

Interventions of Iranian Traditional Medicine for Constipation During Pregnancy

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Received: 23 Aug. 2014

Accepted: 4 Feb. 2015

Abstract

Background: Constipation is a common complaint during pregnancy. Iranian Traditional Medicine (ITM) has some recommendations for this complaint.

Objective: In this study, interventions of constipation in pregnancy have been presented and their efficacy and safety evidence were reviewed from modern literature.

Methods: Interventions selected based upon the chapters related to health protection of pregnant women from ITM literature. Then a literature search was performed in the scientific databases including articles from inception up to March 2014. Articles with a focus on safety or efficacy of the selected herbs during animal or human pregnancy were selected.

Results: Folus (*Cassia fistula*), Shir-khesht (*Cotoneaster numularia* Fisch.), Tamarind (*Tamarindus indica*), Taranjabin (*Alhagi camelorum*), Damask rose (*Rosa damascene*) and almond oil are the most recommended medications for constipation in pregnant women. For all of these herbs, there is some efficacy evidence in animal or human studies. Folus is forbidden during pregnancy due to its anthraquinones ingredients. Shir-Khesht was safe in a study to treatment of constipation in pregnant women. The other mentioned herbs have not been evaluated during pregnancy. There is limited evidence to provide safe advice for consuming these herbs for constipation during pregnancy.

Conclusion: Although there are some animal and human study suggesting the laxative effect of ITM interventions, their safety are not sufficiently documented in modern literature. Scientific studies regarding these herbal remedies during pregnancy and pregnancy outcome are warranted to determine safety.

Keywords: Constipation, Herbal medicine, Iranian Traditional Medicine, Pregnancy

Introduction

The prevalence of constipation in pregnancy is reported to be 11–38% and is due to anatomic and physiologic changes in the gastrointestinal (GI) tract. [1]. Increased bowel transit time (in response to estrogen and progesterone), uterine mechanical obstruction, decreased maternal activity, decreased levels of motilin, increased colonic sodium and water absorption, and routine iron supplementation in the pregnant population are considered as major physiologic factors [2].

Mild Constipation is often self-treated with home remedies including increased fluid and fiber intake and a moderate amount of daily exercise. Bulk forming agents such as psyllium, methylcellulose, or polycarbophil along with water will also be useful for more severe cases. Osmotic and stimulant laxatives are second-line therapy but side effects (e.g., flatulence, bloating, nausea and electrolyte disturbances) may limit their long-term use [3, 4].

Iranian traditional medicine (ITM) as one of the complementary/alternative medicine (CAM) methods tries to propose simple and useful recommendations for health protection and treatment of diseases for different groups of people (e.g., pregnant women). Medicinal plants are the most commonly used ingredients of ITM medications.

The popularity of CAM has increased in recent years. Herbs are the most commonly used CAM therapies [5, 6]. Women are a large group of consumers of healthcare and CAM. Many women use herbal remedies during pregnancy due to, in part, their perceived safety, easy access, and the widespread availability of information about them (i.e., Internet, magazines and books). Despite the insufficiency of studies evaluating the efficacy and safety of herbal therapies, use of herbal

medicines during pregnancy has been reported to be about 7-96% of all people in some countries [7-10]. This frequency has been reported to be about 67% in Tehran (Iran) [10].

Unregulated or inappropriate use of alternative medicine can have negative or dangerous effects, especially in vulnerable groups like pregnant women. Also, the long term use of some medications traditionally is not reliable enough for approving their safety, so scientific evidence is needed to ascertain the efficacy and safety of medicinal plants and traditional practice.

The objective of this study was to review the literature on the efficacy and safety of the most recommended medicinal plants in ITM for treating constipation in pregnancy.

Materials and methods

The selection of herbs to review was based upon the chapters related to health protection of pregnant women from ITM literature. We reviewed the most important ITM recommendations for constipation in pregnancy mentioned by the most famous ITM books including the *al-Qanun fi al-Tibb*, *Khulasat al-hikmah*, *Exir-e-Azam*, *Mufarrih al-qulub*, *Tib-e- Akbari* and *Tadbir-al-Habali*, *al- Atfal*, *al-Sabiban*, *Makhzan-al-Adviah* and *al- Havi* [11-18].

Then a literature search was performed in the databases Google-scholar, PubMed, Scopus, Cochrane, Iranmedex and SID (the last two are Iranian databases) including articles from inception up to March 2014. The search terms were: safety, efficacy, in combination with pregnancy or pregnant, constipation, in combination with scientific names, common names, Persian and traditional names of the above-mentioned herbs. The

reference lists in the literature located were checked for further relevant publications. Articles with a focus on safety or efficacy of the selected herbs during animal or human pregnancy were selected.

