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Original article

A prospective case series exploring the role of Chinese herbal medicine in the treatment of recurrent urinary tract infections

Andrew Flower *, George Lewith

The Complementary and Integrated Medicine Research Unit, Department of Primary Medical Care, University of Southampton, UK

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Abstract

Background: Recurrent urinary tract infections (RUTIs) are common in women and are associated with considerable morbidity and health care costs. Antibiotic prophylaxis is currently successful but infections commonly reoccur and bacterial resistance is an increasing problem. Preliminary data suggests that Chinese herbal medicine (CHM) may have a role to play in managing RUTIs. CHM is a complex intervention that requires a thoughtful process of evaluation and testing. A prospective case series can be used to report 'real world' treatment using CHM and to investigate the feasibility of more rigorous research.

Methods: Fifteen women with RUTIs seen in routine clinical care by an experienced practitioner over a 6-month period were enrolled in a prospective case series. Treatment involved concentrated CHM powders for 12 weeks. Data was collected on common patterns of presentation, and participant response to CHM including compliance, overall changes in urinary tract symptoms, the frequency and severity of recurrent infection; change in use of antibiotics; and wellbeing.

Results: Thirteen out of 14 participants who completed the course of treatment reported improvement in their symptoms and overall wellbeing. Antibiotic use declined. It was possible to detect common diagnostic patterns.

Conclusion: A case series can explore the routine delivery of an intervention and provide information on feasibility for future research. It provided a useful opportunity to introduce case record forms, to assess various outcome measures, to gain an idea of common diagnostic presentations, to assess the safety of CHM, and to explore different treatment strategies. It facilitated the identification of commonly used herbs in the treatment of RUTIs (Fig. 2) and allowed preliminary assessment of a standardised herbal formula for treatment of an acute UTI. However a case series lacks experimental rigour and is subject to considerable bias. The findings from this approach should be interpreted cautiously and seen as preliminary data that can help to inform subsequent more rigorous research.

Keywords: Recurrent urinary tract infections; Chinese herbal medicine; Prospective case series

Introduction

In the UK urinary tract infections (UTIs) are the commonest infection presented by women within the primary care setting [1,2], with approximately 40–50% of women experiencing one episode during their lives [3].

Recurrent urinary tract infections (RUTIs) are commonly defined in the literature as three episodes of UTI in the last 12 months or two episodes in the last 6 months [4]. Between 20 and 30% of women who have had one episode of UTI will have a recurrent UTI [5] and around 25% of these will develop subsequent recurrent episodes [6]. RUTIs can have a significant negative effect on quality of life, and have a high impact on health care costs as a result of outpatient visits, diagnostic tests and prescriptions.

Antibiotics are currently the mainstay conventional treatment for both acute and recurrent UTIs. Whilst antibiotics may be effective in reducing the duration of severe symptoms in acute episodes [7,8], antibiotic resistance leading to increased duration of severe symptoms [2], is currently estimated at 20% for

Abbreviations: ALT, alanine transaminase; b.d., twice a day; CAM, complementary and alternative medicine; CHM, Chinese herbal medicine; MYMOP, Measure Yourself Medical Outcomes Profile; NHS, National Health Service (UK); RCHM, Register of Chinese Herbal Medicine; RUTIs, recurrent urinary tract infections; WBC, white blood cell; UTIs, urinary tract infections; VAS, Visual Analogue Scale.

* Corresponding author at: Complementary and Integrated Medicine Research Unit, Primary Medical Care, University of Southampton, Aldermoor Health Centre, Aldermoor Close, Southampton SO16 5ST, UK.
Tel.: +44 023 8024 1050.
E-mail address: flower.power@which.net (A. Flower).

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Trimethoprim and Cephalosporins, and 50% for Amoxicillin [9]. It is predicted that antibiotic resistance will continue to increase [10].

Antibiotic prophylaxis can be successfully used to prevent RUTIs [4]. However once prophylaxis is discontinued, even after extended periods of up to 5 years, approximately 50–60% of women will become re-infected within 3 months [11,12]. Thus, antibiotic prophylaxis does not appear to exert a long-term effect on the baseline infection rate. The unsatisfactory results of long-term RUTI treatment and the expressed need to develop antibiotic sparing strategies within primary care [2] create what has been termed an "effectiveness gap" in the management of this condition.

