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Brief Report

Suprascapular Nerve Block for Hemiplegic Shoulder Pain Post Stroke: Subgroup Analysis of Pain Response

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Abstract

Background and Aims: Suprascapular nerve block is an effective intervention for hemiplegic shoulder pain post stroke. This study aims to ascertain baseline variables associated with significant shoulder pain reduction in a post-stroke population receiving suprascapular nerve block versus placebo.

Methods: Post hoc subgroup analysis of data from a randomised controlled trial. Participants included 64 patients with hemiplegic shoulder pain (mean onset 12 weeks post stroke); 32 received suprascapular nerve block and 32 received placebo subcutaneous normal saline injection.

Results: Greater rates of pain reduction were found in participants with severe baseline pain ($p=0.0454$) and participants aged under eighty ($p=0.0417$). Persons aged over eighty demonstrated poor response to intervention. Heterogeneity of sex interaction was associated with reduced placebo effect in females ($p=0.036$).

Conclusions: Participants with severe baseline pain or aged <80 years were more likely to have reduced pain following injection. Patients >80 warrant further investigations prior to consideration of this intervention. Stroke subtype and level of spasticity were not associated with response.

Keywords: Stroke; Hemiplegia; Pain; Nerve Block; Treatment; Age

Abbreviations

SSNB: Suprascapular Nerve Block;

VAS: Visual Analogue Scale;

NIHSS : National Institute of Health Stroke Scale;

MAS: Modified Ashworth Scale;

Introduction

Hemiplegic shoulder pain occurs in approximately 25-30% of the post-stroke population [1, 2], but there is a paucity of evidence-based treatments. Multiple aetiologies can contribute to the development of hemiplegic shoulder pain, including soft tissue injuries, changes in motor control, and central nervous system alterations [3]. Initial loss of motor tone can contribute to instability and subluxation, which in turn can lead to soft tissue or nerve injury [3], though there is conflicting evidence regarding the role of subluxation in the development of hemiplegic shoulder pain [4]. The impact of varying aetiologies contributes to the clinician's dilemma in selection of appropriate, evidence-based interventions. Prophylaxis includes positioning and safe manual handling techniques, though there is no causative association demonstrated [5]. Treatment options with increasing evidence base include Botulinum toxin A [6] and functional electrical stimulation⁷, whilst there is conflicting evidence regarding the use of intra-articular steroid injections [7, 8].

The authors' recent randomised controlled study [9] demonstrated statistically and clinically significant benefits of suprascapular nerve block (SSNB) in a post-stroke population. This safe and effective treatment [10] warrants further studies in larger populations to provide greater understanding of characteristics of clinical responders and the impact of effective pain management on independence and quality of life.

Whilst larger scale studies are awaited, it is clinically relevant to consider which patients are the best candidates for the intervention. Reviewing the original trial data, this paper aims to explore the clinical variables associated with greatest reduction in reported pain.

Methods

A 'within study' post hoc subgroup analysis was performed on the data from *Suprascapular nerve block for shoulder pain in the first year after stroke: a randomised controlled trial* (ACTRN12609000621213) [9]. This randomised controlled trial assessed the effectiveness of SSNB on primary outcome of pain (100mm visual analogue scale, VAS) in a population of 64 stroke survivors with hemiplegic shoulder pain >30mm. The original paper [9, 11] outlines the ethics approval, informed consent, full methodology and outcomes. Patients were randomised to receive intervention (SSNB) or placebo injection. Suprascapular nerve block (10ml 0.5% bupivacaine hydrochloride and 1mL of 40mg/mL methylprednisolone) was performed via posterior approach, with use of anatomical landmarks to inject into the suprascapular fossa [12]. The placebo group received 5mL normal saline subcutaneous injection to the same region of the shoulder. Baseline demographics showed that the intervention group (n=32) consisted of 65.6% males, whilst the placebo group (n=32) was 46.9%

males. The majority of participants suffered ischaemic stroke (84.4% in intervention group, 90.6% in control group). There was a greater proportion of elderly participants in the intervention group (25% aged 80 years and over) versus placebo (9.4% aged over 80). Patients were assessed at baseline, and followed up at one week, one month and three months. The intervention group demonstrated a statistically and clinically significant pain reduction when compared to control.

