IMPACT OF TREATMENT WITH ANTI-PARASITE (IVERMECTIN) DURING PREPARTUM PERIOD ON MASTITIS AND POSTPARTUM REPRODUCTIVE PERFORMANCE IN BALADI COWS

A. I. Damarany

Department of Animal and Poultry Production, Faculty of Agriculture and Natural Resources, Aswan University, Egypt

Submitted: 13/3/2022; Accepted: 12/5/2022; Published: 6/7/2022

SUMMARY

The current investigation was designed to determine the effect of treatment with anti-parasitic (Ivermectin) on mastitis and postpartum reproductive performance of Baladi cows. Twenty-four Baladi cows were used in this study, the cows were divided into two groups. The G1 (n= 12 cows) were injected two months prepartum with two consecutive doses (15- days in- between) of IVOMEC® Plus solution subcutaneously at the rate of 1ml/50kg live body weight (prescribed by the manufacturer), whilst G2 (n= 12 cows) was used as a control group. The present results revealed that the occurrence of mastitis in treated cows group was significantly (P <0.05) lower (16.7%) than control cows’ group (41.7%). The conception rate in treated cows group was significantly (P <0.05) higher (66.7%) compared with (33.3%) in control group. The time from calving to conception in treated cows was significantly (P <0.05) lower (86.5± 11.4 days) compared to 123.3±13.2 days in the control group (P <0.05). The occurrence of anestrous was significantly (P <0.05) lower (86.5± 11.4 days) compared to (33.3%) in control group. The time from calving to conception in treated cows was significantly (P <0.05) lower (86.5± 11.4 days) compared to 123.3±13.2 days in the control group (P <0.05). The occurrence of anestrous was significantly (P <0.05) lower (8.3%) in treated cows than in the control group (25%). The results of this study showed that Ivermectin injection to pregnant Baladi cows during the last two months of pregnancy (at the rate of 1ml/50kg live body weight) was useful in reducing the incidence of mastitis, as well as, in enhancing the reproductive performance of the cows.

Keywords: Ivermectin, mastitis, conception rate, days open, anestrous, Baladi cows.

INTRODUCTION

Endo-and ecto-parasites infestation cause high economic losses in livestock especially farm animals. Economic losses are represented by costs of anthelmintics drugs, higher mortality rate, decline in meat, milk, growth rate and fertility (Mendes et al., 2008). Economic loss was estimated by US $ 3.2 billion per annum worldwide due to liver worm (Fasciola) as one of endo- parasite in the livestock (Spithill et al., 1999). In Brazil, Grisi et al. (2014) reported that economic losses due to cattle external and internal parasitic total loss nearly 14.0 million of US$ annually. Lawrence and Ibarbura (2007) estimated the economic losses of internal parasites (gastrointestinal nematode) control in beef cattle and reported that there was a 34% decrease in the break-even price for cattle that were not treated by deworming. Mavrogianni et al. (2012) and Mavrogianni et al. (2014) reported that there is a correlation between endo-parasitic infections and increased frequency of clinical or subclinical mastitis during the first two weeks post-partum in ewes. Food and drugs administration (FDA) has approved Ivermectin as broad spectrum anti-parasitic agent (Gonzalez Canga et al., 2008). Ivermectin is considered to be an effective drug due to its anti-parasitic activity against both internal and external-parasites and has multiple applications in veterinary and human medicine (Geary, 2005, Crump, 2017 and Sharun et al., 2019). Sajid et al. (2006) and Jameel et al. (2015) reported that Ivermectin have immune-potentiating activity in cows. Yates and Wolstenholme (2004), Chaccour et al. (2013) and Suarez et al. (2013) showed that Ivermectin is effectively and widely used against a lot of external and internal parasites. Pregnancy rates were higher in cows after treatment with anti-parasitic drugs (Ivermectin and Eprinomectin) compared with non-treated cows (Loyacano et al., 2002, Kaley et al., 2019 and Volk et al., 2019). Andresen et al. (2017) observed a marked improvement in reproductive performance of cows and heifers after administration of anti-parasites treatment compared to untreated controls group. Infected buffalo cows having the liver worm (Fasciola) needed a long time from calving to conception (Selim et al., 2010). Dairy cows treated with anti-parasitic drugs needed less time to conception postpartum (Sanchez et al., 2002). Liver fluke infections (Fasciolosis) in cows were accompanied by ovarian inactivity and other infertility problems (Ahmed, 2007). Recently, Ivermectin was used as an antiviral drug because of its effects on a number of RNA viruses including human immunodeficiency virus (HIV)-1 and SARS-CoV-2 (COVID-19) (Wagstaff et al. 2012, Caly et al., 2020 and Kumar et al., 2020). There is no information, on the effect of anti-parasitic treatment on the reproductive performance in Baladi cows that are reared under the environmental conditions of Aswan governorate. The current investigation was planned to study the effect of treatment with the anti-parasitic drug (Ivermectin) on mastitis and some postpartum reproductive parameters of Baladi cows.
MATERIALS AND METHODS