There is a growing interest in the potential of complementary and alternative medicine (CAM) therapies to fill this gap. Cranberry products, for example, have been subject to considerable analysis and a Cochrane review of the use of herbal cranberry for UTIs [13] concluded there was some supportive evidence for this approach for women with RUTIs, with a reduction in recurrence risk estimated at between 10 and 20% [14].

Another alternative approach is Chinese herbal medicine (CHM). CHM has a recorded history of treating the symptoms of UTIs for over 2000 years [15]. More recent clinical research in China has provided some supportive evidence that CHM can alleviate the symptoms of UTIs [16–19] and reduce the rate of recurrence 1 year post treatment from 30% when antibiotics were used alone to 4.4% when antibiotics and CHM were combined [18]. Despite these encouraging preliminary reports the methodological quality of the Chinese RCTs are frequently poor [20,21] and there is currently little rigorous and reliable data supporting the potential role of CHM in managing acute and preventing recurrent UTIs. There is therefore a clear need for further research. In accordance with the UK Medicine Research Council (MRC) recommendations for the investigation of poorly evidenced complex interventions such as CHM [22], a strategic, phased, research development process is essential.

In response to these guidelines one of the authors (AF), a CHM practitioner, conducted a retrospective audit on a number of his cases involving the use of CHM for the treatment of RUTIs. Results, although obviously anecdotal, were generally positive. There was an early indication of recurrent patterns of diagnosis, treatment strategies and herb selection. In order to provide a more structured, deeper and more careful evaluation of these clinical findings a more comprehensive, prospective case series evaluation from the same practitioners clinical practice, involving 15 new women with RUTIs was proposed.

A case series can be defined as 'a study reporting on a consecutive series of patients with a defined disorder treated in a similar manner, without a concurrent control group' [23]. It is a methodology that facilitates an early testing of a particular approach to treatment for a pre-defined condition. It allows an evaluation of routine care without the artificial constraints and financial demands imposed by randomised controlled trials, and can provide clinically important information for a practitioner and a provisional assessment of the feasibility of an intervention for those involved in research.

The main objectives for this case series were:

- To establish the feasibility of delivering a 12-week program of CHM for the treatment of RUTIs. In particular could participants manage to take CHM encapsulated powders, and what were the rates of compliance during the course of the study?
- To assess the credibility of this intervention amongst the participants.
- To explore which outcomes measures worked and why.
- To examine, in terms of traditional Chinese medicine theory, whether there were common patterns (syndromes) of diagnosis for RUTIs.
- To gain a preliminary idea of the effectiveness of the herbal intervention and to identify key individual herbs and herbal combinations that could be used in future research.
- To investigate the safety of CHM for the treatment of RUTIs.

The Research Committee of the main UK professional association for CHM, the Register of Chinese Herbal Medicine (RCHM) reviewed this proposal and approved it. This work was not undertaken as a project under the auspices of the University of Southampton and was regarded a service evaluation within usual care. As a consequence formal University or NHS ethical approval was not considered necessary.

Methods

Recruitment was undertaken via an information sheet posted in two CHM clinics in Hove and London, UK. In addition all members of the RCHM (approximately 400) were informed of this case series by post and via e mail and invited to refer appropriate patients. Inclusion criteria were women aged over 18 years with at least 3 episodes of recurrent UTI in the previous 12 months, or two in the previous 6 months, with at least one urine culture positive for pathogenic bacteria. The primary reason for a positive urine culture was to distinguish a recurrent UTI from similar presentations such as painful bladder syndrome, urethral syndrome and interstitial cystitis which can present with overlapping symptoms. Unfortunately most patients were not informed by their GPs of the exact nature of the causative organism. Women with a history of liver or renal disease, who were pregnant or breast feeding, who had diabetes, or suffered from psychosis, dementia or terminal illness were excluded from taking part.

Treatment was delivered in the usual setting of the author's (AF) CHM clinic in Hove and London, UK. The evaluation commenced in February 2011 and concluded in October 2011 having successfully recruited 15 women.

Herbal treatment

Part of the rationale for this case series was to investigate the feasibility of delivering CHM as encapsulated concentrated herbal powders for the treatment of RUTIs. These powders originated from the Sheng Jiang Pharmaceutical Company in Taiwan and were supplied by Balance, UK, a member of the RCHM's Approved Supplier Scheme which, in a previous clinical trial

Table 1
Acute formula herbs.

