A randomized, control and comparative study of polyherbal formulation use for Malaria (*Plasmodium falciparum*)

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Abstract: *Plasmodium falciparum* is the most well-known reason for extreme and life-debilitating malaria. Falciparum malaria causes more than 1 million deaths annually. Malaria remains a noteworthy reason for major morbidity and mortality in the tropics, with *Plasmodium falciparum* accountable for the mainstream of the disease weight and *Plasmodium vivax* being the geologically greatest broadly dispersed cause of malaria. The controlling of severe malaria comprises quick direction of suitable parenteral anti-malarial agents and initial acknowledgement and treatment of the complications. This clinical trial was piloted in 100 patients, in which 50 received the test drug (Malarina) and 50 received the control drug (Quinine Bisulphate). The age range of patients was 12 years to above 50 years. The sample paired t-test was applied to evaluate the significant level. Malarina was very effective in treating malaria sign and symptoms. The new treatment Malarina was safe and well tolerated in all patients.

Keywords: Herbal formulation, clinical trial, Malaria treatment, *Plasmodium falciparum.*

INTRODUCTION

Malaria remains a staggering worldwide medical issue. On the planet, an expected 300-500 million individuals contract malaria each year, 1.5 to 2.7 million passings every year (Muentener, Schlagenhauf *et al*., 1999, Sachs and Malaney, 2002). Because of the expansion in worldwide movement and travel people in endemic territories of malaria, the frequency of malaria cases in created nations have expanded. Around 10,000 to 30,000 voyagers from industrialized nations malaria is required to contract yearly (Kain and Keystone, 1998). What's more, plasmodium falciparum impervious to proceeding with malaria drugs distribute and present all regions the world.

Plasmodium transmitted basically by the nibble of a contaminated female anopheline mosquito, however infections can likewise happen by presentation to tainted blood products (transfusion malaria) and inborn transmission. In industrialized nations, most instances of malaria happen immigrant or military explorers coming back from zones malaria endemic (imported malaria). Especially, locally transmission by mosquitoes (indigenous malaria). In patients with unexplained fever or clinical weakening who have come back to the past from an endemic region within a couple of years, malaria ought to be incorporated into the differential conclusion. The evaluation of these cases ought to dependably be a worldwide travel history. Postponements in acknowledgment and increment the proper treatment of malaria dreariness and mortality (Kain *et al*., 1998). Approximately 94.9 million of Pakistan's 160.9 million individuals, approximately 59.9% of Pakistan's populace, living in malaria endemic districts (Williams and Meek, 2011). After annihilation endeavors in the 1960s, malaria surged back to a pestilence level in the 1970s. As of late, an uptick in malaria can be in part ascribed to surges that influenced roughly 19.9 million individuals in more than 61 areas (Williams and Meek, 2011). Regardless of a settled malaria control program, 500,000 malaria diseases and 50,000 malaria inferable passings happen every year in Pakistan (Mukhtar, 2006), with roughly 36.9% of cases evaluated to happen in areas along the outskirts with Afghanistan and Iran (Kakar *et al*., 2010).

Plasmodium vivax (in charge of roughly 63.9% of diseases) and Plasmodium falciparum (causing 35.9% of contaminations) are the 2 common Plasmodium classes in Pakistan (Organization, 2015), and malaria is basically found in the regions of Khyber Pakhtunkhwa, Balochistan, Sindh and the Federally Administered Tribal Areas (Kakar *et al*., 2010). Malaria spread is thought to be temperamental, with real *P. vivax* transmission cresting from June to September and again in April to June, when backslides of contaminations gained the past season are watched (Bouma *et al*., 1996). The important spread time frame for P. falciparum in Pakistan is between August and December (Bouma *et al*., 1996).

