Serum GRP levels may be a useful indicator of disease severity of AD.

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References

1 Tominaga M, Ogawa H, Takamori K. Histological characterization of cutaneous nerve fibers containing gastrin-releasing peptide in NC/Nga mice: an atopic dermatitis model. *J Invest Dermatol* 2009; **129**:2901–5.
2 Lee CH, Yu HS. Biomarkers for itch and disease severity in atopic dermatitis. *Curr Probl Dermatol* 2011; **41**:136–48.
3 Kasutani K, Fujii E, Ohyama S *et al.* Anti-IL-31 receptor antibody is shown in a murine model to be a potential therapeutic option for treating itch and dermatitis in mice. *Br J Pharmacol* 2014; **171**:5049–58.
4 Kagami S, Sugaya M, Suga H *et al.* Serum gastrin-releasing peptide levels correlate with pruritus in patients with atopic dermatitis. *J Invest Dermatol* 2013; **133**:1673–5.
5 Andoh T, Kuwazono T, Lee JB, Kuraishi Y. Gastrin-releasing peptide induces itch-related responses through mast cell degranulation in mice. *Peptides* 2011; **32**:2098–103.
6 Sukhtankar DD, Ko MC. Physiological function of gastrin-releasing peptide and neuromedin B receptors in regulating itch scratching behavior in the spinal cord of mice. *PLoS ONE* 2013; **8**:e67422.

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Severe postherpetic neuralgia and other neuropathic pain syndromes alleviated by topical gabapentin

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Dear Editor, Herpes zoster reactivation (shingles) affects 0·2% of the population.[1] Complications include secondary bacterial infection, postherpetic neuralgia (PHN), ulceration and scarring, pneumonitis, hepatitis, Ramsey–Hunt syndrome, meningoencephalitis and paralysis. PHN occurs in 10–15% of patients following an episode of shingles, with the greatest risk in the elderly.[2] The risk of PHN can be reduced by early treatment, at the onset of the cutaneous eruption, with antivirals, amitriptyline, opioid analgesics or oral gabapentin.[3] However, among patients over 50 years of age, 20% reported persistent pain 6 months after resolution of the cutaneous eruption, despite thymidine kinase antiviral treatment.[4,5] Established PHN is characterized by severe burning and lancinating pain, which is often intractable, lasting in some cases > 20 years, and it is a considerable cause of suffering and disability.[6,7] The chronic pain in PHN can be difficult to alleviate, despite the reported efficacy of many different treatments including analgesics, topical lidocaine, topical capsaicin, nerve blocks, biofeedback, tricyclic antidepressants, gabapentin and pregabalin.[8]

Following local National Health Service Research and Development and ethics approval we retrospectively reviewed 23 consecutive patients attending a tertiary complex pain clinic (University Hospital of Wales, Cardiff and Vale University Local Health Board) treated with topical gabapentin (Gaba-Gel™) manufactured at an MHRA licensed unit as a pharmaceutical special (St Mary's Pharmaceutical Unit, Cardiff and Vale University Health Board, Cardiff, U.K.). Three of these patients had PHN, all female, aged 74, 83 and 85 years. The remaining 20 patients (four male) treated with topical gabapentin had other severe chronic pain conditions: postsurgical pain, complex regional pain syndrome, painful diabetic polyneuropathy, vulvovaginodynia (VVD), trigeminal neuralgia, autonomic cephalalgia, pudendal neuralgia and coccygodynia.

The median age of the PHN group was 83 years and the mean duration of PHN was 9 months (range 3–24), involving the ophthalmic division of the trigeminal nerve (n = 2) and the intercostal nerve. All continued to suffer pain, described as pins and needles, prickly, sensitive to touch, with occasional stabbing (n = 1) or burning (n = 1). Previous and ongoing treatments included lidocaine patches, codeine, paracetamol, capsaicin cream, oral pregabalin or gabapentin, lidocaine and depot steroid local infiltration, acupuncture and Botox injection. All three patients with PHN reported intolerance to oral pregabalin and/or gabapentin.

The pretreatment median pain severity, using the Brief Pain Inventory 11-point numerical rating scale (0, no pain to 10, worst possible pain),[9] was 7 (range 4–10) for PHN and 8 (range 6–10) for the other chronic pain group. The median quality-of-life (0, low to 10, high) and Chronic Pain Sleep Inventory (0, maximal disruption to 10, no disruption) scores pretreatment were 3·5 (range 2–5) and 6 (range 6–9) for PHN and 5 (range 0–9) and 6 (0–10) for other chronic pain, respectively. A topical formulation of 6% w/w gabapentin was applied three times per day to the affected site, maximal area 20 cm^2, and all patients were assessed monthly for pain, quality-of-life and Chronic Pain Sleep Inventory scores over a period of 6 months (Fig. 1).

