IN-DEPTH REVIEWS

Treatment of Brachioradial Pruritus: A Systematic Review

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ABSTRACT

Importance: Brachioradial pruritus (BRP) is a poorly understood disease and can severely impact quality of life. However, there is currently no clear treatment.
Objective: To identify effective behavioral, topical, oral, and invasive treatment options for BRP, and to discuss the quality of the data currently found in the literature.
Evidence Review: The PubMed and CINAHL databases were systematically reviewed for articles from 1968 to the present containing search terms "brachioradial OR solar OR forearm AND pruritus OR itching." Results were narrowed to articles written in English, focusing specifically on BRP, and that stated precise treatment modalities. Evidence quality was determined using the Oxford Centre for Evidence-Based Medicine Criteria based on the study type.
Findings: Thirty-six articles discussing treatments for BRP are included in this review with a total 399 patients. Six studies (n=68) report on the efficacy of capsaicin cream, eight studies (n=26) on oral gabapentin 300 mg daily to six times daily and four studies (n=98) on sun protection. The remaining articles comprise of low-quality, small-scale studies on further oral medications, physical therapy, minimally-invasive procedures, and surgery.
Conclusions and Relevance: Low-quality evidence supports the use of sun protection, topical capsaicin, or oral gabapentin as effective therapeutic modalities for BRP. Clinicians should be aware of possible underlying cervical spine pathology and include thorough imaging as part of BRP work-up. Further high-quality studies on BRP treatments would help elucidate clear management for this disorder.

INTRODUCTION

Brachioradial pruritus (BRP) is an uncommon disorder first described in the late 1960s as "pruritus of the upper extremities."[1] While originally thought to be caused by excessive sunlight exposure, later reports demonstrate a neuropathic component.[2,3] Due to uncertain pathology, a wide variety of treatment options have been trialed. Over 50 years later, there is still no clear therapeutic modality for BRP.

BRP occurs with higher prevalence in women (72% to 87.4%) and patients with fair skin tones (52% to 86%). Patients present over a wide age range from 12 to 84 years, however the fifth decade is the average age at diagnosis.[4–7] BRP is described as pruritus, tingling and/or stinging on unilateral or

bilateral dorsolateral aspect(s) of the upper extremity(ies) without overt cutaneous findings, and may spread to the upper torso.[5,8] Disease etiology includes local neurocutaneous damage from ultraviolet (UV) radiation and/or cervical spinal nerve injury.[2,3,8] Retrospective studies demonstrate 34.1% to 77% of patients have worsening symptoms in summer, 48.6% to 59% note exacerbation after sun exposure, and 30% to 80.5% have cervical spine abnormalities.[3–7] While BRP appears to be a benign disease, it causes significant impairment in patient quality of life (QOL).[6,7,9] Typical pruritus treatments, such as corticosteroids or antihistamines, are unsuccessful in treating BRP. Current BRP treatments focus on preventing sun exposure or addressing potential neuropathic aspects, however, many lack efficacy. In this systematic review, we evaluate the literature surrounding BRP, and aim to answer the question: what is the most effective treatment for BRP?

METHODS

A systematic literature search was performed using PubMed and CINAHL databases with search terms “brachioradial AND pruritus OR itching,” “solar AND pruritus OR itching,” and “forearm AND pruritus OR itching” in August 2018. All clinical trials, observational studies, case series, case reports, and commentaries from 1968 to the present were included. Exclusion criteria consisted of articles that were in a language other than English, articles that did not state a clear, effective treatment modality for each case of BRP, or articles that did not distinguish an effective treatment for BRP from other forms of neuropathic itch (notalgia paresthetica, post-herpetic neuralgia, *etc.*). The evidence quality level for each study was determined using the Oxford Centre for Evidence-Based Medicine Criteria.

RESULTS

In total, 169 individual articles were screened. After exclusion criteria, 36 articles were reviewed consisting of one randomized clinical trial (RCT), five prospective cohort studies, eight retrospective studies, seven case series, fourteen case reports, and one commentary. After removing duplicate data (Pinto *et al.*/Waccholz *et al*. and Pereira *et al*./Stienke *et al*.), 399 patients with BRP were included.[4,9–11] Given that most data on BRP treatment comes from case series and reports, the overall quality of the evidence reviewed is low (Table 1-4).