In spite of the fact that the greater part of malaria cases in Pakistan is caused by *P. vivax*, inclines in the previous couple of decades have demonstrated that P. falciparum contamination is on the ascent. The World Health

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Organization (WHO) announced that in Pakistan the extent of malaria contaminations ascribed to P. falciparum ascended from 33.9% of every 1987 to 53.9% of every 1990 (Bouma *et al*., 1996, Bouma *et al*., 1996). The recurrence of P. falciparum among microscopy-positive cases ascended from 44.9% of every 1995 to 67.9% out of 2006 in the city of Quetta in Balochistan area and in Jhangara city of Sindh territory (Durrani *et al*., 1997, Rab *et al*., 2001). In 2010, 73,857 (30.9%) of 240,591 aggregate announced malaria cases in Pakistan were *P. falciparum* (Organization, 2012).

The ascent of *P. falciparum* in parts of Pakistan might be mostly inferable from fizzled treatment of chloroquine-safe diseases (Nizamani *et al*., 2006). Chloroquine resistance in P. falciparum was accounted for interestingly from Pakistan in 1984 and later affirmed as far reaching (Ghanchi *et al*., 2011, Organization, 2012, Rana and Tanveer, 2004, Robinson *et al*., 1984). A current report found that 90% of P. falciparum tests gathered in the areas of Balochistan and Sindh conveyed the pfcrt 76 T allele in charge of presenting chloroquine resistance (Rawasia, Sridaran *et al*., 2012). In spite of the fact that chloroquine is prescribed just for treatment of *P. vivax, P. falciparum* contaminations are regularly treated with chloroquine, as possible analysis or empiric treatment is typically in light of clinical side effects in asset restricted nations like Pakistan (Parikh *et al*., 2010).

MATERIAL AND METHODS

This was an experimental study of randomized control trial with an open intercession. The doctor chose patients arbitrarily for Unani drug and modern drug. 100 patients were chosen randomly from Civil Hospital, Quetta. The patients were separated into two groups, test groups and control group, the two groups comprises 50, 50 patients individually. Test consequences of trials of test group and control group were expected to investigate the viability of the two medications and followed the aftereffects of best entertainer sedate. Arbitrarily 50 patients were given Malarina (test medication), and 50 patients were given Quinine Bisulphate (control medicine) after the positive blood test MP for Plasmodium falciparum. Results were isolated into two classes, impact on malarial parasite, stand positive or negative after treatment, and help in manifestations which additionally classified in various class, 1: Complete improvement, 2: Moderate improvement, 3: Mild improvement, 4: No change

Selection Criteria

Test Group

The test group was treated with Unani medicine (Herbal) formulation of Malarina 250 mg twice a day for three days when patient was positive with *Plasmodium falciparum* and presented with uncomplicated symptoms. The Malarina was prepared with medicinal plants include *Azadirachta indica* L., *Swertia chiraitta, Aconitum nepallenis, Tinospora cordifolia, Caesalpinia bondus, Picrorrhiza kurroa, Echinops echinatus, Bamboo manna,* and *Rheum emodii*.

Control group

The control group was treated with modern medicine, already known with proven evidence as antimalarial effects in modern research. The modern medicine, Quinine Bisulphate (300 × 2 = 600 mg) twice a day for three days.

Clinical history

The physical examination of every patient was directed to conclude the severity of the disease. Patients were examined and set criteria for complicated or uncomplicated malaria and regulate whether go for treatment or not and physical examination whether patient is serious and had sever malaria caused by *Plasmodium falciparum*.

Diagnosis

On the basis of signs and symptoms, suspected patients' blood sent for microscopic examination for confirmation of *Plasmodium falciparum*.

Eligibility

Inclusion Criteria

- The patients were selected with following criteria
- All age groups 12 years and above
- Male and female
- Patients were selected from Civil Hospital, Quetta, where people came from all over Baluchistan
- Only those patients were selected who were positive with *Plasmodium falciparum*
- Only uncomplicated patients were selected

Exclusion Criteria

- Less than 12 years
- Patients positive with other type of malaria i.e. *Plasmodium vivax* while *Plasmodium ovale* and *Plasmodium malariae* do not exist in Pakistan.
- Complicated patients like malaria with splenomegaly
- Cerebral malaria-sever malaria
- Patient who were positive with *Plasmodium falciparum* but had had other disease accompanying with malaria
- Pregnancy

Consent

The verbal consent was taken from all patients according to protocol approved by the appropriate Ethical Committee of Faculty of Eastern Medicine, Hamdard University, Karachi, Pakistan.