Climatic conditions and farm location:

This study was conducted at a private farm located in a village in Kom Ombo city (32, 31° 23’ East and 22, 28° 09” North), Aswan governorate. Average of the ambient temperature was (Min.12.3-22.1°C) and (Max. 24.2-35.0°C), relative humidity (18-24) during the experimental period which extended from September to April.

Management and feeding of herd:

Table 1. Specifications (Mean±SE) of Baladi cows at starting of treatment and at calving

<table>
<thead>
<tr>
<th>Status of cow</th>
<th>Untreated cows</th>
<th>Treated cows</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of cows</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Body weight (kg) at starting of treatment</td>
<td>305.5± 6.5a</td>
<td>315.7± 9.4a</td>
</tr>
<tr>
<td>Body weight (kg) at calving</td>
<td>310.3±5.4a</td>
<td>370.6±15.6b</td>
</tr>
<tr>
<td>Age (year)</td>
<td>8.5±1.2a</td>
<td>7.4±1.1a</td>
</tr>
<tr>
<td>Parity</td>
<td>3.5</td>
<td>3.5</td>
</tr>
<tr>
<td>BCS at calving</td>
<td>&lt;3</td>
<td>≥3</td>
</tr>
</tbody>
</table>

Table 2. Specifications of IVOMEC® Plus drug (Ivermectin + Clorsulon) adapted to US FDA (Food and Drug Administration) 2015

<table>
<thead>
<tr>
<th>Drug</th>
<th>Drug Type</th>
<th>Dosage Form</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ivermectin+ Clorsulon</td>
<td>Anti-parasitic</td>
<td>Subcutaneous</td>
<td>Control of internal/external parasites in cows</td>
</tr>
</tbody>
</table>

Detection of heat and pregnancy diagnosis:

The cows were checked for the occurrence of heat twice daily (at 6 am & 6 pm). The sexual behavior of the cows was also visually observed. The cows were naturally mated once the standing behavior of the oestrous cows was observed. Rectal palpation was used (after 60 days post-service), to diagnose pregnancy.

Mastitis diagnosis:

Cows with acute or sub-clinical mastitis were diagnosed using California Mastitis Test according to the steps described by the manufacturer.

Sub-clinical mastitis: Sub-clinical mastitis infected cows do not show any symptoms unless reagents are used. (Kathiriya et al., 2014).

Postpartum reproductive efficiency determination:

Conception rate: estimated as the percentage of animals, that were pregnant from the first service post-partum.

Conception rate = Number of pregnant cows in each group /Total number of served cows in each group x 100

Postpartum ovarian dysfunction determination:

Anestrous cases: Cows did not display any visible signs of estrus during = 60th day postpartum according to Kamal et al. (2012).

True anestrous case: Cows considered have true anestrous case when rectal check ovaries are smooth, small and inactive with the absence of corpus luteum and plasma progesterone concentration remain in the basal levels (1ng/ml) (Kamal et al., 2012).