Herbs	Botanical name	Proportion in the formula (%)
Tu Fu Ling	Rhizoma Smilax glabra ROXB.	16.8
Chong Lou	Rhizoma Paris polyphylla SMITH var. yunnanensis	8.4
Pu Gong Ying	Herba Taraxacum mongolicum HAND.-MAZZ.	11.2
Bai Jiang Cao	Herba Patrinia scabiosaefolia FISCH. EX. TREV.	8.4
Shi Wei	Folium Pyrosia lingua (THUNB.) FARWELL	8.4
Ze Xie	Rhizoma Alisma orientalis (SAM) JUZEP.	6.7
Che Qian Cao	Herba Plantago asiatica L.	8.4
Tong Cao	Medulla Tetrapanax payferus (HOOK.)K. KOCH.	3.3
Huang Bai	Cortex Anemarrhena aspheloides BGE	6.7
Ku Shen	Radix Sophora flavescens AIT.	5
Yi Mu Cao	Herba Leonurus heterophyllus (SWEET)	8.4
Wu Yao	Radix Lindera aggregata (SIMS) KOSTERM.	5
Gan Cao	Radix Glycyrrhiza uralensis FISCH.	3.3

has been acknowledged as a proxy for acceptable dispensary standards by the MHRA [24]. Unfortunately in April the new EU Traditional Medicines Directive came into operation and it became apparent that herbal dispensaries were no longer able to provide encapsulated products. As a consequence most participants received concentrated herbal powders that they were required to mix with hot water to produce a herbal drink. One participant who had advanced MS and was being fed via a nasogastric tube could only take the herbs as a decoction. Participant compliance and preliminary data relating to the effectiveness of this method of administering CHM treatment were also considered to be valid objectives for this case series.

Each participant was seen by the practitioner (AF) and a full case history was taken, including tongue and pulse observations. Subsequent consultations were held at 2–4 weekly intervals (again reflecting normal practice). All participants were given 2 herbal formulae. One was labelled "acute herbs" and was to be taken during any episode of an acute UTI. It comprised of a standardised combination of 14 Chinese herbs (see Table 1) that the author (AF) had identified following his retrospective audit. Dosage for this was either 5 × 500 mg capsules every 4 h or 3 level teaspoons (approximately 4 g) of powder 2–3 times a day depending upon the severity of the episode. A second "preventative" herbal formula was also dispensed to each participant. This formula was individualised according to the different, more constitutional, presentation that the practitioner identified as underlying the acute infection. These data were used to help establish common patterns of CHM diagnosis in the treatment of RUTIs. The dosage for the preventative formula was either 5 × 500 mg capsules twice a day (b.d.) or 3 teaspoons of powder b.d. These dosages reproduced routine practice. Treatment duration was 12 weeks.

Outcomes

The Devilly and Borkovec [25] questionnaire was completed prior to the initial consultation to assess how credible the participants considered the treatment and what their expectations were for the study. Baseline liver (ALT) and renal (serum creatinine) levels were measured using a desk-top Reflotron blood testing machine. These readings were repeated at the end of the study, or earlier in the event of any reported adverse effects. The primary final outcome was a VAS score rating the degree of change in symptoms during the study with secondary outcomes provided by a series of scales recording the frequency, severity of any infections, changes in wellbeing and changes in the use of antibiotics during the study (see Fig. 1). These outcomes measures were not validated for use in recurrent UTIs because validated outcomes measures providing these data could not be found at the time of this study. However it was an important objective of this audit to explore which kinds of outcome measures would be most useful for a subsequent clinical trial.

MYMOP, a validated quality of life measure [26], was originally proposed for use during the study but in practice it did not prove to be useful and its use was discontinued.

Analysis

This is a small case series using un-validated outcomes measures. It is not designed to provide anything other than very preliminary exploratory data on feasibility, and as a reflection of clinical practice including differential diagnosis, herb selection and dosage. Only descriptive statistics have been used to analyse the baseline characteristics of the participants and to summarise the overall findings of the study.

Results

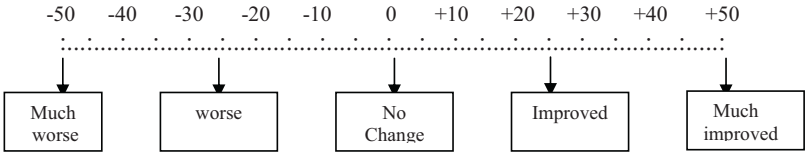
Baseline characteristics

Baseline characteristics are recorded in Table 2.

Treatment results

Fifteen women were successfully recruited to the study. 12 of the women were recruited via practitioner referral and 3 via the clinic information sheet. The occupational status of the women reflects the rather skewed sample derived from this recruitment with 6/15 working in CAM fields that included acupuncture and massage. The symptoms that most bothered

1. Please mark the place on the scale below that reflects how your urinary symptoms have changed during the course of this treatment?