Sample selection

The study conducted in 2013 and 2014 during peak and off-season malaria in Quetta. The sample selected from

OPD in the Civil Hospital Quetta, on the basis of signs and symptoms and after confirmation of the microscopic examination of the blood of malaria parasite. We selected patients with Plasmodium falciparum positive and followed an inclusion and exclusion criteria.

STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS (version 22), sample paired T test were pragmatic and determined the statistical results. All variances were measured statistically significant by producing a *p*-value from test statistics. The noteworthy result with *p*-value less than 0.05 is considered as statistically significant.

RESULTS

This study were conducted on 100 patients (n = 50 Test drug group); (n = 50 control drug group). Out of 100 patients none of patient stated any adverse or side effect. Following symptoms of malaria were evaluated after treatment with test drug and control drug, nausea, headache, sweating, vomiting, paroxysm of fever, myalgia, bitter taste of mouth, anorexia, rigors, malaise, and abdominal pain. Participant's age distribution; sex distribution and frequency distribution of Test group and control group are shown in fig. 1 and fig. 2 respectively.

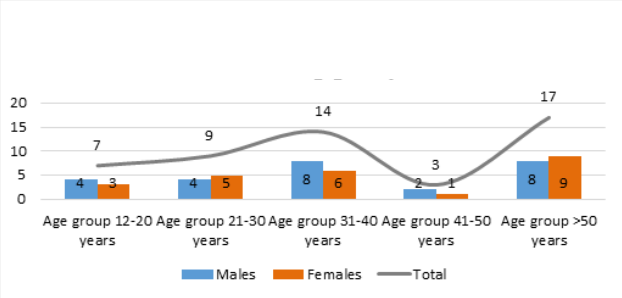

Fig. 1: Patients age distribution and frequency test group

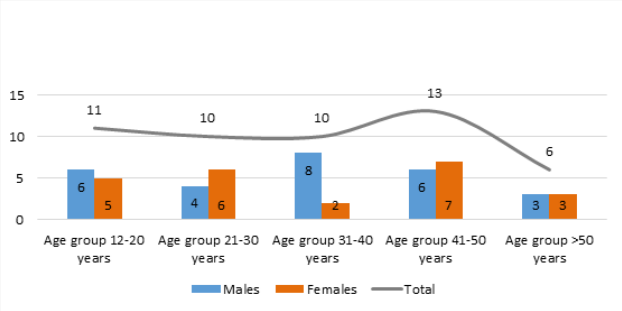

Fig. 2: Patients age distribution and frequency control group

Nausea

Nausea symptom has been evaluated in both groups. In Test group 34% patients show complete improvement, 30% show moderate improvement, 16% show mild improvement and 20% show no improvement. In control group 48% patients show complete improvement, 26% show moderate improvement, 10% show mild improvement and 16% show no improvement. The overall effects of Test drug and control drug on nausea after treatment is shown in table 1 and fig. 3.

