Section 1

02

Clinical Trials

The Efficacy of *Prunus africana* (Rosaceae) in the Management of Symptomatic Benign Prostatic Hyperplasia

Tanzania

Rogasian Mahunnah and Jichola J.J. Masanja

Urology Unit, Department of Surgery,
Lugalo Military Hospital, Bagamoyo Road,
Dar es Salaam
Tanzania
Tel.: +255 712 144 974
Email: jicholam@gmail.com

Duration: April 2006 - January 2007

Summary

A placebo-controlled, double blind randomized clinical trial was conducted among patients with symptomatic benign prostatic hyperplasia (BPH) at Muhimbili National Hospital, Dar es Salaam, Tanzania, from April 2006 to January 2007. The aim of the study was to evaluate the efficacy and safety of *Prunus africana* (Hook. f.) Kalm (family Rosaceae) in the treatment of symptomatic BPH.

Patients were divided into two groups in order to compare the drug to a placebo. Patients allocation to treatment and placebo were done by permuted blocks randomization.

In the treatment group, there were 26 (65.0%) patients who reported improvement in International Prostate symptom Score (IPSS) from the baseline and 21 (52.5%) patients reported improvement in quality of life.

In the placebo group there were 28 (73.7%) patients who reported improvement in IPSS from the baseline and 22 (57.9%) patients reported improvement in quality of life. Among all patients, the proportion of patients who reported improvement in IPSS in the treatment group was 26 (48.1%) as compared to 28 (51.9%) in the placebo group; the difference was not statistically significant. There was also no significant difference in the proportion of patients with improvement in quality of life between the treatment group 2 1(48.8%) as compared to 22 (51.2%) in the placebo group.

Generally the trend of the results in this study showed that the drug is not superior to the placebo.

Background and Justification

Medical therapy for clinical has a major role in the improvement of symptoms associated with bladder outlet obstruction. Medical therapy focuses on two aspects of the pathophysiology of BPH: (i) a dynamic (physiological, reversible) component related to the tension of prostatic smooth muscle in the prostate and bladder neck and (ii) a fixed (structural) component related to the bulk of the enlarged prostate compressing the urethra. Medical therapy for clinical BPH has developed over decades and the general mechanism of action of prescribed drugs is either to relax the smooth muscle tone and/or reduce the size of the prostate. Pharmaceutical extracts derived from plants are widely used throughout the world for the treatment of various medical conditions. The phytotherapeutic agents used in the treatment of lower urinary tract symptoms (LUTS) secondary to BPH are extracted from the roots, seeds, barks, or fruits of plants. Active components in plant extracts include phytosterols, fatty acids, lectins, flavonoids, plant oils and polysaccharides.

A clinical trial was conducted to evaluate the efficacy of *Prunus Africana* (Hook. F.) Kalm. (family Rosaceae) for clinical BPH

Description

A randomized double blind placebo controlled clinical trial was conducted from April 2006 to January 2007. The study population were divided into two treatment groups in which one group received a drug derived from *P. Africana* and the other group received a placebo. Both drug and placebo were made in capsules with similar colour (red) but coded by different names, "amest" and "alba". The disclosure of the codes was done by the manufacturer after the analysis.

After meeting patients, they were given an International Prostate Symptom Score (IPSS) and their quality of life (QoL) was assessed.

A total of 82 patients were enrolled and followed for a period of 10 months. Each patient was followed at 4-week intervals for a duration of 3 months. Four patients were lost to follow up and excluded from the study.

No any adverse drug reactions were reported in either group and there were no reported deaths.

Results

As shown in Table 1, of the 78 patients who completed the study, the largest number, 29 (37.2%) belonged to the group with a mean age 65.5 years. Among whole population, 40 (51.3%) patients were allocated to the treatment group, and 38 to the placebo group.

Mean age (years)	Drug	Placebo	Total
≤ 50	3	0	3 (3.8%)
55.5	5	10	15 (19.2%)
65.5	17	12	29 (37.2%)
75.5	11	14	25 (32.2%)
> 80	4	2	6 (7.7%)
Total	40 (51.3%)	38 (48.7%)	78 (100.0%)

Table 1: Distribution of study population by mean age and treatment group.

Baseline IPSS	Drug	Placebo	Total
0-7	6 (37.5%)	10 (62.5%)	16
8-19	33 (54.1%)	28 (45.9%)	61
20-35	1 (100.0%)	0 (0.0%)	1
Total	40	38	78

Table 2: Baseline International Prostate Symptom Score (IPSS) among the study population by group allocation.

	Treatment allocation		
IPSS:	Drug	Placebo	Total
Improved	26 (48.1%)	28 (51.9%)	54
Not improved	14 (58.3%)	10 (41.7%)	24
Total	40	38	78

Table 3: Comparison in improvement in International Prostate Symptom Score (IPSS) between the treatment group and the placebo group. Table 2 shows the baseline IPSS scores and reveals no difference between the treatment and control group at the beginning of the trial (95% C.I, P = 0.31). At the end of the trial (Table 3) there were no significant differences in the proportion of patients who reported improvements in IPSS between the treatment group and the placebo group (95% C.I, P=0.47).