Collectively 20 of the 23 patients benefited from topical gabapentin, with a reduction in mean ± SD pain scores from 8·2 ± 1·4 to 5·6 ± 1·7 after 1 month (11 achieved a clinically meaningful 30% reduction in pain). A Wilcoxon signed-rank test indicated a strong tendency for analgesia ($P < 0·001$, Table 1). Two of the three patients with PHN benefited from treatment, with reduction in pain (60%, 57% and 0%),

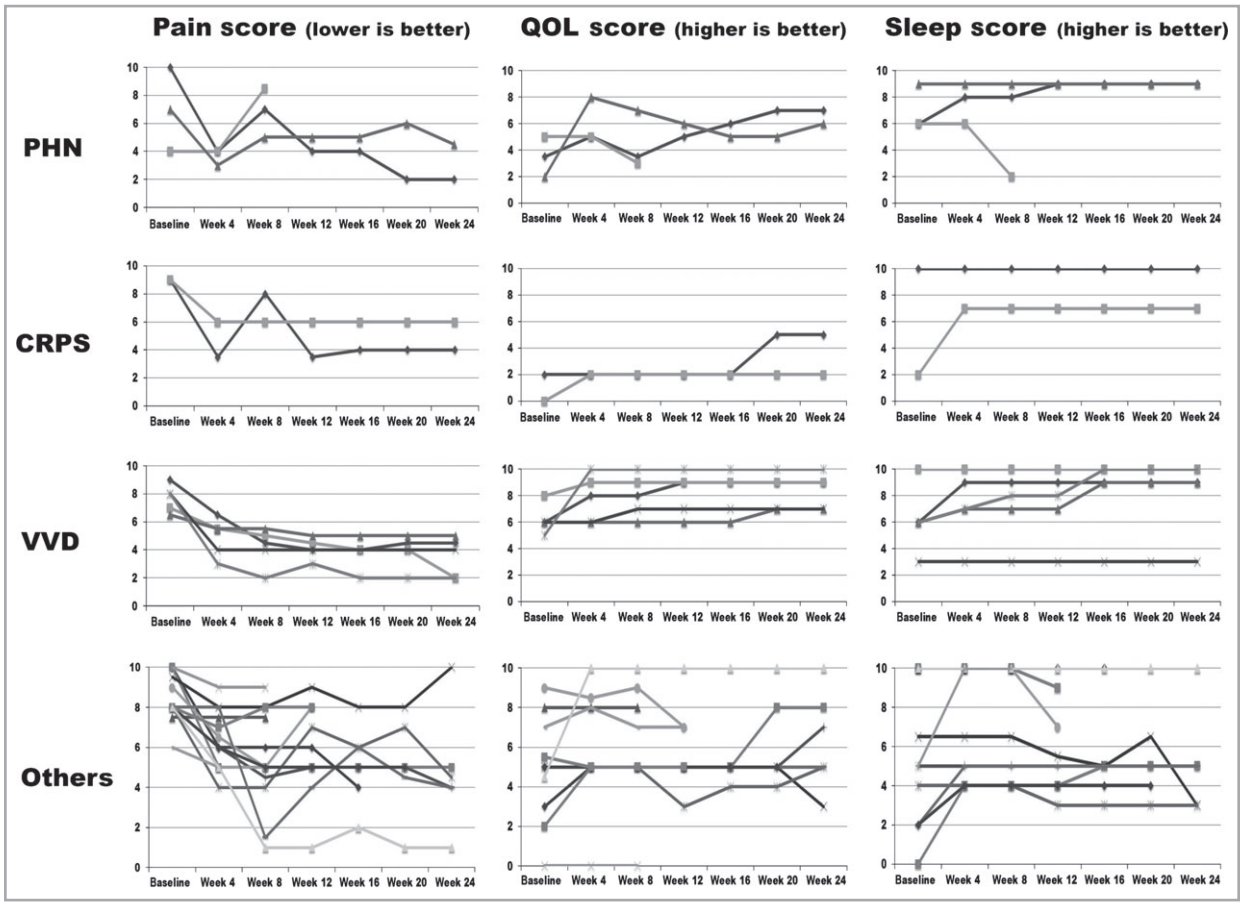

Fig 1. Efficacy of topical gabapentin in treating chronic pain. Topical gabapentin was administered to patients with a variety of recalcitrant chronic pain conditions including postherpetic neuralgia (PHN), complex regional pain syndrome (CRPS) and vulvovaginodynia (VVD). The response of each individual patient was recorded at baseline and monthly using the Brief Pain Inventory 11-point numerical rating scale (pain score), the pain quality-of-life (QOL) index and Chronic Pain Sleep Inventory (sleep score).

improvement in quality of life (42%, 300% and 0%) and sleep (33%, 0% and 0%) after 1 month. Interestingly, all of the patients who responded to topical gabapentin treatment experienced pain relief within 1 h of application. Six patients withdrew from the study because of lack of efficacy: PHN (n = 1), postoperative pain (n = 3), pudendal neuralgia (n = 1) and right-thigh hyperaesthesia (n = 1). One patient with PHN and concurrent normal-pressure hydrocephalus stopped the treatment early because of loss of balance, unsteadiness, sleep disturbance and generalized skin irritation. No other patients reported local or systemic adverse effects to treatment. Four of the 18 patients who responded were able to reduce their systemic analgesia, and one patient was able to discontinue all oral analgesics.