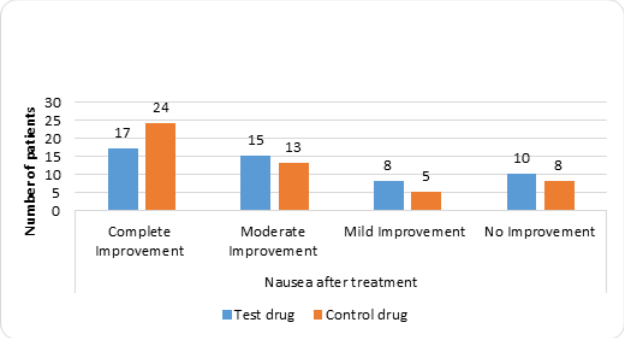

Fig. 3: Comparison of nausea after treatment in test group and control group

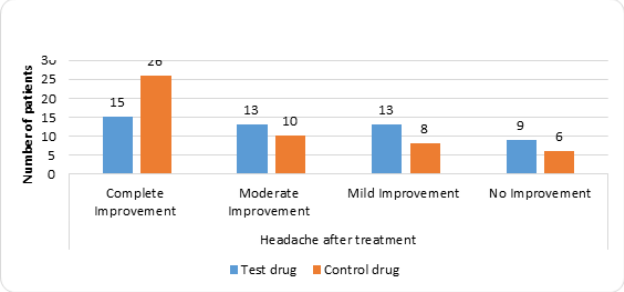

Fig. 4: Comparison of headache after treatment in test group and control group

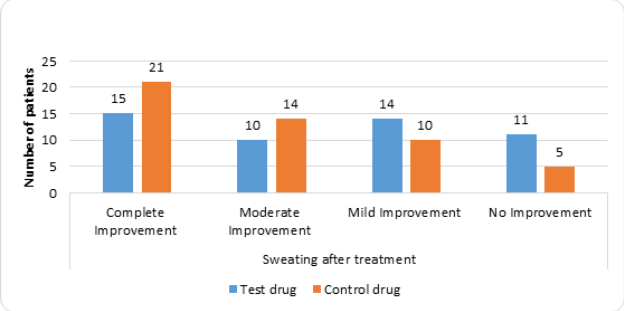

Fig. 5: Comparison of sweating after treatment in test group and control group

Headache

Headache symptom has been evaluated in both groups. In Test group 30% patients show complete improvement, 26% show moderate improvement, 26% show mild improvement and 18% show no improvement. In control group 52% patients show complete improvement, 20% show moderate improvement, 16% show mild improvement and 12% show no improvement. The overall effects of Test drug and control drug on headache after treatment is shown in table 2 and fig. 4.

Table 1: Comparison of nausea after treatment in test group and control group

Level of Improvement	Complete improvement	Moderate improvement	Mild improvement	No improvement	*P* value
Test drug	17(34%)	15(30%)	8(16%)	10(20%)	0.033
Control drug	24(48%)	13(26%)	5(10%)	8(16%)	

Table 2: Comparison of headache after treatment in test group and control group

Level of Improvement	Complete improvement	Moderate improvement	Mild improvement	No improvement	*P* value
Test drug	15(30%)	13(26%)	13(26%)	9(18%)	0.043
Control drug	26(52%)	10(20%)	8(16%)	6(12%)	

Table 3: Comparison of sweating after treatment in test group and control group

Level of Improvement	Complete improvement	Moderate improvement	Mild improvement	No improvement	*P* value
Test drug	15(30%)	10(20%)	14(28%)	11(22%)	0.026
Control drug	21(42%)	14(28%)	10(20%)	5(10%)	

Table 4: Comparison of vomiting after treatment in test group and control group

Level of Improvement	Complete improvement	Moderate improvement	Mild improvement	No improvement	*P* value
Test drug	19(38%)	8(16%)	11(22%)	12(24%)	0.023
Control drug	24(48%)	15(30%)	4(8%)	7(14%)	

Table 5: Comparison of myalgia after treatment in test group and control group

Level of Improvement	Complete improvement	Moderate improvement	Mild improvement	No improvement	*P* value
Test drug	14(28%)	17(34%)	12(24%)	7(14%)	0.030
Control drug	27(54%)	12(24%)	6(12%)	5(10%)	

Table 6: Comparison of bitter taste of mouth after treatment in test group and control group

Level of Improvement	Complete improvement	Moderate improvement	Mild improvement	Not improvement	*P* value
Test drug	14(28%)	12(24%)	16(32%)	8(16%)	0.037
Control drug	25(50%)	12(24%)	4(8%)	9(18%)	

