

ORIGINAL RESEARCH



A preliminary investigation of the effects of labour inducing plant, *Cissampelos mucronata*, on the outcomes of pregnancy using rat models

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Abstract

Background

The use of traditional remedies in pregnancy has been associated with bad obstetric outcomes including uterine rupture and foetal distress. These outcomes may ultimately lead to maternal and child mortality or morbidity. Few studies have been done to measure the effects of various herbs in pregnant women or a developing fetus. This study investigated the effects of the commonly used labour inducing plant, *Cissampelos mucronata*, on pregnancy outcomes using a rat model.

Methods

Pregnant female rats were divided into 3 groups of 10 each. The first group was the control. The second group was treated with the aqueous extract of *Cissampelos mucronata* at mid-pregnancy. The third group was treated with *Cissampelos mucronata* close to full term. All the groups were left to give birth and outcomes were recorded.

Results

Rats treated at mid-term had significantly low number of pups when compared to the control group as well as the close to term treated group (4.1 ± 0.54 vs. 6.4 ± 0.60 ; 6.2 ± 0.56). The mid-term treated rats had pups with significantly lower body weight when compared to the control and the close to term treated groups (3.73 ± 0.36 g vs. 5.37 ± 0.16 g; 4.27 ± 0.1 g). The average gestation period was significantly short in the mid-term treated group when compared to the control and the close to term treated groups (18.16 ± 0.50 days vs. 20.40 ± 0.44 days; 20.12 ± 0.37 days). There were no uterus ruptures observed in all study groups 3 days after delivery.

Conclusion

Administration of *Cissampelos mucronata* during pregnancy leads to early induction of labour.

Key words: herbal medicine; pregnancy; labour; maternal mortality

Introduction

Developing regions accounted for approximately 99% of global maternal deaths in 2015 with Sub-Saharan Africa alone accounting for roughly 66%¹. Maternal mortality rate in Malawi remains one of the highest in the world despite a global decrease in maternal mortality rates between 1990 and 2015 by 44%¹. According to the World Health Organization (WHO), Malawi's maternal mortality ratio in 2015 was estimated to be 634 per 100,000 live births which is far from the overall maternal mortality ratio of other developing countries at 239 per 100,000¹. Malawi still has a long way to go as the current Sustainable Development Goal's target is to reduce the global maternal mortality ratio to less than 70 per 100,000 live births with no country having more than double the global average maternal mortality rate by 2030¹.

The complications that account for majority of maternal deaths includes ante partum and or post partum haemorrhage, sepsis, hypertensive disorders in pregnancy, unsafe abortion,

obstructed labour and ruptured uterus^{1,2}. Most of these complications are preventable and treatable^{1,2}. The use of herbal medicines in pregnancy and labour has been reported to be a contributing factor to the high maternal mortality among women especially in poor resource countries³. The use of traditional remedies in pregnancy has been associated with bad obstetric outcomes including uterine rupture and foetal distress³. These outcomes may ultimately lead to maternal and child mortality or morbidity³⁻⁵.

Many women around the world use therapeutic herbs during pregnancy as well as during childbirth². Herbal medicines are used in pregnancy although there is very little evidence of safety; few animal or human studies have been conducted on the safety of herbal medicines in pregnancy or while nursing. Herbal medicines use during labour leads to strong, continuous contractions not corresponding to the slow dilatation of the cervix⁶. Several studies have found herbal medicines use in pregnancy to be associated with congenital malformations, intrauterine growth restriction,

decreased foetal distress, foetal hypoxia and premature delivery as a result of uterine hyper-stimulation which may lead to perinatal mortality⁶⁻⁹. Hyper-stimulation of the uterus may also lead to complications such as rupture of the uterus¹⁰. Other concerns range from an increased risk of maternal bleeding or impact on neonatal hormones due to the hormonal nature of the herbal medicine⁶⁻¹¹. Decision to use the traditional medicine is most commonly made by grandmothers or mothers and, where mother in-laws are involved, refusal is often very difficult as it would show disrespect⁶. This would suggest that the use might be more than is documented as most literature suggests that the prevalence of use is uncertain.

Few studies have been done to measure the effects of various herbs in pregnant women or a developing foetus. There is lack of scientific research and evidence on the effective use of herbs¹². This study was therefore aimed at establishing the relationship between intake of a labour inducing plant extract, *Cissampelos mucronata*, and the outcome of delivery using a rat model.

Methodology

Plant collection

Roots of a herbal medicinal plant, *Cissampelos mucronata*, were obtained from a local forest in Mulanje District, Malawi, in the winter season between May and July, 2016. Botanical identification was done at the Malawi National Herbarium and Botanical Gardens and the specimen was given voucher number 5MAL.

