7.5 *Treatments that are not recommended*

Oral hydroxyzine does not appear to be an effective treatment for BPS. B

Oral pentosan polysulfate (PPS) does not appear to be an effective treatment for BPS. A

Long-term antibiotics, intravesical resiniferatoxin, intravesical Bacillus Calmette–Guérin, high-pressure long-duration hydrodistension and long-term oral glucocorticoids are therapies that are not recommended for BPS. ✓

One RCT[89] of 31 patients treated with oral hydroxyzine 10–50 mg daily in titrated doses for 3 weeks, then treated on the highest effective dose for 21 weeks was compared with a placebo group. There was no significant response rate in the treatment group (31%) versus the control group (20%).

PPS is thought to repair the damaged glycosaminoglycan layer, which acts as a protective mechanism for the bladder mucosa.[72] An RCT of 368 patients has shown no statistical significance between oral PPS and a placebo.[90] PPS has the adverse effects of diarrhoea, vomiting, rectal bleeding and alopecia. In view of this evidence and the adverse effect profile, PPS is no longer recommended as a treatment of BPS.

Evidence level 1+

Long-term antibiotics should not be used as a treatment option. One RCT[91] reported on 50 patients randomised to receive an 18-week course of antibiotics (rifampicin plus a sequence of doxycycline, erythromycin, metronidazole, clindamycin, amoxicillin and ciprofloxacin for 3 weeks each) or placebo. There was 48% symptomatic improvement in the treatment group and 24% in the placebo group, but this was not significant. Due to the high rate of adverse effects in the treatment group (80%), these are not recommended.

Intravesical resiniferatoxin was evaluated in a systematic review[92] of eight RCTs, but failed to show symptomatic improvement and caused pain, which reduced treatment compliance.

Intravesical Bacillus Calmette–Guérin has been studied in two RCTs[93,94] on 282 patients compared with a placebo. While it may be effective, there are a large number of adverse effects, including arthralgia, headaches and infection.

Evidence level 1–

High-pressure, long-duration hydrodistension with pressures greater than 80–100 cm of water over more than 10 minutes may cause sepsis or bladder rupture. Two observational studies[95,96] showed a wide range of efficacy rates between 22% and 67%, with at least one case of bladder rupture in each study. The risks of this treatment far outweigh the benefits.

Evidence level 3

Long-term oral glucocorticoid administration is not recommended due to its long-term adverse effect profile.[97,98]

Evidence level 4

8. Further management (see Appendix IV)

8.1 *Who should manage BPS?*

History, urinalysis and physical examination should be carried out in primary care. ✓

In primary care, a careful history should be taken enquiring about type, duration and location of pain, urinary symptoms and QoL. Primary care should also check that all conservative measures have been taken. A urine dipstick or midstream specimen of urine is recommended to rule out a UTI. An abdominal and vaginal examination may be performed to assess for tenderness, abdominal masses and urinary retention. Patients should be commenced on first-line conservative treatments, such as analgesia, stress relief, dietary modification, exercise and physical therapy, and if these fail to resolve or improve symptoms, a referral to secondary care should be considered. It is expected that these conservative measures may take between 3 and 6 months to improve symptoms. Referral to a urogynaecologist or urologist with a special interest in BPS would be preferable rather than a general gynaecologist when the main symptoms are pelvic pain and urinary in character.

Evidence level 4

8.2 *Who should be referred to secondary care?*

Patients who fail to respond to conservative treatment should be referred to secondary care. ✓

Patients should be referred to secondary care after 3–6 months of conservative management if symptoms persist.

8.3 *What is the role of the MDT – physiotherapist, pain team, clinical psychologist?*

Referral to a physiotherapist should be considered as BPS symptoms may be improved with physical therapy. B

Consider referring patients with refractory BPS for psychological support or counselling if it is impacting on their QoL or the patient requests a referral. ✓

Patients with refractory BPS should be referred to an MDT in order to explore alternative treatment options. Those patients who may benefit from neuromodulation should be referred to an MDT before treatment is commenced. ✓

An electronic questionnaire[42] revealed that 74.2% of patients experienced symptomatic improvement with massage therapy, 61.5% with physical therapy and 66.1% through physical therapy with internal treatment. Internal massage releases the pelvic floor from painful trigger points and areas of myofascial tenderness or restriction. A randomised study[99] of 10 scheduled treatments of myofascial physical therapy versus global therapeutic massage on 81 women showed a reduction in pain, frequency and urgency in both groups with no significant difference in therapies.

Evidence level 1–

Some patients benefit from speaking to a counsellor or clinical psychologist and engaging in behavioural therapy to modify their lifestyles and improve their QoL.