Pharmacological treatments

Topical medications

Topical therapies, specifically capsaicin, are typically first-line treatment for BRP. Six studies (one RCT, one prospective cohort study, one retrospective study, two case series, and one case report), address the effectiveness of capsaicin 0.025% to 0.1% cream for BRP (n=68).[5,12–16] In the RCT, thirteen patients with bilateral BRP were treated with capsaicin cream 0.025% to one arm and placebo cream to the other five times daily for one week, then three times daily for four weeks. Capsaicin was not significantly more effective than placebo, with both demonstrating over 60% pruritus resolution.[12] A non-blinded trial of capsaicin cream 0.025% to one arm four times daily compared to no treatment of the second arm (n=15) showed a 76% reduction in pruritus by capsaicin after three weeks.[13] While many case reports note improvement in symptoms with topical capsaicin, they describe an unpleasant burning sensation and a

recurrence of symptoms after treatment is discontinued.[13–16]

Capsaicin 8% patch is another treatment option for BRP. Two prospective cohort studies and one case series (n=30), have reported on its effective use in BRP after one hour of application.[9,11,17] One study described an 85% reduction in itch as soon as three weeks post-treatment and lasting three months, while two others reported a statistically significant decrease in pruritus six months after treatment .[17,9,11] While 27% of patients require another patch applied at three months, and 13.7% another at six months, all patients noted a significant improvement in QOL.[9,11] Side effects include intense burning, which can be mitigated by pre-treatment with topical lidocaine.[17]

Other topicals studied for BRP include amitriptyline 1%/ketamine 0.5% cream, topical steroids, doxepin cream and local anesthetics. One retrospective study and one case report described topical amitriptyline 1%/ketamine 0.5% for BRP (n=12). Complete resolution of pruritus was noted in 33.3% of patients with daily use, while 25% noted only improvement.[5,18] Historically, topical steroids such as hydrocortisone, triamcinolone, and fluocinonide have been tried for BRP without much success.[1,5,6,15,16,19,20] The use of topical steroids, doxepin cream, and local anesthetics has been described in one retrospective study. Of patients treated with topical steroids (n=22), 18% noted complete resolution of symptoms and 27% reported improvement. In the same study nine patients were treated with doxepin cream with 22% describing complete resolution and another 22% noting some improvement. As for topical anesthetics (n=42), no patients reported complete resolution of symptoms with pramocaine cream or lidocaine patches, and only 12.5% noted some improvement with pramocaine.[5]

Systemic Medications

Oral medications used for BRP include anticonvulsants, antidepressants, antipsychotics, neurokinin (NK)-1 receptor inhibitors, non-steroidal anti-inflammatory drugs (NSAIDs), and antihistamines. The most commonly cited oral medication for BRP treatment is gabapentin with eight articles (three retrospective studies, one case series, four case reports; n=26) reporting on gabapentin efficacy.[4,5,10,19,21–24] Effective doses range from 300 mg once daily to six times daily.[19,21–23] However, side effects such as sedation and gastrointestinal upset may limit the upper limit of dosing in some patients.[22] Retrospective studies note complete resolution of BRP in 20% to 42% of patients, while partial symptomatic control was achieved in 20% to 28.5%.[5,10]

Other anticonvulsants used for BRP include pregabalin, lamotrigine, and carbamazepine.[5,25,26] One prospective study and one case report (n=4) noted improvement in pruritus with pregabalin. Seventy-five percent of patients attained complete resolution with 75 mg pregabalin twice daily, while 25% required 225 mg daily.[26,27] In one case, lamotrigine 200 mg daily produced symptomatic resolution.[25] Similarly, in another case, carbamazepine demonstrated symptomatic improvement, however no dose was reported.[5]

Antidepressants, such as amitriptyline, doxepin and fluoxetine, and antipsychotics, such as risperidone, pimozide and chlorpromazine, have occasionally been used to treat BRP.[4,5,10] Two retrospective studies (n=53) noted these medications have a similar effect as gabapentin, with a majority

of patients noting either “excellent” or “good” reduction in pruritus. Unfortunately, no doses were reported.[4,10]

