite – extremity level</td>
<td>P. multocida</td>
<td>Saline Ringer solution + amoxicillin + ampicillin</td>
</tr>
<tr>
<td>8</td>
<td>9</td>
<td>M</td>
<td>Owner</td>
<td>08 19</td>
<td>Bite – face and arms</td>
<td>P. multocida</td>
<td>1% solution of iodated povidona + amoxicillin + ampicillin</td>
</tr>
<tr>
<td>9</td>
<td>19</td>
<td>M</td>
<td>Unknown owner</td>
<td>08 20</td>
<td>Bite – arms and legs</td>
<td>P. multocida</td>
<td>1% solution of iodated povidona + amoxicillin + clavulanate</td>
</tr>
<tr>
<td>10</td>
<td>17</td>
<td>F</td>
<td>Unknown owner</td>
<td>08 21</td>
<td>Bite – face and extremities</td>
<td>P. multocida</td>
<td>1% solution of iodated povidona + amoxicillin + ampicillin</td>
</tr>
</tbody>
</table>

Conclusions

1st lot:
- 20 cats – Common (13), Burmese (4), Siamese (2), Persian (1);
- At bacteriological test were isolated some species of Pasteurella multocida (15 cases) and Pasteurella septica (5 cases);
- The cats having clinical symptoms with pasteurelosis (cases 3, 4, 10, 13, 15, 18) were treated with ampicillin and chloramphenicol;
- After the treatment there was an improvement of general state in most of the cases (excepting case 18).

2nd lot:
- 13 dogs – German Shepherd dog (5 cases), Commune (5 cases), Chow-chow (2 cases), Pitbull (1 case);
- The etiologic agent isolated from bitten wounds was represented by P. canis biotype I (6 cases), P. multocida (4 cases) and P. septica (3 cases);
- The treatment was realized with sodic sulphamidine injectable solution (7 cases) and ampicillin + amoxicillin (6 cases).
3rd lot:
- 10 persons of 6-34 years old, attacked by dogs or cats;
- The aggression of 6 cats: Commune (3 cases), Siamese (1 case), Burmese (1 case), Persian (1 case) and 4 dogs: German Shepherd dog (2 cases), Commune (2 cases);
- The bacteriological test permitted \( P. \) multocida isolation;
- The local treatment was realized with iodated povidone and saline Ringer solution;
- Antibiotherapy was realized with ampicillin and amoxicillin (5 cases) and amoxicillin + clavulanat (3 cases);
- The prophylaxis and struggle will be achieved through the creation of a means plan vise: the elimination of commune cats and dogs and of the owners to avoid bites; the meticulous disinfection of ulcers especially of those caused by bites, keeping evidence of the persons which work with animals, as well as of those immunocompromised or pregnant ones.

References
4. BOYCE JD, ADLER B. How does Pasteurella multocida respond to the host environment?. Curr Opin Microbiol; 9:117. 2006
Achievement of an efficacious human and companion animal’s therapy in Pasteurella multocida infections

23. JORGENSEN, JH, HINDLER, JF. New consensus guidelines from the Clinical and Laboratory Standards Institute for antimicrobial susceptibility testing of infrequently isolated or fastidious bacteria. Clin Infect Dis; 44:280. 2007
29. MARINELLA MA. Community-acquired pneumonia due to Pasteurella multocida. Respir Care; 49:1528. 2004
37. IVANA SIMONA, Bacteriologie generală. Editura Ştiinţelor Medicale 118; 2005
38. IVANA SIMONA, Bacteriologie specială, Editura Ceres, 242-246; 2002
40. IVANA SIMONA, Microbiologie medicală veterinără, vol II, Editura Orienturi, 240-247; 2008
41. IVANA SIMONA, Tratat de bacteriologie medical veterinara si introducere in micologie, Editura Ştiinţelor Medicale, 730-760; 2006