Table 7: Comparison of paroxysm of fever after treatment in test group and control group

Level of Improvement	Complete improvement	Moderate improvement	Mild improvement	Not improvement	*P* value
Test drug	15(30%)	12(24%)	13(26%)	10(20%)	0.044
Control drug	23(26%)	12(24%)	9(18%)	6(12%)	

Table 8: Comparison of anorexia after treatment in test group and control group

Level of Improvement	Complete improvement	Moderate improvement	Mild improvement	Not improvement	*P* value
Test drug	16(32%)	14(28%)	12(24%)	8(16%)	0.014
Control drug	25(50%)	14(28%)	7(14%)	4(8%)	

Table 9: Comparison of rigors after treatment in test group and control group

Level of Improvement	Complete improvement	Moderate improvement	Mild improvement	Not improvement	*P* value
Test drug	19(38%)	11(22%)	11(22%)	9(18%)	0.022
Control drug	28(56%)	10(20%)	9(18%)	3(6%)	

Table 10: Comparison of malaise after treatment in test group and control group

Level of Improvement	Complete improvement	Moderate improvement	Mild improvement	Not improvement	*P* value
Test drug	15(30%)	14(28%)	13(26%)	8(16%)	0.020
Control drug	26(52%)	13(26%)	7(14%)	4(8%)	

Table 11: Comparison of abdominal pain after treatment in test group and control group

Level of Improvement	Complete improvement	Moderate improvement	Mild improvement	Not improvement	*P* value
Test drug	13(26%)	16(32%)	12(24%)	9(18%)	0.043
Control drug	23(46%)	14(28%)	4(8%)	9(18%)	

Sweating

Sweating symptom has been evaluated in both groups. In Test group 30% patients show complete improvement, 20% show moderate improvement, 28% show mild improvement and 28% show no improvement. In control group 42% patients show complete improvement, 28% show moderate improvement, 20% show mild improvement and 10% show no improvement. The overall effects of Test drug and control drug on sweating after treatment is shown in table 3 and fig. 5.

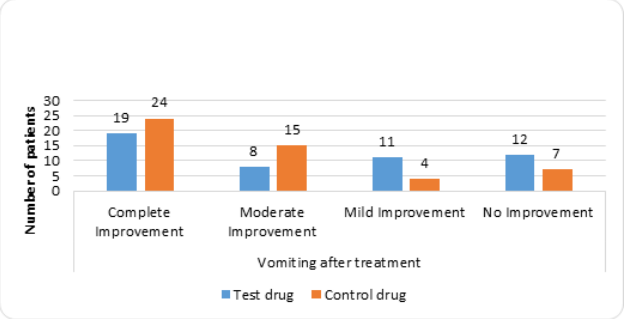

Fig. 6: Comparison of vomiting after treatment in test group and control group

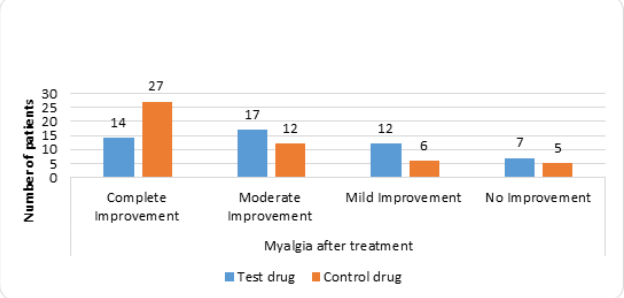

Fig. 7: Comparison of myalgia after treatment in test group and control group

Vomiting

Vomiting symptom has been evaluated in both groups. In Test group 38% patients show complete improvement, 16% show moderate improvement, 22% show mild improvement and 24% show no improvement. In control group 48% patients show complete improvement, 30% show moderate improvement, 8% show mild improvement and 14% show no improvement. The overall effects of Test drug and control drug on vomiting after treatment is shown in table and fig. 6.