Antihistamines and NSAIDs are rarely prescribed for BRP. While antihistamines are classically thought to be anti-pruritic, they are typically ineffective in BRP. [1,6,15,16] Only 10% of patients prescribed antihistamines note some improvement in pruritus (n=10).[5] In cases of cervical-pathology related BRP, successful treatment has been noted with NSAIDs, with and without a combination of physical therapy (n=5).[20,28,29] One patient noted improved pruritus in as little as three days after daily 100 mg oral ketoprofen.[29]

A novel medication being used in BRP is the NK-1 receptor antagonist, aprepitant. In a case of recalcitrant BRP, oral aprepitant 80 mg daily gave symptomatic improvement. However, symptoms returned after treatment cessation and were not as well-controlled after a second course of medication.[30]

Procedural treatments

Invasive treatments have been tried for refractory BRP or those with clear cervical spine pathology.[28,31–34] One case noted dramatic improvement with botulinum toxin (100 IU total) injected at 1.5 cm intervals over the symptomatic area every five to six months.[31] Similarly, epidural steroid injections in four patients gave 75% of patients lasting relief from pruritus after one injection, while 25% required multiple injections to gain long-term relief. [33,35] A case of BRP associated with spinal cord injury was treated with stellate ganglion catheter placement and ropivacaine infusion, achieving partial pruritus relief. Side effects including upper extremity temperature change, piloerection, and conjunctival injection were noted.[34]

Surgical treatment of BRP is reserved for cases with correctable cervical pathology. For example, one case of BRP was secondary to a cervical rib. Of note, surgery was not pursued until additional neurological symptoms, including paresthesia and restricted range of motion, were noted in the BRP-affected arm.[28]

Non-pharmacological treatments

Behavioral intervention

Initially BRP was only described in patients with excessive sun exposure, and treatments were directed at sun avoidance and protection.[1] Four articles (one retrospective study, one case series, one case report, and one commentary; n=98), report on the effectiveness of long-sleeve clothing for BRP.[1,7,36,37] High sun protection factor (SPF) sunscreens were effective in two studies for relieving pruritus (n=58).[7,37] Sun protection relieves pruritus in as little as four weeks, and can provide continuing relief if behavioral modification is sustained.[7,37]

Physical therapy

In the 1980s, the role of nerve damage in BRP was first reported.[20] Three retrospective studies and one case series (n=22), report cervical physical therapy or cervical traction and/or manipulation as effective treatment for BRP.[5,20,28,38] In one case series, all patients (n=5) with cervical degenerative changes and BRP had improvement in pruritus with either physical therapy, cervical traction and/or manipulation.[20] Another study demonstrated that cervical spine manipulation resolved pruritus from two days up to permanently in 100% of patients with a history of neck problems (n=6), and 50% of patients with no neck problems (n=8).[38] A further case series (n=3) noted a reduced

number of patients (33%) with pruritus resolution after cervical physical therapy when the cervical pathology was unknown.[5]

Cutaneous field stimulation or acupuncture

One prospective study (n=9) using cutaneous field stimulation, daily electrical stimulation of pruritic skin patches, on BRP patients demonstrated effectiveness at reducing pruritus intensity in all patients. However, symptoms returned for 88.9% of patients 3 to 12 months after treatment.[39] Similarly, one retrospective study (n=10) described the use of acupuncture in BRP, and found all patients achieved relief of pruritus with deep cervical paravertebral muscle stimulation. Again, 40% demonstrated symptomatic relapse 1 to 12 months later.[40]

DISCUSSION

While a wide variety of therapeutic modalities have been tried for BRP, many have not been studied in large-scale RCTs. There is no strong consensus on the most effective treatment – for instance, in one retrospective study, 19 different treatment modalities had been tried on BRP patients over ten years, with 54% of patients being prescribed more than one therapy. Only 12% of patients reported complete resolution of pruritus with treatment.[5]

This shot-gun approach to BRP treatment may be related to the disorder's ambiguous etiology. BRP pathogenesis is most likely multifactorial, involving UV-induced neurocutaneous damage and cervical radiculopathy.[3,41] In a prospective cohort study, patients with BRP have significantly reduced levels of calcitonin gene-related protein (a sensory nerve marker) and total number of intraepithelial nerve fibers in symptomatic skin. These findings are similar to findings after serial phototherapy, which is consistent with the hypothesis that prolonged UV damage plays a role in the development of BRP.[41] However, another prospective study reported a significant relationship between cervical stenosis and nerve compression, as seen by MRI, correlating to dermatomal pruritus in BRP.[3]

Although many cases of BRP do not have a clear cause, cervical pathology is noted frequently enough to recommend that patients follow with a neurologist and cervical imaging is performed. Similarly, if cervical pathology is noted, physical therapy or other non-pharmacologic options may be useful with or without the addition of further medications. While evidence supporting the effectiveness of sun protection in BRP is low, dermatologic benefits associated with sun avoidance are such that it is worth advising patients to add protection to their treatment regimen.