2. Please mark the number that describes how many urinary tract infections you have had whilst on the RUTI trial?

0 1 2 3 4 5 6 or more

If you have had no infections please go to question 5.

3. Please mark the number that best describes how frequent your urinary tract infections are now compared to before taking part in the RUTI trial?

1	2	3	4	5
much more frequent	more frequent	no change	less frequent	much less frequent

4. If you have had a urinary tract infection whilst being on the trial how bad have the symptoms been compared to your previous experience?

1	2	3	4	5
much worse	worse	no change	improved	much improved

5. Overall how would you rate your overall wellbeing now compared to how it was at the beginning of the trial?

1	2	3	4	5
much worse	worse	no change	improved	much improved

6. If you use antibiotics to manage your bladder infections has your use of antibiotics increased or decreased whilst being on the trial?

1	2	3	4	5	6
increased a lot	slightly decreased	no change	slightly decreased	decreased a lot	completely stopped

Fig. 1. RUTI study outcomes.

these women were the classic triad of urgency, burning and frequency, together with abdominal pain and irritability and malaise, which affected 7/15 of the women. Common reported triggers for a UTI included intercourse, alcohol, stress, dehydration, fatigue, and poor diet.

Of the 15 women who were enrolled in the study, 13 completed a full course of treatment and provided data that has been used in this analysis. One woman withdrew from the study at 8 weeks due to a probable viral infection (see below) but she did complete a final outcomes analysis. One woman dropped out at the outset of her treatment because she could not tolerate the taste of the herbs. Apart from this case there was no problem with compliance with the CHM treatment.

The outcomes measures were easy to complete and correlated well with the clinical assessment of the practitioner–researcher (AF). The results of the case series audit are summarised in Table 3.

In addition to the standardised herbal formula for acute infection it was possible to identify 55 herbs that were used in various combinations to treat constitutional factors that were considered to underlie these acute episodes. Twenty-four herbs were used in 3 or more cases and 13 herbs were used in 8 or more cases (see Fig. 2).

It was possible to detect shared diagnostic patterns in this sample of participants. The commonest presentation for an acute UTI was, in terms of traditional Chinese medicine (TCM)

Table 2
Baseline data.

	Data		Comments
Age	Mean age	38.7 yrs	
	SD	11.4 yrs	
	Min	17 yrs	
	Max	60 yrs	
Duration of disease	Mean duration	6.8 yrs	
	SD	4.4 yrs	
	Max	>15 yrs	
	Min	2 yrs	
Recruitment	Practitioner network	12	The practitioner network might be an important means of recruitment for future CHM trials
	Clinic advert	3	
Occupation	Involved in CAM	6	
	Working in other jobs	5	
	Retired	1	
	Disabled	1	
	Full time students	2	
Underlying TCM syndromes	Spleen Qi deficiency + Damp	13/14	The commonest presentation was Spleen Qi deficiency + Damp combining with Liver Qi stagnation to produce D/H and then toxic heat in the lower jiao. This was compounded by an underlying Kidney deficiency, particularly in women over the age of 45
	Liver Qi stagnation	12	
	Kidney deficiency (yin/yang)	8	
	Heart Fire	1	
	Heart Qi xu	1	
	Blood xu	1	
	Blood stagnation	1	
Pre-trial treatment options	Antibiotics	12/14	No women were on prophylactic A/Bs (this should probably be in the exclusion criteria of the trial)
	Cranberry products	5	
	CAM therapies (Ac/herbs/diet)	3	One woman advised to go on prophylaxis but symptoms resolved with CHM
	OTC sachets	2	

Table 3
Results.