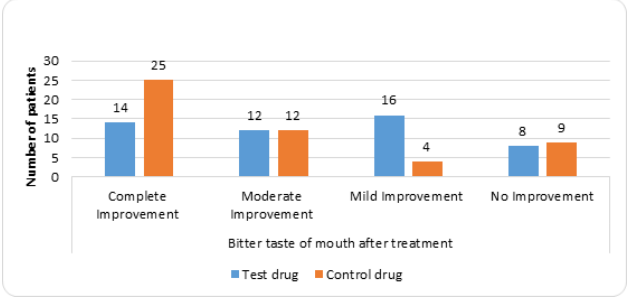

Fig. 3: Comparison of bitter taste of mouth after treatment in test group and control group

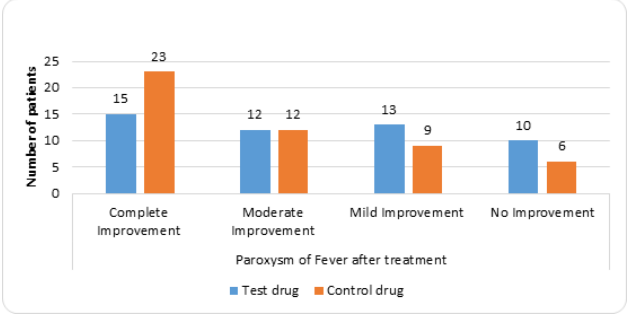

Fig. 4: Comparison of paroxysm of fever after treatment in test group and control group

Myalgia

Myalgia symptom has been evaluated in both groups. In Test group 28% patients show complete improvement, 34% show moderate improvement, 24% show mild improvement and 14% show no improvement. In control group 54% patients show complete improvement, 24% show moderate improvement, 12% show mild improvement and 10% show no improvement. The overall effects of Test drug and control drug on myalgia after treatment is shown in table 5 and fig. 7.

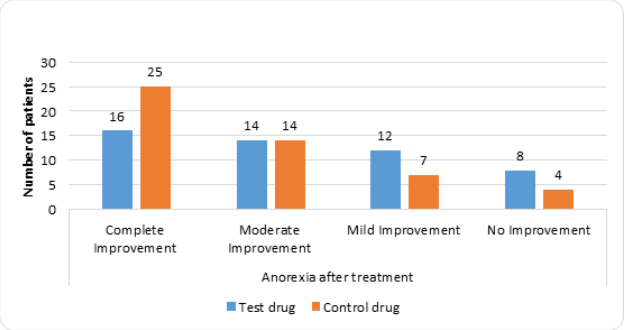

Fig. 5: Comparison of anorexia after treatment in test group and control group

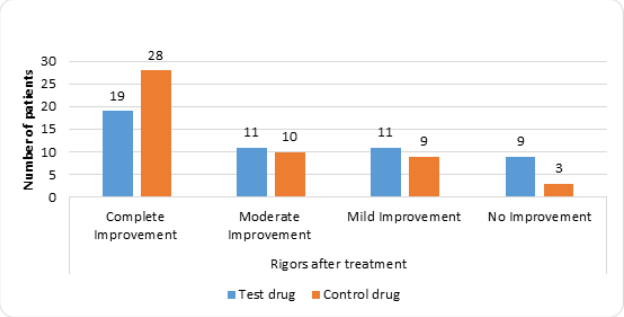

Fig. 6: Comparison of rigors after treatment in test group and control group

Bitter taste of mouth

Bitter taste of mouth symptom has been evaluated in both groups. In Test group 28% patients show complete improvement, 24% show moderate improvement, 32% show mild improvement and 16% show no improvement. In control group 50% patients show complete improvement, 24% show moderate improvement, 8% show mild improvement and 18% show no improvement. The overall effects of Test drug and control drug on bitter taste of mouth after treatment shown in table 6 and fig. 8.

Paroxysm of fever

Paroxysm of fever symptom has been evaluated in both groups. In Test group 30% patients show complete improvement, 24% show moderate improvement, 26% show mild improvement and 20% show no improvement. In control group 26% patients show complete improvement, 24% show moderate improvement, 18% show mild improvement and 12% show no improvement.