Current treatments focus on blockade of nerve sensation at the local or systemic level. Unmyelinated C-fibers play a prominent role transmitting epidermal itch sensation through thermosensors, which modulate itch, heat, and pain, as well as the NK-1 receptor which binds substance P.[42,43] Capsaicin modulates the itch pathway by depleting substance P and regulating thermosensor expression.[44] Further upstream, modulation of excitatory neurotransmitters with gabapentin can change itch perception through afferent neuron signal transmission and central hypersensitivity.[45]

Of the topical treatments reviewed, capsaicin has the most evidence supporting its use in BRP. While the only RCT on topical capsaicin cream demonstrated no significant improvement in pruritus versus placebo,

difficulty blinding capsaicin's burning sensation may have limited study quality. It would be beneficial to repeat this study with placebo cream that better mimics capsaicin's side effects. The capsaicin patch is an appealing alternative, given the need for less frequent application.

Topical amitriptyline/ketamine cream may also be a promising treatment option, however large-scale studies are needed to determine its true effectiveness and long-term adverse effects.

Oral gabapentin is the most commonly discussed systemic treatment. Gabapentin inhibits calcium ion channels on afferent neurons thus preventing excitatory neurotransmitter release.[45] Evidence for gabapentin's use in BRP is low given the lack of RCTs and prospective studies. While anecdotally, it seems to be an effective medication, high doses are required to provide symptomatic relief. Side effects, such as sedation and gastrointestinal upset, may prevent its use by patients.[22] Pregabalin may be a useful alternative for BRP, however there is a paucity of high-quality evidence for its use as well.

Some antidepressants (amitriptyline, doxepin, fluoxetine) and antipsychotics (risperidone, pimozide) can be equally as effective as gabapentin in treating BRP, and may provide an affordable option for patients.[10] Duloxetine and mirtazapine have been used for the treatment of neuropathic pruritus, however large-scale RCTs using antidepressants and/or antipsychotics in BRP have not been done.[46,47] Aprepitant, an NK-1 receptor antagonist originally approved for the prevention of chemotherapy-induced nausea and vomiting, has also been reported to be effective in chronic pruritides.[30,48] Anecdotal evidence demonstrates effect in BRP, however more studies are needed to support this medication.[30]

Invasive treatment is appropriate when there is clear cervical pathology for BRP. Epidural steroid injections improve C-fiber functionality and provide long-term symptomatic control in BRP.[35] Surgical treatment is appropriate with underlying correctable cervical spine pathology.[8] Even then, surgical treatment is considered as a last option and is not typically pursued unless additional neurological symptoms, such as weakness, paresthesia or pain, are present.[28,49] It is important to carefully consider risks and benefits of invasive treatment options given the lack of high-quality evidence, and thoroughly counsel patients before attempting these modalities.

Limitations to this review include the current lack of RCTs and high-quality prospective studies investigating therapies for BRP. Although many medications show promise, their use is supported by small studies, case series and case reports. While ideally more studies should be performed to better assess efficacy and adverse events of existing treatment modalities, new therapies are currently being developed that may benefit BRP patients. Modulators of the protease pathway, such as nafamostat mesillate and tetracyclines, target protease-activated receptor (PAR)-2 and modulate the cowhage itch pathway. Cannabinoids target vanilloids, impacting itch perception. Furthermore, future therapies may target centrally and effect dorsal root ganglion molecules.[50]

CONCLUSION

BRP is an uncommon disorder that can have a large impact on patient QOL and morbidity. Currently there are no clear, effective treatment choices. It is important that

clinicians are aware of possible underlying cervical spine etiology, and disease follow-up should include thorough imaging work-up for cervical spine abnormalities. Review of the literature demonstrates low-quality evidence supporting sun protection, physical therapy, topical capsaicin cream (0.025% to 0.1%) and patch (8%), as well as oral gabapentin (300 mg daily to six times daily) as effective therapeutic modalities. Many other medications such as topical steroids, antihistamines and anesthetics, as well as oral antihistamines, antidepressants, antipsychotics and NSAIDs have anecdotally been reported to improve symptoms of BRP. Novel treatments such as NK-1 receptors are being investigated for use in BRP.