Outcome	Results	Comments
Change in urinary tract symptoms at the end of the trial.	9 – much improved (+5) 4 – improved (+2 to +4) 1 – no change (0)	
This was a 10 cm VAS scale ranging from −5 as much worse, with 0 as no change, and + 5 as much improved.	Mean +4 SD 1.4 Min +1 Max +5	
Number of UTIs during the trial	0 episodes $n = 7$ 1 episode $n = 4$ 2 episodes $n = 3$	Although 7 women still reported UTis 5/7 reported this occurred with less frequency and 6/7 with reduced severity.
Change in frequency of UTIs at end of trial	Much less frequent $n = 4$ Less frequent $n = 1$ No change $n = 1$ No data $n = 1$	For those who experienced a UTI there was still a positive reduction in episode frequency.
Improvement of symptoms in those reporting a UTI	Improved $n = 6$ No data $n = 1$	Although women did experience UTIs during the trial these were reported as less severe than when not taking CHM.
Change in wellbeing	No change $n = 0$ Improved $n = 10$ Much improved $n = 4$	This is an important outcome that needs to be measured in the RCT.
Change in antibiotic use	Increased $n = 0$ No change $n = 2$ Slightly decreased $n = 1$ Decreased a lot $n = 3$ Completely stopped $n = 3$	This question was added to the outcomes half way through the trial so data are only available for 8/14 women who completed the trial. This needs to be more carefully measured in the RCT. Some confusion with no change-ambiguous.

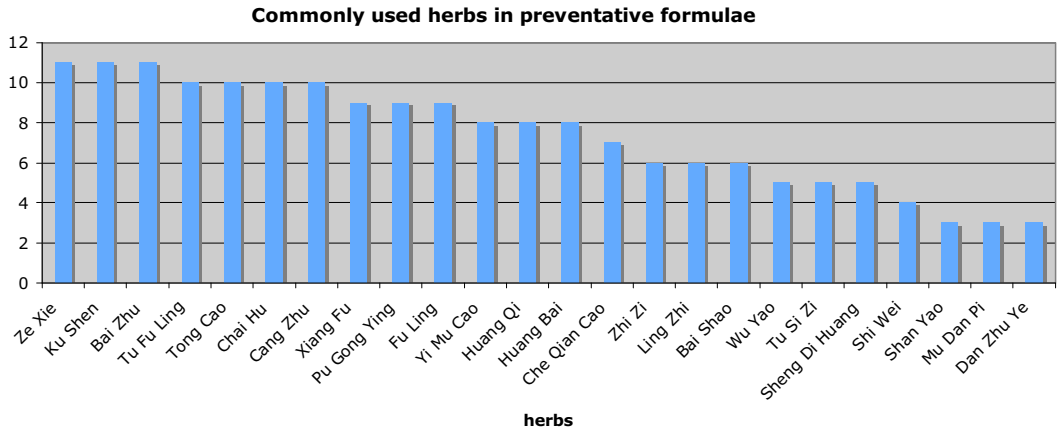


Fig. 2. Commonly used preventative herbs.

theory, Damp-Heat in the Bladder turning into toxic Heat causing disruption in the circulation of Qi and Blood. Underlying factors regularly involved a combination of Spleen Qi deficiency and Liver Qi stagnation. In older participants or those with other co-morbidities a Kidney deficiency was also a common presentation.

There were no instances of serious adverse reactions involving alterations in ALT or serum creatinine. However one woman developed a sore throat that progressed to severe myalgia, fatigue, and palpitations at week 8 of her treatment. Her creatine kinase levels were raised and her WBC count was slightly below normal (2.2 (3.9–11)). These returned to normal after 4 weeks. Her conventional doctor diagnosed an acute viral illness. As a precaution, at this point she stopped taking the Chinese herbs. She was later diagnosed with, and treated successfully for, fairly severe Vitamin D deficiency (20 nmol/L (normal range (50–250 nmol/L). It is highly unlikely that a relatively low dose of CHM taken over an 8-week period could lead to Vitamin D deficiency. To our knowledge Vitamin D deficiency has not been previously reported as an adverse effect of taking CHM. In this instance it is far more likely that the participant, a Japanese woman with a cultural tradition of avoiding sunlight, who had also been working indoors 6–7 days a week for a considerable period of time, became deficient due to inadequate exposure to ultraviolet light.

The cost of this case series was considerably less than anticipated. The total cost of the herbs amounted to approximately £1500.

Discussion

In general the results from this case series were extremely promising. Thirteen out of fourteen women who completed outcomes data for the study reported an overall improvement in their urinary tract symptoms. Nine of these reported maximum possible improvements of +5 on the VAS scores. Only one woman reported no change. Seven women suffered at least one UTI during the course of the study but 5 of these reported this was less frequent than before the trial and 6/7 reported that symptoms were less severe. This suggests that, in these instances, a combination of the individualised preventative herbs and the standardised acute herbs was successful in alleviating recurrent UTIs. Wellbeing in all participants improved and 7/9 women who regularly used antibiotics to manage their condition reported a decrease in their antibiotic use during the study.

Although no formal follow up analysis has taken place several of the participants have been contacted and the benefits appear to have persisted.