Blood samples and biochemical assay:

Blood samples (10 ml) were collected from cows in estrus, 7th and 21st days post estrus into heparinized tubes from the jugular vein. For plasma harvesting the samples were centrifuged at 3000 rpm for 20 minutes. The separated plasma was stored under -18°C until the time of analysis. Progesterone (P4) and estradiol-17β (E2) hormones were determined by radioimmunoassay kit (Immunotech, France). Progesterone and estradiol-17β sensitivity values were stated to be 0.03 ng/ml and 4.0 pg/ml, respectively.

Twelve- four of Baladi cows were used in the current research. Alfa- Alfa alongside the concentrate mixture, wheat bran and wheat hay were offered to cows during the experimental period. The cows treated with the Ivomec two months pre-partum after drying. Table 1 (1) shows the specifications of experiment animals. The cows were kept under the ordinary conditions applied on the farm. The cows were kept under semi open sheds and similar environmental and managerial conditions.
according to manufacturer labeled information. Intra assay coefficient of variation was 6.2% and 12.2% for progesterone (P4) and estradiol-17β (E2), respectively.

Statistical analysis:
The statistical design involved one factor (one-way ANOVA) (treatment effect) on mastitis, postpartum reproductive efficiency and ovarian dysfunction parameters. Chi Square was used to verify the significance of percentage values. The statistical analysis was performed by software (SAS, 2002). Following model was used:

\[ Y_{ij} = \mu + T_i + e_{ij} \]

Where:
- \( Y_{ij} \) = the observation trait; \( \mu \) = overall mean; \( T_i \) = effect of treatment (treated=1 and untreated =2), and \( e_{ij} \) = experimental error

Duncan’s Multiple Range test (Duncan, 1955) was used to check the significance of the differences between means.

RESULTS AND DISCUSSION
Effect of treatment with anti-parasitic drug on occurrence rate of mastitis in Baladi cows:

Figure (1) indicates the percentage of mastitis in treated cows was significantly (P <0.05) lower (16.7%) than the control group (41.7%). The current result agrees with that reported by Mavrogianni et al. (2012) and Mavrogianni et al. (2014) who found increased frequency of clinical or subclinical mastitis in the first two weeks post-partum in ewes that suffer from endo-parasitic infections. Staphylococcus aureus is considered one of the major pathogenic agents of the udder that causes mainly subclinical infection (mastitis) (Tenhagen et al., 2001, Leitner et al., 2003 and Olde Riekerink et al., 2008). Infections by endo-parasites lead to decreasing weight gain, reduced nitrogen balance, negative affect on metabolism of proteins and suppress immune response in calves (Randall and Gibbs, 1981 and Wiggin and Gibbs, 1990). Ashraf et al. (2018) showed that cows treated with Ivermectin exhibited anti- Staphylococcus aureus activity than other cows. Uhlir (1991) observed that antibody activity is increased after treatment with Ivermectin in rabbits. Backes (2016) reported that white blood cells and lymphocytes were greater in cows treated with anti-parasitic than control cows group. Similar results were reported by Sajid et al. (2006) and Jameel et al. (2015) who stated that treated cows with Ivermectin lead to increase total number of white blood cells and lymphocyte cells in those cows and the reflection of this on the raising of the immunity in animals. Torres et al. (2016) observed that Ivermectin drug was effective against biofilm formation by Staphylococcus aureus. Recently, Heidary and Gherebaghi (2020) discovered that Ivermectin drug has many effects against some diseases and was highly effective against many microorganisms. It worked as antimicrobial, antiviral, and anti-cancer drug. Mastrangelo et al. (2012) reported that Ivermectin acts as an anti-viral agent to flavivirus by inhibiting its replication activity. Recent studies by Lv et al. (2018) and Yamasmith et al. (2018) underlined the effective potential of Ivermectin as an antiviral drug able to reduce viral load in the host. Furthermore, Lim et al. (2013) and Omansen et al. (2015) suggested that Ivermectin acts as antibacterial activity against Mycobacterium tuberculosis and Mycobacterium ulcerans. In the light previous studies lower percentage of mastitis in treated cows group than untreated in the present study may be attributed to the anti-microbial effect of Ivermectin (anti- Staphylococcus aureus) in cows udders.