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Table 1. Summary of articles describing topical treatment options for BRP.

Author (year)	Study type (quality)	No. of patients	Patient characteristics	Treatment	Study results
Pereira *et al.*[11] (2018)	Prospective cohort study (2)	29	65.5% F Mean age 61.5 y/o 86.2% with cervical spine abnormalities on MRI, decreased intraepidermal nerve fiber density	8% capsaicin patch applied for 1 hr (1 hr pretreatment with topical lidocaine) 8 patients needed reapplication at 3 mo and 4 patients at 6 mo 6 mo F/U	Pruritus significantly decreased at 3 wk, 3 mo, and 6 mo Significant improvement in quality of life
Steinke *et al.*[9] (2017)	Prospective cohort study (2)	25	75% F Mean age 61.3 y/o Mean disease duration 16.9 mo	8% capsaicin patch applied to the pruritic area for 1 hr Repeat patch application at 3 mo and 6 mo if symptomatic 6 mo F/U	Pruritus significantly decreased Quality of life significantly improved
Zeidler *et al.*[17] (2015)	Case series (4)	5	80% F Age range 54-69 y/o C5-C6 dermatomal pruritus Reduced intraepidermal nerve fiber density on punch biopsy	8% capsaicin patch for 1 hr (1 hr pretreatment with topical lidocaine) 3 mo F/U	85% reduction in itch after 3 wk and 3 mo
Poterucha *et al.*[18] (2013)	Case report (5)	1	41y/o M R arm pruritus, summer exacerbations progressed to year-round C3 and C5 narrowed interspaces on radiography	1% amitriptyline/0.5% ketamine cream applied 2-3 times/d 4 yr F/U	Complete pruritus relief
Lane *et al.*[16] (2008)	Case report (5)	1	46 y/o F L arm pruritus, no seasonal variation, hx of C4-C6 discectomy with	Topical capsaicin cream (dose N/A, F/U time N/A)	Moderate pruritus relief

			osteophytes on MRI		
Barry and Rogers[14] (2004)	Case series (4)	7	57.1% F with b/l arm pruritus 42.9% exacerbation in sunlight 57.1% with cervical spine disease	0.025% capsaicin cream 4 times/d 8 wk F/U 25 mg/d amitriptyline if no response to capsaicin	57.1% with significant improvement in pruritus after 6-8 wk with topical capsaicin 28.6% with no relief from capsaicin but relief with amitriptyline
Wallengren[12] (1998)	Double-blind randomized, controlled trial (1)	13	69.2% F Average age 52 y/o 100% with b/l arm pruritus 92.3% with seasonal variation (worse in summer)	0.025% capsaicin cream applied to one arm 5 times/d for 1 wk, then 3 times/d for 4 wk Placebo cream applied to the other arm	Capsaicin cream reduced itch by 63.1 +/- 2% Placebo cream reduced itch by 65.5% +/- 2.9% 84.6% had recurrent of symptoms the following summer
Knight and Hayashi[13] (1994)	Prospective cohort study (2)	15	50% F Majority age 30-49 y/o 100% b/l arm pruritus No seasonal variation in symptoms No report of cervical spine abnormalities	0.25% capsaicin cream to one arm 4 times/d for 3 wk Other arm left untreated as control	76% noted significant decrease in pruritus after 3 wk 2 patients dropped out due to intolerable burning sensation 6 patients had recurrence of pruritus 1 wk-7 mo later
Goodless *et al.*[15] (1993)	Case series (4)	2	<u>Patient 1</u> 60 y/o M B/l arm pruritus, chronic sun exposure, hx of rheumatoid arthritis	<u>Patient 1</u> 0.033% capsaicin cream4-5 times/d for 2 wk 4 mo F/U	<u>Patient 1</u> Pruritus resolved in 2 wk

			Patient 2 50 y/o F B/l arm pruritus, hx of MVA	Patient 2 0.1% capsaicin cream used 4-5 times/d for 2 wk 4 mo F/U	Patient 2: Pruritus resolved in 2 wk

Table 2. Summary of articles describing systemic treatment options for BRP.