Plant crude extract preparation

The air-dried plant material was ground using an electric grinder into a homogenous thin powder. The crude extract was prepared by making a suspension of 100g of the powder in 500mL of water to come up with an aqueous extract. The suspension was left to stand overnight at room temperature, with constant agitation and then filtered. This was to mimic how, traditionally, the plant material is extracted. The solution was concentrated in a vacuum at 40°C using a rotor vapour until crystals were formed. The crude extract yield was 4.75% (4.75g/100g raw material).

Animals and animal treatment

Albino rats were used to study the efficacy of *Cissampelos mucronata*. The animals were kept in standard cages and housed in the animal house. In these experiments 30 female rats of 90 days or older were used. Mating was performed by housing 30 females with 30 adult males (each male with a female in the cage) overnight and the females were checked daily to confirm pregnancy by examining vaginal smears for the presence of sperm. Pregnant females were maintained individually in cages in a room at 25°C with lights on from 6:00 to 18:00 hours. They were fed standard rat chow and water ad libitum.

The pregnant rats were divided randomly into 3 groups (10 in each). The first group was the control, which was not treated with anything until they gave birth. The second group was treated with a dosage (200mg-1 kg-1 rat-1 day) of aqueous extract of *Cissampelos mucronata* at day 11 (mid-pregnancy) and left to give birth. The third group was treated with a crude extract (200mg-1 kg-1 rat-1 day) of *Cissampelos mucronata* at day 19 (close to full term) and left to give birth. The drug was administered to the animals through oral intubation.

In all the groups, the pups were examined for mortality,

deformities and they were weighed. The mothers were observed for 3 days to check for mortality or labour-associated complications and thereafter killed. The uterus was isolated and checked for any ruptures.

Data analysis

The results were analysed on the Prism 7 statistical program (Graph Pad, San Diego, CA, USA). All data are expressed as mean \pm SEM. One-way ANOVA (with Bonferroni post hoc test if $P < 0.05$) was used for statistical analysis. Differences were regarded statistically significant if $P < 0.05$.

Ethical consideration

This study was approved by the College of Medicine Research and Ethics Committee (COMREC).

Results

Table 1 below shows the pregnancy and pup outcomes for different study groups. Rats treated at mid-term had significantly low number of pups when compared to the control group as well as the close to term treated group (4.1 \pm 0.54 vs. 6.4 \pm 0.60; 6.2 \pm 0.56). The mid-term treated rats had pups with significantly lower body weight when compared to the control and the close to term treated groups (3.73 \pm 0.36g vs. 5.37 \pm 0.16g; 4.27 \pm 0.1g). The average gestation period was significantly short in the mid-term treated group when compared to the control and the close to term treated groups (18.16 \pm 0.50 days vs. 20.40 \pm 0.44; 20.12 \pm 0.37 days).

Table1: Pregnancy and pup outcomes for different study groups

Study group	Average number of pups	Average weight of pups(g)	Average gestation period(days)
Control	6.4 \pm 0.60	5.37 \pm 0.16	20.40 \pm 0.44
Treated midterm	4.1 \pm 0.54*#	3.73 \pm 0.36*#	18.16 \pm 0.50*#
Treated close to Term	6.2 \pm 0.56	4.27 \pm 0.11	20.12 \pm 0.37

The observation studies did not show any ruptures of uteruses in all the groups. It was observed that 3 mothers in the mid-term treated group ate all their pups immediately after delivering. However, these pups were included in the average totals for this group.

Discussion

The results in this study have indicated that the labour inducing herbal medicinal plant, *Cissampelos mucronata* had an effect on the outcomes of pregnancy in the rat model by influencing the number of pups delivered, average body weights of the pups, and the gestation period. It was observed that rats which were administered with *Cissampelos mucronata* in the mid-term of pregnancy were more affected than those administered close to term. Most of the plants claimed to have the potential to induce labour are reported to increase the spontaneous activity of the uterus causing increase in contractions⁸. We speculate that *Cissampelos mucronata* works in a similar way as observed by a shortened gestation period when rats were administered with the drug during the mid-pregnancy. This could also be the reason why the pups were of low body weights.

The observation that some pregnant rats that were treated at mid-term ate their offspring could probably be attributed to the stress induced by the early contractions of the uterus caused by *Cissampelos mucronata* treatment. Some studies have reported that high levels of maternal stress lead to cannibalism in rodents¹³⁻¹⁵.

Conclusion

The findings of this study have demonstrated that *Cissampelos mucronata* has oxytocic effects on rat uterus and does affect the outcomes of pregnancy by inducing early labour. If administered early, *Cissampelos mucronata* may cause premature delivery of offspring with low birth weights. We therefore speculate that consumption of herbal medicinal plant, *Cissampelos mucronata*, by pregnant women could be one of the reasons for negative outcomes of labour in Malawi and other countries where it is used. Further studies will indicate how *Cissampelos mucronata* influence shortened gestation period.

Author contributions

All authors were involved in the conception and designing of the study, data collection, drafting, revision and final approval of the manuscript.

Competing interests

All authors declare that they have no competing interests related to this work.

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