Effect of treatment with anti-parasitic drug on conception rate (%) in Baladi cows:

Figure (2) shows that the conception rate (%) in treated cows was significantly (P <0.05) higher (66.7%) compared with untreated cows (control group) (33.3%). The present findings agree with those reported by Backes (2016) who found that treatment with Long-Acting Eprinomectin (an anti-parasitic drug) lead to increasing conception rates compared to control group (89 vs. 50%). Higher pregnancy rate (94%) was observed for beef cows that treated with anti-parasitic drugs compared with untreated beef cows 82% (Stromberg et al., 1997). Larson et al. (1995) reported that pregnancy rate was higher (56.4%) in beef heifers that treated with Ivermectin than control heifers (25.6%). Pregnancy rate was 72%
and 87% in control cows group and Ivermectin treatments group, respectively in Ontario cow (Kaley et al., 2019). Loyacano et al. (2002) stated that pregnancy rate was higher (78%) in beef heifers that were treated with Ivermectin than no treatment heifers (54%). Volk et al. (2019) reported that beef heifers which treated with Eprinomectin (anti-parasites) recorded greater (84%) pregnancy rate compared with control group heifers (68%). Orellana et al. (1999) reported that treatment with anti-parasites was associated with increasing the conception rate in dairy cows. Seliem et al. (2010) showed that higher pregnancy rate in buffaloes that were treated with anti-Fasciola drugs (67.7%) than control group buffaloes (16.7%). Hammam et al. (2011) found that the pregnancy rate in the healthy treated buffaloes was higher (55.6%) than buffaloes infected with liver worm (Fasciola hepatica) (30.8%). Hawkins (1993) and Gross et al. (1999) stated that anthelmintic-treated beef cows recorded higher conception rate and calving rate compared to untreated controls. The present results indicate increase in the conception rate in treated cows by anti-parasitic drug compared to untreated cows which may be due to improve weight gains and general body condition score of treated cows during postpartum period than untreated cows. Larson et al. (1995) reported that treatment of beef heifers with Ivermectin improved weight gains and pregnancy rate during a 60-d breeding season. Barakat et al. (1995) showed that acute infection with nematodes worms (internal parasites) was associated with low incidences of conception rate and ovarian activity in cows and buffaloes. Somchez et al. (2002) stated that removing external and internal parasites around calving improved the energy balance through the postpartum period and therefore improved the reproductive performance of cows. Maintaining of body weight and body condition score during postpartum period led to increase energy balance and have also positive effect on reproductive performance of beef cows (Hess et al., 2005). Improving of body weight and body condition score of beef heifers which were treated with extended-release Eprinomectin (anti-parasites) during breeding season may be the main cause to improved their reproductive performance (Volk et al., 2019). Marked improvement was showed in reproductive performance of cow and heifers after administration of anthelmintic treatment compared to untreated controls (Andresen et al., 2017). Rehbein et al. (2013) reported that treatment with deworming drugs led to reduce worm burdens and increase weight gains in cattle. Infections with trematode (internal parasite) caused depressed appetite and feed intake in affected sheep hence decreased available energy (Taylor et al., 2007 and Rojo-Vázquez et al., 2012). El-Khadrawy et al. (2008) reported that buffalo-cows with (internal parasites) (Fasciola) recorded lower concentrations of serum Zn, Cu, Fe and Se compared to healthy animals. Ahmed et al. (1998) stated that buffaloes which have lowered Cu or Zn in blood suffered weak growth and infertility.

![Conception rate (%) in treated and untreated Baladi cows.](image)