Author (year)	Study type (quality)	Number of patients	Patient characteristics	Treatment	Study results
Atis and Kaya[26] (2017)	Prospective cohort study (2)	3	100% F with b/l arm pruritus No seasonal variation No x-ray or MRI abnormalities in cervical spine	75 mg pregabalin BID for 1 wk, reduced to 100mg daily for 1 mo 2 mo F/U	66.6% with complete resolution of pruritus 33.3% needed 225mg pregabalin daily to reach complete resolution
Wachholz *et al.*[10] (2017)	Retrospective study (3)	49	73.5% F Mean age 58 y/o 81.6% Caucasian	Oral amitriptyline, doxepin, gabapentin, risperidone, pimozide, fluoxetine, chlorpromazine, and hydroxyzine prescribed for BRP for any period of time between 2011-2014 Average 36 mo F/U	38.8% patients reported excellent reduction in pruritus (gabapentin, amitriptyline, doxepin, risperidone, pimozide) Best reduction noted with higher intensity pruritus and longer therapy period
Pinto *et al.*[4] (2016)	Retrospective study (3)	49	73% F Mean age 56.1 y/o 77.6% b/l arm pruritus 59.2% exacerbated with sun exposure 61.2% narrowing of cervical intervertebral spaces	Oral tricyclic antidepressants (TCAs), doxepin, antipsychotics, anticonvulsants, serotonin reuptake inhibitors (SSRIs) and antihistamines prescribed for any period of time for BRP between 2011 and 2014 Average 35 mo F/U	59.2% of patients treated with monotherapy 33.3% used TCAs, 22.8% doxepin, 18.1% antipsychotics, 10.6% anticonvulsants, 6.1% SSRIs 79.2% with treatment effectiveness “very good” or “good”

Vestita *et al.*[27] (2016)	Case report (5)	1	47 y/o F R arm pruritus, worse in summer R C6-C7 disc herniation and C4-C7 arthrosis	75 mg pregabalin BID for 90 d Physiotherapy with cervical traction 10 mo F/U	Resolution of pruritus in 15 days Continued relief at F/U
Carvalho *et al.*[19] (2015)	Case report (5)	1	60 y/o F R arm pruritus, no seasonal variation C6-C7 nerve compression	900 mg/d gabapentin indefinitely 3 mo F/U	Significant control of pruritus
Ally *et al.*[30] (2013)	Case report (5)	1	61 y/o F B/l arm pruritus, seasonal exacerbations C4-C6 foraminal stenosis	80 mg/d aprepitant for 7 d, followed by 80 mg/d for 14 d after relapse 48hrs off medication 6 wk F/U	Significant improvement after 7 d course with relapse 48hrs after d/c Some improvement in pruritus after 14 d course, but not well controlled
Mirzoyev *et al.*[5] (2013)	Retrospective study (3)	111	72% F Mean age 59 y/o 75.7% b/l arm pruritus 45.9% seasonal exacerbations 33% with cervical abnormalities on imaging	Topical treatments (capsaicin, triamcinolone, pramocaine, doxepin, amitriptyline/ketamine, hydrocortisone, lidocaine, fluocinonide) and oral treatments (gabapentin, pregabalin, carbamazepine, oxymetazoline, cetirizine, hydroxyzine, diphenhydramine, allegra, desloratadine), and physical therapy prescribed for BRP for any period of time between 1999-2011 Average 18.5 mo F/U	75 patients completed F/U 9 had complete resolution (amitriptyline-ketamine cream, topical capsaicin, topical doxepin) 13 had improvement (topical capsaicin, triamcinolone, carbamazepine, gabapentin, topical doxepin)
Yilmaz *et al.*[24] (2010)	Case report (5)	1	64 y/o M	300 mg/d gabapentin indefinitely	Markedly reduced pruritus at 4 wks