An interesting possible additional benefit from CHM treatment occurred when two participants, who had been trying to conceive without success, tested positive for pregnancy. Both women had completed their herbal treatment for RUTIs. One woman has now had a live birth, the other, a 41-year old woman with a prior history of previous miscarriage, unfortunately had another miscarriage.

Diagnostically there were several key features according to traditional Chinese medicine theory. Weakness in the Spleen, which correlates in general to the digestive function, leading to Damp stagnation commonly combined with Liver Qi stagnation resulting from emotional stress to produce Damp-Heat. This pathogenic complex tends to sink and settles in the Bladder where it may become toxic heat and take on the common features of a UTI infection. In several women, particularly women over the age of 45 or in women with accompanying health problems, such as hypothyroidism, there was also an underlying Kidney deficiency. This correlates well with previous acupuncture research on RUTIs involving 67 women in Norway where 90% of the participants were found to have either Spleen and Kidney deficiency or Liver Qi stagnation [27]. It will be interesting to see if these patterns correlate with the experience of other CHM practitioners and to see how strongly they present in a proposed systematic review of Chinese clinical trials. If this is the case then it may be possible to simplify the CHM treatment of RUTIs for the purposes of a clinical trial without seriously undermining the model validity of Chinese medicine in the process.

Although this analysis may appear archaic, CHM pathophysiology is a sophisticated, complex account of the disease process that has its own consistent internal logic. Translating CHM terminology into biomedical concepts can lead to a rather unhelpful over-simplification and it is beyond the remit of this paper to present a more detailed exploration of the

parallels between these two medical systems. For a comprehensive account of basic CHM theory the reader is referred to [14].

The strength of an audit using a prospective case series is that it reflects the 'real world' management of RUTIs in a typical CHM clinic. Although the occupation of the participants reflects a strong interest and support in CAM this is not an untypical population for a CHM clinic. It is extremely likely that patients recruited via general practice will be less sympathetic towards CHM and this might be one important factor in explaining any disparity between the kind of results achieved in this case series and a full RCT.

The case series was a useful way of developing a case record form that could be used for the trial and in exploring different types of outcomes measure. The range of data that were captured reflected the kinds of changes experienced by the participants. Any future trials need to find validated equivalents of these outcomes measures. Although MYMOP was used at the outset it quickly became apparent that it was not an appropriate measure for episodic illnesses such as recurrent UTIs and it stopped being used early in the study. This is a useful check of outcomes measures that could save a lot of trouble from inappropriate measures being used in subsequent trials.

The study was interesting in terms of the application of CHM. Although 14 herbs were used in the standardised acute remedy, 55 herbs were used in prescriptions for the individual preventative formulae. However it was possible to identify commonly used herbs and these are evident in Fig. 2. These data may be useful in the design of a standardised preventative remedy to be used in a clinical trial. Unfortunately it was not possible to explore the viability of using encapsulated herbal products. 11/14 women who took the herbs had to make them into a herbal drink. The recommended dose of 24 g of concentrated herbs per day was a clinically realistic dose but considerably more than the 8 g herbs delivered by using encapsulated powders. 8 g of herbs produces16 × 500 mg capsules/day which may be at the edge of participant compliance. It is possible that many of the benefits experienced by women during the trial could be attributed to the relatively large dose of herbs they were able to take and it is not yet clear whether encapsulated products can deliver the same benefits. Only three women received these products during the study but these too reported positive benefits.

The weaknesses of this study are all too apparent. Without randomisation into parallel treatment arms, allocation concealment and blinding these results are subject to all kinds of bias affecting practitioner and participant that may distort these results. It may be that a substantial proportion of the benefits experienced have little to do with the herbs themselves and more to do with the contextual effects of positive expectation, receiving a treatment, and establishing a strong therapeutic relationship with a practitioner. The extent of these contextual influences and confounders will not become apparent until a blinded RCT has been undertaken.

Recruitment of participants to a CHM practice led to a sample population that is likely to be considerably different to any sample recruited via NHS primary care networks. Several women (6/15) were involved in CAM activities and a pre-study Credibility & Expectation questionnaire [25] showed relatively high mean scores of 7.1 and 7.3 respectively out of a maximum of 10. Expectation has been shown to have an influence on reported outcomes [25] and it is likely that this has some bearing on the extremely positive findings of this study. However, interestingly, the two women who reported the lowest rates of improvement (VAS scores of +2 and +1) both had above average expectations (7.6 and 8) prior to treatment and conversely women with the two lowest expectations (4.3 and 4.7) reported high global improvement of +5/5 and +4/5 respectively. It is clear that the link between expectation and outcome is multi-faceted and far from straightforward.