The overall effects of Test drug and control drug on paroxysm of fever after treatment is shown in table 7 and fig. 9.

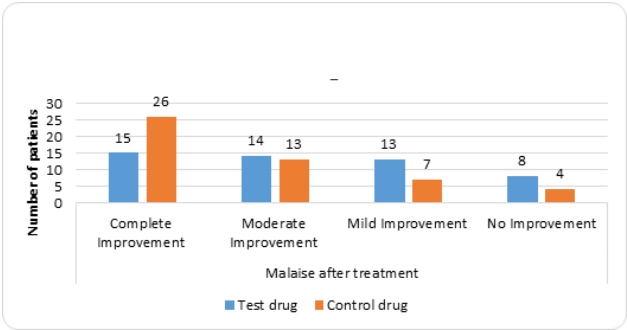

Fig. 7: Comparison of malaise after treatment in test group and control group

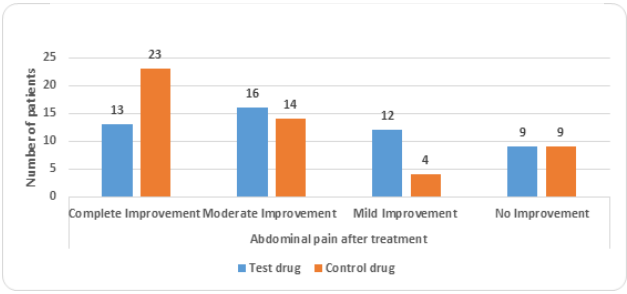

Fig. 8: Comparison of abdominal pain after treatment in test group and control group

Anorexia

Anorexia symptom has been evaluated in both groups. In Test group 32% patients show complete improvement, 28% show moderate improvement, 24% show mild improvement and 16% show no improvement. In control group 50% patients show complete improvement, 28% show moderate improvement, 14% show mild improvement and 8% show no improvement. The overall effects of Test drug and control drug on anorexia after treatment is shown in table 8 and fig. 10.

Rigors

Rigors symptom has been evaluated in both groups. In Test group 38% patients show complete improvement, 22% show moderate improvement, 22% show mild improvement and 18% show no improvement. In control group 56% patients show complete improvement, 20% show moderate improvement, 18% show mild improvement and 6% show no improvement. The overall effects of Test drug and control drug on rigors after treatment is shown in table 9 and fig. 11.

Malaise

Malaise symptom has been evaluated in both groups. In Test group 30% patients show complete improvement, 28% show moderate improvement, 26% show mild improvement and 16% show no improvement. In control group 52% patients show complete improvement, 26%

show moderate improvement, 14% show mild improvement and 8% show no improvement. The overall effects of Test drug and control drug on malaise after treatment is shown in table 10 and fig. 12.

Abdominal pain

Abdominal pain symptom has been evaluated in both groups. In Test group 26% patients show complete improvement, 32%, moderate improvement, 24% mild improvement and 18% show no improvement. In control group 46% patients show complete improvement, 28% moderate improvement, 8% mild improvement and 18% show no improvement. The overall effects of Test and control drug on abdominal pain after treatment is shown in table 11 and fig. 13.

DISCUSSION

With the issues of expanding drug resistance levels and challenges in poor ranges approach powerful antimalarial drugs, conventional solutions could be an essential and maintainable wellspring of treatment (Willcox and Bodeker, 2004). WHO suggests that a satisfactory clinical reaction is a more valuable measure of the adequacy of the treatment. This reaction is characterized as the nonattendance of parasitism on day 14 or without fever (regardless of parasitism), without meeting the criteria for early treatment disappointment (Organization, 2003).

CONCLUSION

Our study results showed that Malarina poly herbal formulation is effective in the treatment of sign and symptoms of malaria without any side effect. The new treatment Malarina was safe and well tolerated in all patients.

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