			R arm pruritus, no seasonal variation MRI with right foraminal stenosis at C4-C5 and C6/C7 disc protrusion	1 yr F/U	with complete resolution by 4 mo Recurrence of pruritus if treatment interrupted
Crevits[25] (2006)	Case report (5)	1	54 y/o F R arm pruritus followed by L arm pruritus after L shoulder injury MRI with midcervical spondylosis	1st course: 200 mg/d lamotrigine for 18 mo 2nd course: 100 mg/d lamotrigine for 8 wks 3 yr F/U	Complete resolution of R arm pruritus while on lamotrigine and for 6 mo after d/c treatment, at which time a L shoulder injury precipitated L arm pruritus, resolved with 100 mg/d lamotrigine No recurrence after d/c 2nd course
Kanitakis[22] (2006)	Case report (5)	1	54 y/o M B/l arm pruritus, no seasonal variation or relation to sun exposure X-ray with cervical arthrosis of C5-C7	400 mg gabapentin TID for 2 mo, 600 mg TID for 4 mo, 1200 mg/d to 600 mg/d for 2 mo 8-9 mo F/U	Some improvement with gabapentin at 400 mg TID Significant symptomatic improvement with the addition of topical 8% calamine and essential fatty acid cream Side effect at 600 mg TID: sedation and diarrhea Recurrence of pruritus after gabapentin d/c
Winhoven *et al.*[21] (2004)	Case series (4)	2	<u>Patient 1</u> 67 y/o F B/l arm pruritus, no seasonal variation	<u>Patient 1</u> 300 mg gabapentin TID, then transitioned to 300 mg/d indefinitely F/U time N/A	<u>Patient 1</u> Significant relief with TID and daily dosing

			X-ray with moderate degenerative changes from C4 downwards Patient 2 51 y/o F B/l arm pruritus X-ray with b/l cervical ribs and degenerative changes at C5-C6	Patient 2 300mg gabapentin TID indefinitely F/U time N/A	Patient 2 Significant relief
Bueller *et al.*[23] (1999)	Case report (5)	1	54 y/o F L arm pruritus, initially worse in summer, then became year-round, exacerbated with sunlight MRI with left and central bony ridging at C5-C6	300 mg gabapentin 6 times/d indefinitely 4 mo F/U	Complete resolution of symptoms
Abbot[29] (1998)	Case report (5)	1	74 y/o M L arm pruritus X-ray with cervical foraminal narrowing at C2-C7	100 mg/d ketoprofen for 3 d F/U time N/A	Patient noted complete improvement in pruritus Sporadic recurrent episodes of pruritus since treatment

Table 3. Summary of articles describing procedural interventions for the treatment of BRP.

Author (year)	Study type (quality)	Number of patients	Patient characteristics	Treatment	Study results
Weinberg *et al.*[33] (2018)	Case series (4)	3	100% F Average 66 y/o B/l arm pruritus 100% with foraminal stenosis on cervical imaging	CT-guided epidural injection of 2:1:1 ratio dexamethasone, bupivacaine, and lidocaine Repeat injections at 3 mo and 6 mo after initial injection	Patient 1 Complete resolution of symptoms after 1 injection Patient 2 Near complete resolution after 1 injection and oral

				Patient 1 – 2 mo F/U Patient 2 – 3 mo F/U Patient 3 – 15 mo F/U	pregabalin indefinitely Patient 3 Complete resolution of pruritus after 3 injections and oral mexiletine indefinitely
Kavanagh and Tidman[31] (2012)	Case report (5)	1	59 y/o F B/l arm pruritus, no report of seasonal variation No cervical abnormalities	10 uL botulinum A toxin (100 IU/3mL saline total) injections at 1.5 cm intervals over symptomatic area every 5-6 mo 2 yr F/U	Significant relief Recurrence 5-6 mo after treatment
De Ridder *et al.*[35] (2010)	Case report (5)	1	56 y/o M L arm pruritus MRI showing foraminal stenosis at L C4-C5 and b/l C5-C6	Fluoroscopically-guided injection of 80 mg methylprednisolone and 40 mg lidocaine at C6 and C8 midline 6 mo F/U	Improved pruritus, continued relief
Crane *et al.*[34] (2009)	Case report (5)	1	18 y/o F L arm pruritus Traumatic spinal cord injury at C6	Stellate ganglion block with ropivacaine, then stellate ganglion catheter with ropivacaine infusion 34 mo F/U	Block with 2 d pruritus relief Catheter placement with 4 wk relief and return of pruritus at milder severity
Rongioletti[28] (1992)	Case series (4)	2	Patient 1 22 y/o M Year-round L arm pruritus C7 transverse process hypertrophy on x-ray Patient 2 58 y/o F Year-round left arm pruritus Supernumerary short cervical rib	Diclofenac (dose N/A) and cervical physical therapy for both patients for 1.5 wk Surgical resection of cervical rib in patient 2 after development of cervico-brachialgia, paresthesias, and restricted motion 6 mo after physical therapy 6 mo F/U	Patient 1 Improvement in pruritus, continued relief after therapy Patient 2 Improvement in pruritus, Total resolution of pruritus post-surgery