Results

Masters of ITM have always paid attention to the role of nutrition in preventing and treating diseases. For treating mild constipation in pregnancy, it is recommended to eat soft foods that are digested quickly and doing light exercise and mild jogging. In

severe cases, using some medicinal plants and their preparations are recommended as laxatives [19]. Folus (*Cassia fistula*), Shir-khesht (*Cotoneaster numularia* Fisch.), Tamarind (*Tamarindus indica*), Taranjabin (*Alhagi camelorum*), Damask rose (*Rosa damascena*) and almond oil are the most recommended medications. Using purgatives such as *Viola odorata* (violet), *Althae officinalis* (marsh-mallow) and *Malva silvestris* (common mallow) is prohibited during pregnancy due to their emmenagogue (stimulator of menstrual bleeding) and abortive effects [11-18].

Table 1 - Provides a summary of the studies on the safety and/or efficacy of the above-mentioned herbs in constipation of pregnancy

Scientific name	Medicinal part for constipation	Reference for efficacy	Type of study	Dosage	results	Reference for safety in pregnancy
<i>Cassia fistula</i>	ripe pulp	Akanmu M.A. 2004	In vitro study	4-8mg/ml Pulp of fruit	Infusion relaxed the ileum	
		Mozaffarpur S.A. 2012	Controlled clinical trial	0.1g/kg/day Pulp of fruit	laxative effect of the herb more than mineral oil in children	
<i>Cotoneaster numularia</i> Fisch.	manna	Changavi F. 2005	Controlled clinical trial	4g/day	Laxative effect with out side effects in pregnant women	Changavi F. 2005
<i>Alhagi persarum</i> Boiss.	Manna	Kazerani H.R. 2009	Experimental study	2.5g/kg	suggested laxative effect	
		Noorbakhsh M.F. 2009	Experimental study	2.5 and 5g/kg	Taranjabin is an osmotic laxative	
<i>Tamarindus indica</i>	fruit pulp	Souza A. 2007	In vitro study	10 ⁻⁸ - 10 ⁻² mg/ml Aqueous extract of fruit	spasmogenic effect on guinea-pig taenia coli	

Table 1- Continued

Scientific name	Medicinal part for constipation	Reference for efficacy	Type of study	Dosage	results	Reference for safety in pregnancy
<i>Rosa damascena</i>	Petals	Abbaszadeh M. 2010	Experimental study	180 mg/kg/day aqueous extract	Laxative effect in dogs	
		Arezoomandan R. 2011	Experimental study	1.5g/kg aqueous extract	osmotic laxative effect In rats	
		Sadraei H. 2013	In vitro study	1-8 mg/ml hydro-alcoholic extract	Stimulatory effect on rat ileum smooth muscle	
		Dolati K. 2013	In vitro study	0.66, 0.83, 1.3 mg/ml Aqueous extract	Mild excitatory effect on guinea-pig ileum contraction	
		Heshmati Moghaddam M.R. 2013	In vitro study	0.16- 0.83, mg/ml Aqueous extract	Stimulatory effect on guinea-pig ileum and jejunum	
<i>Amygdalus Communis</i> L.	ripe fruit and the oil	Davis PA. 2001	Experimental study	200 g almond /kg of total diet	Improvement of colon movement and bowel transit in rats	

Folus (*Cassia fistula*)

It is a member of Caesalpinaceae family and commonly known as “golden shower” or “Purging cassia” and in ITM called, “Folus” or “Khiar shanbar” [20]. It is said to be warm and wet in nature (temper). The ripe pulp of *C. fistula* is used in ITM for children and pregnant women as a mild laxative [17]. It is recommended to use Folus with almond oil or sugar to alleviate its intestinal side effects [20]. It is also used in Indian medicine as a laxative suitable for children and pregnant women [21].

The herb which contains organic acids and pectin is said to be a laxative. It can also be a purgative in higher dosage [22]. It is also said

to have cathartic and laxative effect because of the anthraquinone derivatives isolated from the pulp of the fruits [23, 24].

The in-vitro effect of *C. fistula* infusion in comparison with senna fruit (Senokot® tablet, control group) on isolated guinea-pig ileum has been studied [25]. The infusion of *C. fistula* fruit (4-8 mg/ml) relaxed the ileum [25].