Table 1 Changes in clinical measures, month 1 vs. baseline

Measure	ψ	95% confidence interval
Pain	−0·988	−0·999 to −0·644
Sleep	0·640	0·169 to 0·853
Quality of life	0·601	0·126 to 0·831

Psi is the generalized Wilcoxon measure, as defined in Newcombe.[11]

Multiple studies have already demonstrated the efficacy of oral gabapentin in treating chronic neuropathic pain;[9] however, efficacy is often limited by dose-dependent toxicity. To our knowledge this is the first report describing topical 6% gabapentin in the treatment of PHN. Preliminary *in vitro* Franz diffusion cell studies, examining the transport of topical gabapentin 10% w/w across human skin, show that 0.6% active permeates after application of a 1g dose. Extrapolation of this data suggests that peak plasma gabapentin concentration after topical application (0.01 μg mL^{-1}) (S. Hiom & C. Martin, unpublished), is significantly lower than that reported for oral gabapentin (2–20 μg mL^{-1}).[12] Similarly to our findings, a retrospective study of 35 patients with VVD found that topical gabapentin led to a > 50% reduction in pain within 8 weeks in 28 (80%) of the patients studied.[10] Although our population of patients with PHN was small, in lieu of placebo-

controlled trials, our findings lend weight to support the efficacy of topical gabapentin in the treatment of PHN and potentially other painful neuropathy.

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References

1 Gnann JW Jr, Whitley RJ. Herpes zoster. *N Engl J Med* 2002; **347**:340–6.
2 Hope-Simpson RE. Postherpetic neuralgia. *J R Coll Gen Pract* 1975; **25**:571–5.
3 Johnson RW, Dworkin RH. Treatment of herpes zoster and postherpetic neuralgia. *BMJ* 2003; **326**:748–50.
4 Scott FT, Leedham-Green ME, Barrett-Muir WY *et al.* A study of shingles and the development of postherpetic neuralgia in East London. *J Med Virol* 2003; **70**(Suppl. 1):S24–30.
5 Dworkin RH, Schmader KE. Epidemiology and natural history of herpes zoster and postherpetic neuralgia. In: *Herpes Zoster and Postherpetic Neuralgia* (Watson CPN, Gershon AA, eds), 2nd edn. New York: Elsevier Press, 2001; 39–64.
6 Kost RG, Strauss SE. Post herpetic neuralgia pathogenesis, treatment and prevention. *N Engl J Med* 1996; **335**:33–43.
7 Johnson RW, Rice AS. Pain following herpes zoster: the influence of changing population characteristics and medical developments. *Pain* 2007; **128**:3–5.
8 Sampathkumar P, Drage LA, Martin DP. Herpes zoster (shingles) and postherpetic neuralgia. *Mayo Clin Proc* 2009; **84**:274–80.
9 Moore RA, Wiffen PJ, Derry S, McQuay HJ. Gabapentin for chronic neuropathic pain and fibromyalgia in adults. *Cochrane Database Syst Rev* 2011; **2011**:CD007938.
10 Boardman LA, Cooper AS, Blais LR, Raker CA. Topical gabapentin in the treatment of localized and generalized vulvodynia. *Obstet Gynecol* 2008; **112**:579–85.
11 Newcombe RG. Generalised Wilcoxon measure. In: *Confidence Intervals for Proportions and Related Measures of Effect Size* (RG Newcombe, ed.). Boca Raton, FL: CRC Press, 2012; 369–400.
12 Gabapentin. Summary of product characteristics. Available at: www.medicines.org.uk/emc/medicine/17095 (last accessed 21 May 2015).

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First-line combination therapy with rituximab and corticosteroids provides a high complete remission rate in moderate-to-severe bullous pemphigoid

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Dear Editor, Bullous pemphigoid (BP) is the most common autoimmune blistering disease, mainly affecting the elderly. Despite improvements in treatment modalities, the 1-year

Table 1 Demographics of patients with bullous pemphigoid receiving first-line combination (R) and conventional therapy (C)

Patient no.	Age (years)	Sex	BPDAI (per 360)	IIF titre	Blood eosinophil count (per μL)	Comorbidities	Total prednisolone dose in 1 year (mg)	Rx results	AEs	Death within 1 year
R1	82	M	97	–	2575	–	3310	CRoff	–	–
R2	63	M	84	1 : 320	704	COPD, DM	3045	CRon	–	–
R3	57	F	57	1 : 80	3287	Hypothyroidism	6120	CRoff	–	–
R4	82	F	49	1 : 320	1720	CVA, DM, HTN	4340	CRon	–	–
R5	83	F	27	1 : 40	480	Cervical cancer, dementia	1840	PRon	UTI, cellulitis	+
R6	74	M	36	1 : 160	378	Dementia, PD	3500	CRoff	–	–
R7	74	F	47	1 : 20	381	CHF, CVA, dementia	2415	CRon	UTI	–
R8	79	F	55	1 : 320	684	CVA, dementia, HTN	3080	CRoff	UTI, pneumonia, SIADH	+
R9	99	M	34	1 : 80	864	CAD, CVA, HTN	1260	CRoff	–	–

(continued)