QoL score	Drug	Placebo	Total
4	14 (43.8%)	18 (56.3%)	32
5	18 (52.9%)	16 (47.1%)	34
6	8 (66.7%)	4 (33.3%)	12
Total	40	38	78

Table 4: Baseline score in quality of life (QoL) among the study population by group allocation. There were no significant differences in quality of life baseline scores between the two groups at baseline (95% C.I, P = 0.38).

	Treatment allocation		
QoL:	Drug	Placebo	Total
Improved	21 (48.8%)	22 (51.2%)	43
Not improved	19 (54.3%)	16 (45.7%)	35
Total	40	38	78

Table 5: Comparison in improvement in quality of life (QoL) between the treatment group and the placebo. By the end of the trial, there were no significant differences in the proportion of patients who reported improvements in QoL between the treatment group and the placebo groups (95% C.I, P=0.66).

No adverse drug reactions were reported in either group and there were no reported deaths.

Discussion

Although patients in both treatment and placebo groups improved their IPSS scores, there was no significant difference between the groups. However, the improvements of IPSS in this study were not different from those found by Breza *et al*. (1998), which was 31-40% reduction at a dosage of *Prunus africana* 50 mg twice daily for a two-month duration. The findings in this study were also comparable to those of Chatelain et al. (1999), who compared *P. africana* at dosing once daily to 50 mg twice daily dosing and found more than 40% reduction in the mean IPSS from the baseline. Likewise, there were no significant differences in improvement in the QoL between the treatment group 21 (48.8%) patients as compared to 22 (51.2%) patients in the placebo group (Table 5). However, improvement in QoL in this study was greater than the 31-40% reported by Breza J. *et al*.

The proportion of patients who had improvements in IPSS and QoL showed satisfactory outcome with the drug under trial. In addition, three patients in the treatment group and one patient in the placebo group reported improvement in their sexual function. However, improvement in sexual function was not among the primary outcomes measure in this study.

The results show that, although a certain number of men with clinical BPH may improve their IPSS without intervention, the authors encourage phytotherapy in selected cases since the drug showed an acceptable degree of efficacy.

Partnerships

The study was conducted in collaboration between Muhimbili University of Health and Allied sciences and the Institute of Traditional Medicine of the Muhimbili University of Health and Allied Sciences, Dar-es-Salaam, Tanzania.

Impact

The results of the study showed satisfactory outcome in improvement in IPSS and QoL. There are now more patients with BPH consulting the Institute of Traditional Medicine to source the product. However, a need for long term and multi-centre clinical trial is recommended. The product is relatively cheap, affordable and accessible to a larger population. The source of the *materia medica, P. africana*, is a globally threatened plant species, hence conservation programmes are paramount (Maximillian and O'Laughlin, 2009). These results adds value to the existing policy and legislation that promote the contribution of traditional medicine in healthcare delivery in Tanzania (United Republic of Tanzania, 2002).

Replicability

A large number of patients are in demand for the product (drug). The drug should be available and accessible to patients. The drug need approval by Food and Drug Administration Authority. Applications for registration have been filed through the Institute of Traditional Medicine and are being processed.

Lessons Learned

It was not possible for most patients to undergo ultrasound estimation for prostate size as most of them could not afford to do so. Among those who came with their reports, most reports were not specific on prostate parameters and therefore it was not feasible to evaluate changes in prostate size. The increased use of the herbal product should be consistent with availability of the respective *materia medica*. It is likely, however that strictly selected cases can do better with phytotherapeutic agents.

Future Plans

A long term multi-centre clinical trial is recommended for further evaluation of the product. Conservation of *P. africana* plant species in the wild and through cultivation is needed to scale up production to meet increasing demand for the product.

References

- McConnell J.D. (1998). Epidemiology, etiology, pathophysiology and diagnosis of benignprostatic hyperplasia. In: Walsh PC, Retik AB, Vaughan ED,Wein AJ, eds. Campbell's Urology. 7th ed. Philadelphia, PA: WB Saunders; 1429-52.2.
- Berry S.J., Coffey D.S., Walsh P.C., et al. (1984). The development of human benign prostatic hyperplasia with age. J Urol. 132:474- 479.
- Lucchetta G, Weill A, Clavert A, et al. (1984). Reactivation of the secretion from the prostatic gland in case of reduced fertility. Urology International. 39: 222-2244.
- Breza J, Dzurny O, Hanus T, et al. (1998). Efficacy and acceptability of tadenan® *(P. africana* extract) in the treatment of benign prostatic hyperplasia a multicentre trial in central Europe. Current Medical Research and Opinion. Urology. 14(3):127-139.
- Chatelain C, Autet W, Brackman F. (1999). Comparison of once and twice daily dosage forms of *P. africana* extract in patients with benign prostatic hyperplasia: a randomized, double-blind study, with long- term open label extension. Urology; 54(3):473-478.
- United Republic of Tanzania (2002). Traditional and Alternative Medicine Act.
- Maximillian, J.R. and J. O'Laughlin (2009). Towards sustainable harvesting of Africa's largest medicinal plant export (*Prunus africana*): a case study in Tanzania: Southern Forests: a Journal of Forest Science; 71: 303-309.