A randomized clinical trial was carried in Babol, Iran on 81 children (age range: 4 – 13 years) with functional constipation. They received *C. fistula* emulsion (CFE) or mineral oil (MO) randomly for three weeks. Dose of CFE was 0.1 g/kg/day, based on dried pulp of

fruits of *C. fistula*. Eighty four percent of children in the CFE group and 50% in the MO group ($p = 0.002$) improved. It was concluded that CFE was more effective than MO in the 3-week treatment of children with functional constipation [26].

In the case of pregnant women, the use of laxatives containing anthraquinones (like senna and aloe and Folus) is said to be potentially dangerous, because the ingredients can induce uterine contractions, increase blood flow to the uterus and its attachments, increasing the risk of fetal loss. Although, there are no studies to approve the safety of Folus in human pregnancy, it is recommended that products containing anthraquinones should be avoided during pregnancy, especially in the first trimester [22-26].

Shir-Khesht

It is the Persian name for *Cotoneaster discolor* which is a glucomannan produced by an insect (*Scolytus rugolosus* Mull) on the *Cotoneaster numularia* Fisch. (or *C. numularioides* Pojak.) which are from Rosaceae family. The common name is “purgative manna” or “cotoneaster” [27]. Its nature is said to be warm in heat and moderate in humidity [17].

Glucomannan is a water-soluble polysaccharide that is considered a dietary fiber. It is said to be an osmotic laxative due to its sugar content [20].

Glucomannan has been investigated for the treatment of constipation. Marzio et al (1989) studied the mouth-to-cecum transit time in 13 patients affected by chronic idiopathic constipation and 18 control subjects. A 10-day diet including either glucomannan (1 g three times a day orally) or placebo administered in a double-blind manner. Mouth-to-cecum transit time in the group with constipation

increased statistically significant. No difference in transit time was noted with placebo [28].

A non-controlled study was done to evaluate the efficacy of glucomannan derived from *Amorphophallus konjac* plant. Ninety three patients with chronic constipation were evaluated for number of days per week with bowel movements, number of enemas and abdominal symptoms. The study had an initial phase (treatment with 1g of glucomannan three times a day for 1 month) and a maintenance phase (1g bid for one month). All parameters improved significantly after one month and lasted through the second month [29].

In a study on 50 pregnant women affected by constipation, sachets containing a preparation of glucomannan (1.45 g) and lactulose (4.2 g) were administered for 1-3 months. The preparation of glucomannan induced a normal frequency of weekly number of defecation (4.9-5.8/week) in comparison with the control group, while being well-tolerated [30].

In a randomized clinical trial, sixty four pregnant women with constipation were allocated randomly to receive powdered Shir-Khesht (4g with a cup of water/BD) or magnesium hydroxide (2 spoons every night) for 1 month. At the end of the study, the frequency of defecation in the first group (Shir-Khesht) was significantly more than the second group and stool was significantly softer. No side effects were reported [31].

Common dosage for *C. discolor* is 50 mg/kg for children and 150 mg/kg for adults. It must be taken with water or other fluid [32].

There are no reported side effects from using Shir-Khesht or other types of glucomannan in pregnancy.



Taranjabin

Alhagi pseudalhagi is a glucomannan produced by an insect (*Poophilus nebulosus*) on the *Alhagi persarum* Boiss. & Buhse or *Alhagi camelorum* L. (Camelthorn), which are plants from Papilionaceae family. It is also called "Persian manna" and "Oshtorangebin" (Camel honey).

It is said to be warm and wet in nature (temper) and it is recommended for constipation in pregnancy [17]. Common dosage for *A. pseudalhagi* is 100 mg/kg three times daily [32].

In preparation of the solution, 20 - 30 g of the crude manna is dissolved in hot water followed by filtration of solid impurities, after cooling the solution is consumed [33].

The chemical constituents of Taranjabin are melezitose, *Saccharose*, fructose, gum and mucilage [20].

The laxative and purgative effect of Taranjabin on rats has been studied. In an experimental study, Taranjabin was gavaged to healthy rats (n=7) at single doses of 2.5 g/kg. The feces count; feces weight and feces water percent during the next 24 h following treatment were evaluated and compared with the placebo group (n=7). In the test group, the feces count, feces weight and feces water percentage were significantly higher than placebo group (p<0.001), then the results suggested an efficient laxative effect for Taranjabin in rats [34].

According to the results of the study has been performed in rats to verify the mechanism behind the laxative effect of Taranjabin, it seems to act as an osmotic laxative [35].

There are no safety studies and reported side effects for using Taranjabin during pregnancy.