Referral to a pain clinic or clinical psychologist may need to be considered if conservative and oral treatments have failed. This should be considered before commencing intravesical treatments.

8.4 *What is the role of support groups?*

Patients should be given written information about patient organisations that provide evidence-based information. ✓

Support groups provide a platform to share experiences, exchange information, raise awareness and promote patient self-help management.

There are many patient organisations that may help patients to find relevant information (see section 12).

9. Long-term management and prognosis

9.1 *What should be the duration of follow-up?*

Patients should be followed up periodically in secondary care with consideration for shared care between the pain team and urogynaecology until symptoms become controlled and then they can be followed in primary care if required. ✓

It is difficult to estimate a finite time for follow-up as it is often difficult to achieve symptomatic control to an extent where the patient may be happy, so individualised management plans need to take into consideration response to treatment, effects on QoL and other existing comorbidities.

9.2 *BPS and pregnancy*

Woman can be advised that the effect of pregnancy on the severity of BPS symptoms can be variable. ✓

BPS treatment options considered safe in pregnancy include oral amitriptyline and intravesical heparin. ✓

Although one course of DMSO may be used prior to pregnancy for symptom remission with good pregnancy outcomes (delivery at term, normal birth weight and postnatal symptom control), DMSO is known to be teratogenic in animal studies. D

There is little published information about the changes in symptoms that may occur during pregnancy.[100] The IC Association conducted a patient survey about symptoms and pregnancy in 1989, where patients who described their symptoms as 'mild' experienced worsening symptoms during pregnancy, which persisted up to 6 months after delivery. In contrast, patients who described their symptoms as 'severe' had a significant improvement in symptoms during the second trimester, which lasted up to 6 months after delivery or for the duration of breastfeeding. BPS was not affected by the mode of delivery. Another study[101] found that only 7% of patients stated that their BPS symptoms had improved during pregnancy. Evidence level 3

Of the commonly used oral treatments, amitriptyline has the lowest risks in pregnancy.[100] Heparin is the safest intravesical treatment because it is unlikely to be absorbed from the bladder or to cross the placenta and is not excreted in breast milk. Lidocaine does cross the placenta and there is no information about the safety of chronic exposure to the fetus. Systemic corticosteroids are not known to Evidence level 4

have teratogenic effects,[102,103] but the possibility of long-term effects on the hypothalamic–pituitary–ovarian axis cannot be excluded. The absorption of intravesical corticosteroids is unknown. Sacral nerve stimulators should not be placed during pregnancy and, if already present, should be turned off for the duration of pregnancy as the effect on the fetus is unknown.[104]

In a few cases, multiple members of the same family have BPS. This suggests that some patients may have a genetic predisposition, however, there is no documented evidence for this. Unless the pregnant patient belongs to a family that has multiple members with the condition, she can be reassured that the risk for passing it on to her child is low.[100]

Evidence level 4

A prospective study[105] included 12 patients who had a course of DMSO (every 2 weeks for 12 weeks) and all had symptom remission. Pregnancy occurred 6 months to 5 years after the DMSO treatment. Nine patients continued to have good symptom remission throughout pregnancy. The other three had worsening symptoms and two patients terminated the pregnancy because of severe symptoms. Because this small group of patients was more homogeneous than the general BPS population, with all patients having chronic inflammation on bladder biopsy and good remission after DMSO, it is unclear how the results of this study apply to the general BPS population. DMSO is known to be teratogenic in animal studies and has a US Food and Drug Administration rating of grade C, which states there are no adequate human studies, but animal studies show an increased risk or have not been done.[100] In view of this, DMSO should be avoided in pregnancy.

Evidence level 3

10. Recommendations for future research

- Create a single, standardised, validated assessment questionnaire.
- Decide on patient-related outcome measures for BPS.
- Assess the role of conservative treatment, e.g. analgesia, dietary modification and stress management (section 7.1), versus placebo for BPS.
- Assess the role of the clinical psychologist.
- Assess the number of patients with coexisting conditions.
- Assess the therapeutic and cost effectiveness of complementary therapies, such as acupuncture, with robustly conducted randomised clinical trials.

11. Auditable topics

- Proportion of patients with BPS symptoms who receive initial conservative treatments in primary care (100%).
- Proportion of patients with BPS who complete a bladder diary for diagnosis (100%).

12. Useful links and support groups

The following organisations provide support for BPS:

- Cystitis and Overactive Bladder Foundation [http://www.cobfoundation.org].
- Pelvic Pain Support Network [http://www.pelvicpain.org.uk].
- International Painful Bladder Foundation [http://www.painful-bladder.org].
- Urostomy Association [http://www.urostomyassociation.org.uk].

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