An alternative interpretation could be that the absence of narrow and rigid inclusion and exclusion criteria in this case series may broaden the relevance of these findings. Although one of the inclusion criteria was being over 18 years of age we included a 17-year old who was particularly desperate for treatment. She responded well to the CHM intervention. We also included a woman with advanced multiple sclerosis who was catheterised and several other women with complex pathologies that would probably have led to their exclusion from a standard clinical trial. This complexity reflects the real world delivery of any form of medicine and it was useful to be able to take this pragmatic approach and investigate and record the potential benefits of CHM for these conditions. These experiences will inform the discussion around inclusion criteria when we design the protocol for a forthcoming RCT.

Finally, as this research reflected routine care, it was not possible to provide paperwork relating to herbal authentication, GMP, or quality control, and a voucher specimen was not provided for each of the herbs used in the study. These would be requirements for a randomised controlled trial and will, in time, hopefully also become standard practice for the provision of any Chinese herbal products.

Conclusion

A prospective case series provided a useful opportunity to introduce case record forms, to assess various outcome measures, to gain an idea of common diagnostic presentations, to assess the safety of CHM, and to explore different treatment strategies. It facilitated the identification of commonly used herbs in the treatment of RUTIs (Fig. 2) and allowed preliminary assessment of a standardised herbal formula for treatment of an acute UTI (Table 1). It is a pragmatic, affordable and highly instructive way to begin to deepen the research process beyond the idiosyncratic realm of the anecdotal report. It has proved to be an important learning experience for the practitioner–researcher who conducted this work and the source of considerable relief to the women who participated in the study. The open nature of the study, the distorting effects of bias, and the lack of any control group severely limit how reliable, precise and generalisable this research is in relation to the effectiveness of CHM for RUTIs. The specific and contextual mechanisms at work in the delivery of CHM remain entwined in their complex, 'real world' embrace. However a case series can make a valuable pragmatic contribution to the 'evidence mosaic' of CHM as an investigation

of a routine practice and as a prelude to more rigorous controlled research.

After initiating this case series the authors of this paper submitted a funding application to the National Institute for Health Research for a 5-year post doctoral project exploring the potential role of CHM for RUTIs. Funding for the project was approved in August 2011 and it commenced in October 2011. This research will involve a systematic review of related literature and clinical trials, the development of professional consensus on good practice, basic science work to explore possible biological mechanisms involved in CHM treatment, and a double blinded randomized controlled feasibility study to investigate the justification for and feasibility of conducting a larger, more definitive trial. The insights gained from this case series will help to inform important aspects of this new research project and ensure that it is grounded in 'real world' clinical experience.

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Conflict of interest

None.

References

[1] Butler CC, Hillier S, Roberts Z, Dunstan F, Howard A, Palmer S. Antibiotic-resistant infections in primary care are symptomatic for longer and increase workload: outcomes for patients with *E. coli* UTIs. British Journal of General Practice 2006;56:686–92.

[2] Little P, Merriman R, Turner S, Rumsby K, Warner G, Lowes JA, Smith H, Hawke C, Leydon G, Mullee M, Moore MV. Presentation, pattern, and natural course of severe symptoms, and role of antibiotics and antibiotic resistance among patients presenting with suspected uncomplicated urinary tract infection in primary care: observational study. British Medical Journal 2010;340:b5633.

[3] Kunin CM. Urinary tract infections in females. Clinical Infectious Disease 1994;18(1):1–10.

[4] Albert X, Huertas I, Pereiró II, Sanfélix J, Gosalbes V, Perrota C. Antibiotics for preventing recurrent urinary tract infection in non-pregnant women. Cochrane Database Systematic Review 2004;(3):CD001209. Review.

[5] Sanford JP. Urinary tract symptoms and infections. Annual Review of Medicine 1975;26:485–9.

[6] Hooton TM, Scholes D, Hughes JP, Winter C, Roberts PL, Stapleton AE, Stergachis A, Stamm WE. A prospective study of risk factors for symptomatic urinary tract infection in young women. New England Journal of Medicine 1996;335(7):468–74.

[7] Falagas ME, Athanasiou S, Iavazzo C, Tokas T, Antsaklis A. Urinary tract infections after pelvic floor gynecological surgery: prevalence and effect of antimicrobial prophylaxis. A systematic review. International Urogynecology Journal of Pelvic Floor Dysfunction 2008;19(8): 1165–72.