Tamarind (*Tamarindus indica*)

Tamarind is a plant of Caesalpinaceae family. The most used organs of the plant in traditional medicine are fruits and leaves. Phytochemical investigations revealed the presence of phenolic compounds, cardiac glycosides, malic and tartaric acid, pectin, and mucilage as active constituents of *T. indica* [22]. Tamarind fruits are also used for chronic or acute constipation in India, Sahel and Soudan [36, 37].

In ITM literatures, it is said to be cold and dry in nature [17] and Tamarind with Goleghand (combination of Gole Mohammadi with sugar) or Golangabin (combination of Gole Mohammadi with honey) is said to be helpful for constipation in pregnancy [11-17].

The effect of aqueous extract of *T. indica* (AETI) fruit was studied on the guinea pig taenia coli. AETI, at concentrations ranging from 10^{-8} mg/ml to 10^{-2} mg/ml, increased the spontaneous contractile activity of guinea pig taenia coli in a dose-dependent manner (EC₅₀= 4×10^{-6} mg/ml) [38].

No health hazards or side effects are known in conjunction with the proper administration of therapeutic dosage which is 10-50g/day of cleaned Tamarind paste [22].

There are not any scientific studies that support the safe use of this plant in women during pregnancy.

Gole Mohammadi (*Rosa damascena*)

It is a plant of Rosaceae family commonly called Damask rose and also known as Persian rose and Gole Mohammadi in Iran. The medicinal parts are the petals and the essential oils extracted from them [39]. Fatty oil and organic acids were isolated from flowers, petals and hips [22].

In ITM, It is said to be cold and dry in

nature [17]. The pure dried petals are astringent due to the tannin content, but combinations of Persian rose with sugar (is called Goleghand) or honey (is called Golangabin) are used in traditional medicine as laxatives. It is said to be a gentle safe laxative in pregnant women. Dried petals (without seeds and leaves), soaked overnight in water and grated with sugar or honey make Goleghand and Golangabin respectively. It is recommended to use for 3 days to be effective. Fresh flower is more laxative and must not be soaked [11 - 17].

Dried flower petals of *R. damascena* are traditionally used to treatment of constipation while rose water containing *R. damascena* essential oil is said to be effective on bowel spasm [40].

In a study in dogs, the laxative/purgative effects of the boiled extract of *R. damascene* was evaluated. Five Groups of dogs (n=5) received the extract at doses 0.5-8 times that traditionally suggested for human use (180 mg/kg) daily. Placebo and lactulose was considered as the negative and the positive control groups respectively. During 10 days of the experiment, diarrhea was occurred in a dose dependent manner; however the fecal water content did not change significantly. It was concluded that boiled extract of *R. damascena* may have a laxative effect in dogs [41].

Prokinetic effect of the boiled extract of *R. damascena* has been evaluated in comparison with lactulose and salin in rats. In this study, feces number and its percentage of water were significantly increased in response to 1.5 g/kg of the extract, but intestinal transit time was not changed. So, osmotic infiltration of fluids into the intestine was concluded to be the mechanism of laxative effect of *R. damascena* [42].

In a study, the effect of hydro-alcoholic extract of flower petals of *R. damascena* growing in Kashan (Iran), was investigated on ileum motility in rats. Ileum contractions induced by electrical field stimulation (EFS), KCl and acetylcholine (ACh). *R. damascena* extract (10-100 µg/ml) induced a contraction in rat isolated ileum, while at 1 mg bath concentration it had relaxant effect on rat ileum. Hydro-alcoholic extract of *R. damascena* (1-8 mg/ml) concentration dependently inhibited ileum contraction induced by KCl (IC₅₀=3.3 ± 0.9 mg/ml), ACh (IC₅₀=1.4 ± 0.1 mg/ml) and EFS (IC₅₀=1.5 ± 0.3 mg/ml). The vehicle had no significant effect on ileum contractions. It was concluded that microgram concentration of *R. damascena* extract had a stimulatory effect on ileum smooth muscle and it confirms the benefits of *R. damascene* for the treatment of constipation [43].

In another study, the effect of various concentrations (0.66, 0.83, and 1.3 mg/ml) of aqueous fraction of *R. damascena* on contractions of isolated guinea pig ileum was evaluated in comparison with acetylcholine (ACh) in presence and absence of atropine. According to the results, aqueous fractions of *R. damascena* increased basal guinea pig ileum contractions as a dose-dependent manner (p<0.05 to p<0.001). It was concluded that aqueous fraction of *R. damascena* has mild stimulatory effect on ileum contraction and may be considered as a mild laxative agent [44].