Table 4. Summary of articles describing behavioral changes for the treatment of BRP.

Author (year)	Study type (quality)	Number of patients	Patient characteristics	Treatment	Study results
Veien and Laurberg[7] (2011)	Retrospective study (3)	95	87% F Median age 55 y/o 83% b/l arm pruritus 82% seasonal variation 17% year-round symptoms 38.9% cervical foraminal narrowing on imaging	Sun protection (clothing or SPF50+ sunscreen) 3 yr F/U	Pruritus resolved in 40 of 45 (88.9%) with seasonal symptoms and 4 of 5 (80%) with year-round symptoms
Armstrong *et al.*[37] (1997)	Case report (5)	1	47 y/o M B/l arm pruritus, worse in summer, exacerbated by sunlight No cervical spine abnormalities	Sun avoidance (close-knit clothing and high-factor sunscreen) 4 wk F/U	Pruritus resolved in 4 wks
Orton *et al.*[36] (1996)	Case series (4)	2	<u>Patient 1</u> 57 y/o M B/l arm pruritus, no seasonal variation Cervical spondylosis <u>Patient 2</u> 48 y/o M L arm pruritus, no seasonal variation, history of tanning bed use No cervical abnormalities	Sun avoidance (long sleeve, close-knit clothing, no tanning bed use) Patient 1 – 1 yr F/U Patient 2 – 6 mo F/U	<u>Patient 1</u> Pruritus resolved in 6 wks <u>Patient 2</u> Pruritus resolved in 10 wks
Waisman[1] (1968)	Commentary (5)	N/A	Typically M Average age 30-50 y/o B/l or L arm pruritus, summer	Sun protection (long sleeve clothing specifically, no sunscreen)	Improvement in pruritus

			recurrence of symptoms, history of chronic sun exposure		

Table 5. Summary of articles describing non-pharmacological treatments of BRP.

Author (year)	Study type (quality)	Number of patients	Patient characteristics	Treatment	Study results
Stellon[40] (2002)	Retrospective study (3)	10	62.5% F Median age 68 y/o Pruritus from dermatomes C3-C8	Deep intramuscular stimulation to paravertebral muscles correlating to dermatome with symptoms Repeated q1-2 wk	Average 4 treatments, 100% with resolution 4 patients with relapse (1-12 mo later)
Wallengren and Sundler[39] (2001)	Prospective cohort study (2)	9	77.8% F Average age 49.9 y/o 77.8% b/l arm pruritus	0.8 mA continuous-current electrode plate applied to pruritic area for 20 min/d for 5 wk 12 mo F/U	Cutaneous field stimulation reduced pruritus by half All but one patient relapsed 3-12 mo after treatment
Tait *et al.*[38] (1998)	Retrospective study (3)	14	Age range 41-72 y/o 50% b/l arm pruritus 50% seasonal variation 42.9% history of neck problems	Cervical spine manipulation (head rotation away from the symptomatic side with traction for 1-2 sec before click felt) Repeat sessions PRN	71.4% with resolution of pruritus (100% of patients with a history of neck problems, 50% of patients with no neck problems), lasting 2 d to permanently
Heyl[20] (1983)	Retrospective study (3)	14	35.7% F Median age 46 y/o 35.7% b/l arm pruritus 30% seasonal variation (worse in summer) 5 patients with cervical imaging (80% with degenerative changes between C4-C7)	3 patients with degenerative changes on cervical imaging and no history of neck treatment given cervical physical therapy or cervical traction/manipulation	Significant improvement in pruritus noted with cervical physical therapy for 1 patient, cervical traction for 1 patient, and cervical manipulation plus physical therapy for third patient