[8] Little P, Moore MV, Turner S, Rumsby K, Warner G, Lowes JA, Smith H, Hawke C, Leydon G, Arscott A, Turner D, Mullee M. Effectiveness of five different approaches in management of urinary tract infection: randomised controlled trial. British Medical Journal 2010;340:c19.

[9] Christiaens TC, De Meyere M, Verschraegen G, Peersman W, Heytens S, De Maeseneer JM. Randomised controlled trial of nitrofurantoin versus placebo in the treatment of uncomplicated urinary tract infection in adult women. British Journal of General Practice 2002;52(482):729–34.

[10] Kumarasamy KK, Toleman MA, Walsh TR, Bagaria J, Butt F, Balakrishnan R, Chaudhary U, et al. Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: a molecular, biological, and epidemiological study. Lancet Infectious Diseases 2010;10(9):597–602.

[11] Harding GK, Ronald AR, Nicolle LE, Thomson MJ, Gray GJ. Long-term antimicrobial prophylaxis for recurrent urinary tract infection in women. Review of Infectious Disease 1982;4(2):438–43.

[12] Car J, Sheikh A. Recurrent urinary tract infection in women. British Medical Journal 2003;327(7425):1204.

[13] Jepson RG, Craig JC. Cranberries for preventing urinary tract infections. Cochrane Database of Systematic Reviews 2008;(1), http://dx.doi.org/10.1002/14651858.CD001321.pub4. Art. No.: CD001321.

[14] Car J. Urinary tract infections in women: diagnosis and management in primary care. British Medical Journal 2006;332:94–7.

[15] Maciocia G. The practice of Chinese medicine. London: Churchill Livingstone; 1994.

[16] Xu JF, Liu BH, Cui XM, Sun SL, Yu PJ, Gao RJ, Liu X. Observation on therapeutic effect of clearing heat and dredging stranguria in 103 cases of urinary tract infection. Journal of Traditional Chinese Medicine 1989;9(3):163–5.

[17] Liu P. Care of patients with acute urinary tract infection treated by Chinese herbal drugs Zhonghua Hu Li Za Zhi. Journal of Traditional Chinese Medicine 1987;22(3):116–7.

[18] Zhang M, Zhang D, Xu Y, Duo X, Zhang W. A clinical study on the treatment of urinary infection with Zishen Tongli Jiaonang. Journal of Traditional Chinese Medicine 2005;25(3):182–5.

[19] Zhan YL, Li XY, Wu SX. Clinical observation on effect of compound Shiwei Tablet in treating urinary tract infection. Zhongguo Zhong Xi Yi Jie He Za Zhi 2007;27(3):249–51.

[20] Tang JL, Zhan SY, Ernst E. Review of randomised controlled trials of traditional Chinese medicine. British Medical Journal 1999;319:160–1.

[21] Wang G, Mao B, Xiong ZY, Fan T, Chen XD, Wang L, Liu GJ, Liu J, Guo J, Chang J, Wu TX, Li TQ, CONSORT Group for Traditional Chinese Medicine. The quality of reporting of randomized controlled trials of traditional Chinese medicine: a survey of 13 randomly selected journals from mainland China. Clinical Therapeutics 2007;29:1456–67.

[22] Medical Research Council (MRC). A framework for the development and evaluation of RCTs for complex interventions to improve health. London: MRC; 2008. www.mrc.ac.uk/complexinterventionsguidance.

[23] White A. Conducting and reporting case series and audits—author guidelines for acupuncture in medicine. Acupuncture in Medicine 2005;23:181–7.

[24] Flower A, Lewith G, Little P. Combining rigour with relevance: a novel methodology for testing Chinese herbal medicine. Journal of Ethnopharmacology 2011;134:373–8.

[25] Devilly GJ, Borkovec TD. Psychometric properties of the credibility/expectancy questionnaire. Journal of Behaviour Therapy and Experimental Psychiatry 2000;31(2):73–86.

[26] Paterson C. Measuring outcome in primary care: a patient-generated measure, MYMOP, compared to the SF-36 health survey. British Medical Journal 1996;312:1016–20.

[27] Alraek T, Soedal LI, Fagerheim SU, Digranes A, Baerheim A. Acupuncture treatment in the prevention of uncomplicated recurrent lower urinary tract infections in adult women. American Journal of Public Health 2002 Oct;92(10):1609–11.