The mechanism of action of the aqueous fraction of *R. damascena* on the intestinal contractions can be due to its stimulatory effect on histamine and cholinergic receptors of ileum and jejunum [45].

No health hazards or side effects are known in conjunction with the proper administration of therapeutic dosage which is 3 - 6 g daily

[22]. There are no scientific studies that support the safe use of this plant in women during pregnancy.

Almond (*Amygdalus Communis* L.)

Amygdalus Communis L. or Almond (also called *Prunus amygdalus* or *Prunus dulcis*) is a plant of Rosaceae family. The medicinal part is the ripe fruit and the oil extracted from them. Sweet almond oil has laxative effect [20].

According to ITM literature, it is said to be warm and wet in nature [17] and constipation in the last month of pregnancy can be controlled easily by eating some sweet almond oil every morning [11-17].

Essential fatty acids, mucilage and protein substances are the main constituents of sweet almond [22].

Almond oil is prepared from a variety of almonds and is a glyceryl oleate, with a slight odour and a nutty taste. Sweet almond oil is obtained from the dried kernel of the plant. This oil has been traditionally used by massage therapists to lubricate the skin during a massage session, and is considered by many to be an effective emollient [46].

Sweet almond might work as a laxative due to the presence of many fatty acids. In an animal study to assess the effect of almond on colon cancer, effects of whole almond-, almond meal- or almond oil-containing diet on aberrant crypt foci (ACF) in azoxymethane-treated F344 male rats were investigated. Improved movement through the colon and better bowel transit was presented as a secondary objective in this study [47].

There is not enough scientific information available to know if sweet almond is safe to use as medicine especially during pregnancy.

Discussion

In this study, a systematic review was conducted to collect all available types of studies on efficacy and safety of the laxative plants for pregnant women mentioned by ITM. The results show a small number of studies for efficacy of Folus and Shir-khesht on human constipation. The laxative effects of glucomannans derived from other plants have been investigated in human or animal studies. Also there are some animal studies to suggest the laxative effect of Taranjabin, Tamarind, Gole Mohammadi and Almond oil.

Although, the above mentioned herbs are the most recommended ITM (and traditional medicine of other countries) medications for constipation during pregnancy [19, 48], there is not sufficient evidence to approve their safety. There is only one study that was done in pregnant women and concluded the safety of Shir-khesht. Folus cannot be recommended in pregnant women due to its anthraquinones ingredients.

Traditional medicine has maintained its popularity worldwide. The safety and efficacy of traditional medicine have become important concerns for both health authorities and the public.

Requirements and methods for research and evaluation of the safety and efficacy of herbal medicines are more complex than those for conventional pharmaceuticals. A single medicinal plant may contain hundreds of natural constituents, and a mixed herbal medicinal product may contain several times that number. Adverse events arising from consumption of herbal medicines may be due to any one of a number of factors. These include the use of the wrong species of plant by mistake, adulteration of herbal products

with other, undeclared medicines, contamination with toxic or hazardous substances, over dosage, misuse of herbal medicines by either health care providers or consumers and use of herbal medicines concomitantly with other medicines. Therefore, analysis of adverse events related to the use of herbal medicines is more complicated than in the case of conventional pharmaceuticals. Furthermore, herbal medicines are often used for self care; thus, there is a great need to educate consumers and public in their proper use. Long-term use of traditional and folk medicine can be a reason for the efficacy, but it is recommended to conduct scientific studies to approve their efficacy and safety [49]. This is particularly important in vulnerable groups such as pregnant women. All medications should be viewed with caution during pregnancy especially during the first trimester. Without sufficient evidence for safety, it is difficult to provide safe advice.

The data regarding safety of botanicals during pregnancy are very limited. However, study on non-pregnant adults seems to be

possible and acceptable for proving the efficacy of a drug, approving the safety in pregnant women requires scientific evidence conducted during pregnancy. When addressing the safety of herbs during pregnancy, we must look at the totality of the evidence, which includes traditional and contemporary use, animal studies, pharmacological studies, observational studies and clinical trial data, when available [50].

According to the results of this study, conducting some scientific studies especially for approving the safety of these herbs during pregnancy is recommended.

Conclusion

There are some animal and human studies suggesting the laxative effect of ITM interventions. Safety of ITM interventions for constipation during pregnancy are not sufficiently documented in modern literature. Scientific studies, especially prospective observational studies regarding these herbal remedies during pregnancy and pregnancy outcome are warranted to determine safety.

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