**Effect of treatment with anti-parasite on the time from calving to conception (Days open) in Baladi cows:**

Table (3) illustrates that the time from calving to conception in treated cows was significantly (P<0.05) lower 86.5± 11.4 days than untreated cows (control group) 123.3± 13.2 days. The present findings correspond with those reported by Walsh et al. (1995) and Sanchez et al. (2002) who found that the interval from calving to conception was less in dairy cows which were treated with anti-parasitic drugs (Ivermectin or Eprinomectin) compared to untreated cows. Orellana et al. (1999) stated that treatment of cows with an anti-parasite led to reduced interval from calving to conception. Seliem et al. (2010) showed that infected buffaloes with internal parasites liver worm (Fasciola) needed a long time from calving to conception (156.75, days) compared to non-infected group (112.46, day). Mejia et al. (1999) stated that treatment of dairy heifers with anti-parasitic (Ivermectin) caused to increased growth rate and earlier onset of ovarian functions. Ballweber et al. (1997) suggested that used anti-parasites (Doramectin or Ivermectin) in cattle led to significant increase in weight gain in drug-treated groups relative to untreated groups, ranging from 0.132 to 0.272 kg average daily gain. Lacau-Mengido et al. (2000) observed that Ivermectin treated dairy heifers recorded increased serum IGF-1, and this caused to acceleration...
of sexual and somatic maturation. Buffaloes having poor body condition score had less number of small and large follicles in their ovaries hence low incidence of good quality oocytes (Ahmed et al., 1999). Observed in ewes having poor body condition lowering LH secretion or decline its pulse frequency. This effect is mediated through glucose level, or insulin growth factor-1 (IGF-1) (Snyder et al., 1999).

Deficiency of energy is considered as one of most agents detrimental to reproduction of livestock (Dunn and Moss, 1992). McClure (1994) reported that energy deficiency causing to inhibit ovarian function at pituitary synthesis/release of gonadotropin. Level of IGF-1 is very important to ovarian follicular development (Robinson, 1996).

Table 3. Effect of treatment with anti-parasitic on the time from calving to conception (DO) in Baladi cows

<table>
<thead>
<tr>
<th>Items</th>
<th>Treated cows</th>
<th>Untreated cows</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of cows</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>The time from calving to conception (DO) days:</td>
<td>86.5± 11.4a</td>
<td>123.3± 13.2b</td>
</tr>
</tbody>
</table>

a, b: values within the same row having different superscripts are significantly different at (P <0.05)

1- Conception rate calculate from first service

Effect of treatment with anti-parasite on ovarian dysfunction in Baladi cows:

Figure (3) indicates that the proportion of anestrus cases (%) was significantly (P <0.05) lower (8.3%) in treated cows group than untreated cows (control group) (25%). This may be due to improvement of the body condition score of treated cows compared with non-treated cows. The current result agrees with that recorded by Barakat et al. (2001) who found that cows infected by internal parasites (liver worm) was associated with loss of body condition, decreased fertility and prolonged anestrus period. Ahmed (2006) and Ahmed et al. (2006) observed that infected buffaloes with internal parasites liver worm (Fasciola) recorded prolonged anestrus period compared with healthy animals. Stewart et al. (1992) stated that treatment of beef replacement heifers with Ivermectin led to improved weight gain, feed efficiency, and estrous activity. Barakat et al. (1995) showed that acute infection with nematodes worms (internal parasites) was associated with low occurrence of ovarian activity in cows and buffaloes. Anthelmintic treated dairy cattle recorded less time to recovering estrous during postpartum period (Sanyal et al., 1992). Liver fluke infections (Fasciolosis) in bovine were associated with ovarian inactivity and other infertility problems (Ahmed, 2007). Simsek et al. (2007) reported that 58% of repeat breeder cows were suffering from liver worm (Fasciola. hepatica). Jeffcoe et al. (1988) and Fernandez-Abella et al. (2006) found that reduction in ovulation rate and ovarian activity in infected ewes with internal parasites. El-Khadrawy et al. (2008) reported that lower concentrations of serum Zn, Cu, Fe and Se in buffalo which infected by liver worm (Fasciola) compared to healthy animals. Kommisrud (2005) suggested that there is a positive correlation between increased pre-partum blood selenium levels and decreased incidence of ovarian cysts and anestrus/silent estrus during the post-partum period in Norwegian dairy herds.

Concentrations of progesterone and estradiol-17β at estrus, 7th and 21st day post-service in treated and untreated Baladi cows:

Table (4) indicates that concentrations of progesterone and estradiol-17β at the time of estrus were significantly (P <0.05) higher in pregnant cows than non-pregnant. The present result agrees with that reported by Waldman et al. (2001) who reported that a strong inverse association between the probability of non-return to estrus and progesterone concentration at the time of estrus in cows. Busch et al. (2008) showed that pregnant cows have higher progesterone concentration at day 10 post-service compared with non-pregnant cow. The current result is in agreement with that stated by Lemley et al. (2010) who found that increase of progesterone post-service was associated
with elevated pregnancy maintenance and improvement in the development of the embryo. Rivera et al. (2011) observed decreased progesterone concentrations during follicle growth in dairy cows lead to low cow embryo quality production. Higher pre- and post- service progesterone concentrations were associated with improvement of the fertility. Progesterone modifies ovarian and uterine function through direct effects or indirect effects on fertilization and early stages from development of embryo (Cerri et al., 2011). El-Khadrawy et al. (2008) suggested that buffaloes having (internal parasites) (Fasciola) recorded lower concentrations of blood Zn, Cu, Fe and Se compared to healthy animals. Kamada, (2017) and Kassab et al. (2020) reported that supplementation of selenium to diet in dairy and beef cows led to increases in progesterone and estradiol concentrations during estrous cycle. Sadek and Shaheen (2015) showed that there is increasing in serum progesterone in Baladi cows during postpartum after treatment with Ivermectin (anti-parasites) for up to 3 months. Opposite trend showed for estradiol in blood serum and returned to the increasing during three months after treatment. Seliem et al. (2010) observed that increasing in progesterone and decreasing in estradiol in blood serum of buffaloes that treated with (anti-Fasciola-hepatica). Hammam et al. (2011) showed that infected buffaloes with liver worm (Fasciola) had a decrease in estradiol concentrations (28.42±8.64 pg/ml) than the healthy group (39.61±18.23 pg/ml). Lopez-Diaz et al. (1998) found that Friesian heifers infected with liver flukes (liver worm) recorded decline levels of progesterone than healthy animals. They suggested that liver flukes may be able to alter normal metabolism and/or balance of sex hormones.

| Table 4. Concentrations of progesterone and Estradiol-17β at estrus, 7th and 21st day post-service in treated and untreated Baladi cows |
|---------------------------------------------------------------|---------------------------------------------------------------|
| **Hormones** | **Treated cows** | **Untreated cows** |
| **Progesterone (ng/ml):** | **Pregnant** | **Non-pregnant** | **Pregnant** | **Non-pregnant** |
| **At estrus** | 0.37±0.09<sup>a</sup> | 0.24±0.04<sup>b</sup> | 0.25±0.02<sup>a</sup> | 0.17±0.04<sup>b</sup> |
| **7<sup>th</sup> day post-service** | 3.30±0.03<sup>a</sup> | 2.10±0.01<sup>b</sup> | 2.80±0.02<sup>a</sup> | 1.90±0.03<sup>b</sup> |
| **21<sup>st</sup> day post-service** | 7.21±0.12<sup>a</sup> | 0.30±0.01<sup>b</sup> | 5.13±0.12<sup>a</sup> | 0.26±0.01<sup>b</sup> |
| **Estradiol-17β (pg/ml):** | **At estrus** | 37.30±0.32<sup>a</sup> | 13.60±0.22<sup>b</sup> | 22.10±0.11<sup>a</sup> | 12.30±0.31<sup>b</sup> |

<sup>a,b</sup>: values within the same row having different superscripts are different at (P <0.05).

**CONCLUSION**

The results of this study showed that Ivermectin injection to pregnant Baladi cows during the last two months of pregnancy (at the rate of 1ml/50kg live body weight) was useful in reducing the incidence of mastitis, as well as, in enhancing the reproductive performance of the cows.

**REFERENCES**


Kumar, B. S., M. Jeyaraman, R. Jain and T.C. Anudeep, 2020. A wonder drug in the arsenal


Placebo-controlled Trial, in 34th Annual Meeting
the Royal College of Physicians of Thailand-
‘Internal Medicine and One Health’. (Pattaya,
Chonburi, Thailand.

Ivermectin – sensitive glutamate gated chloride
channel subunit from Dicrofilaria immitis. Int. J.
parasitol., 43(9): 1075-81.

Ivermectin – sensitive glutamate gated chloride
channel subunit from Dicrofilaria immitis. Int. J.
parasitol., 43(9): 1075-81.