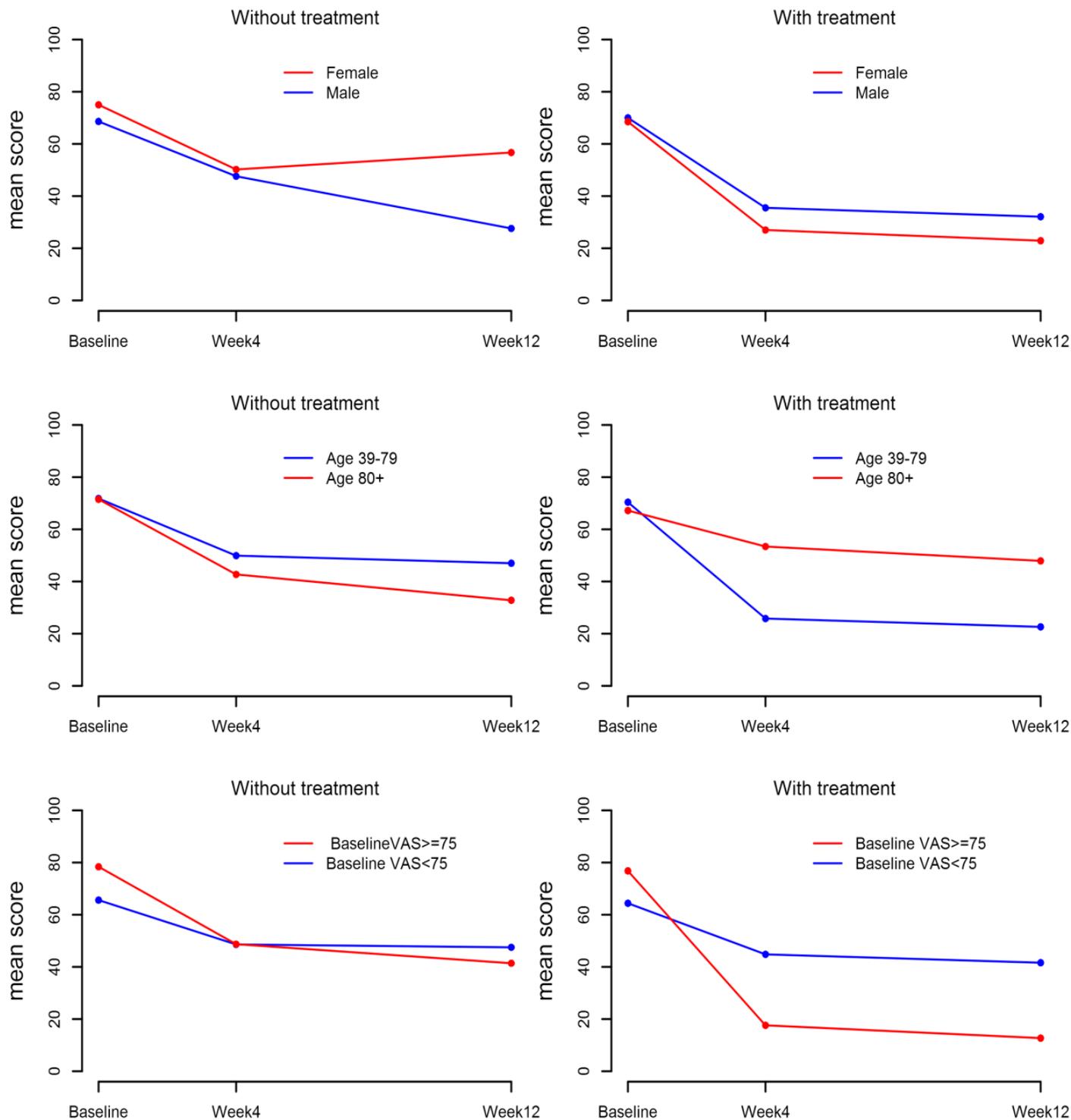
Subgroup analyses were performed to assess the interaction of treatment allocation with seven key baseline variables including age, gender, stroke subtype (infarct vs haemorrhage), upper limb motor deficit on National Institute of Health Stroke Scale (NIHSS) upper limb motor subscale, pain type (movement vs rest / night), spasticity, and VAS. Continuous baseline variables were dichotomised into clinically relevant binary outcomes for the analyses: NIHSS upper limb score definitions were split into 'able to maintain antigravity' (0-2) vs 'unable to maintain antigravity' (3+); severe pain was defined as VAS ≥ 75 mm and mild-moderate pain as < 75 mm [13]; spasticity (Modified Ashworth Scale, MAS) was dichotomised as 'none' (MAS 0) or 'any' (MAS 1+).

Subgroup analyses were conducted by incorporating interaction terms into linear mixed models. The overall treatment effect for the subgroup were calculated by `lsmest` statement with a 2-way interaction term `subgroup*treatment` with `cl` and `diff` option by SAS linear mixed models. Means, mean difference, confidence intervals and p values at different time points were calculated by `lsmeans` statement with a 3-way interaction term `subgroup*treatment*time` with `cl` and `diff` option by SAS linear mixed models. All p values were two sided. Analyses were performed in SAS 9.3 (SAS Institute, Cary NC).

Results

Age under 80 and higher baseline pain scores are associated with more significant response to suprascapular nerve block intervention in hemiplegic shoulder pain. No significant interactions were found between treatment group and stroke type (ischaemic vs haemorrhagic), or baseline level of spasticity, pain type, or upper limb motor deficit, illustrating that treatment effect was not likely to be influenced by these factors. Subgroup analysis (Figures 1 and 2) suggest overall heterogeneity of treatment interactions for sex (p=0.036), age (p=0.0417) and severity of baseline pain (p=0.0454), indicative of impact on response to intervention. Figure 2 outlines p values for separated time points. P values reported test the hypothesis that mean differences (control-intervention) are zero.

Whilst participants aged under 80 had significant response to intervention, those aged over 80 demonstrated poor response. The interaction between treatment and sex appears related to the reduced impact of placebo on females (Figure 1), with equivalent effect of active intervention in both males and females.



VAS Visual Analogue Scale

Figure 1. Subgroup analysis - treatment and time effects.

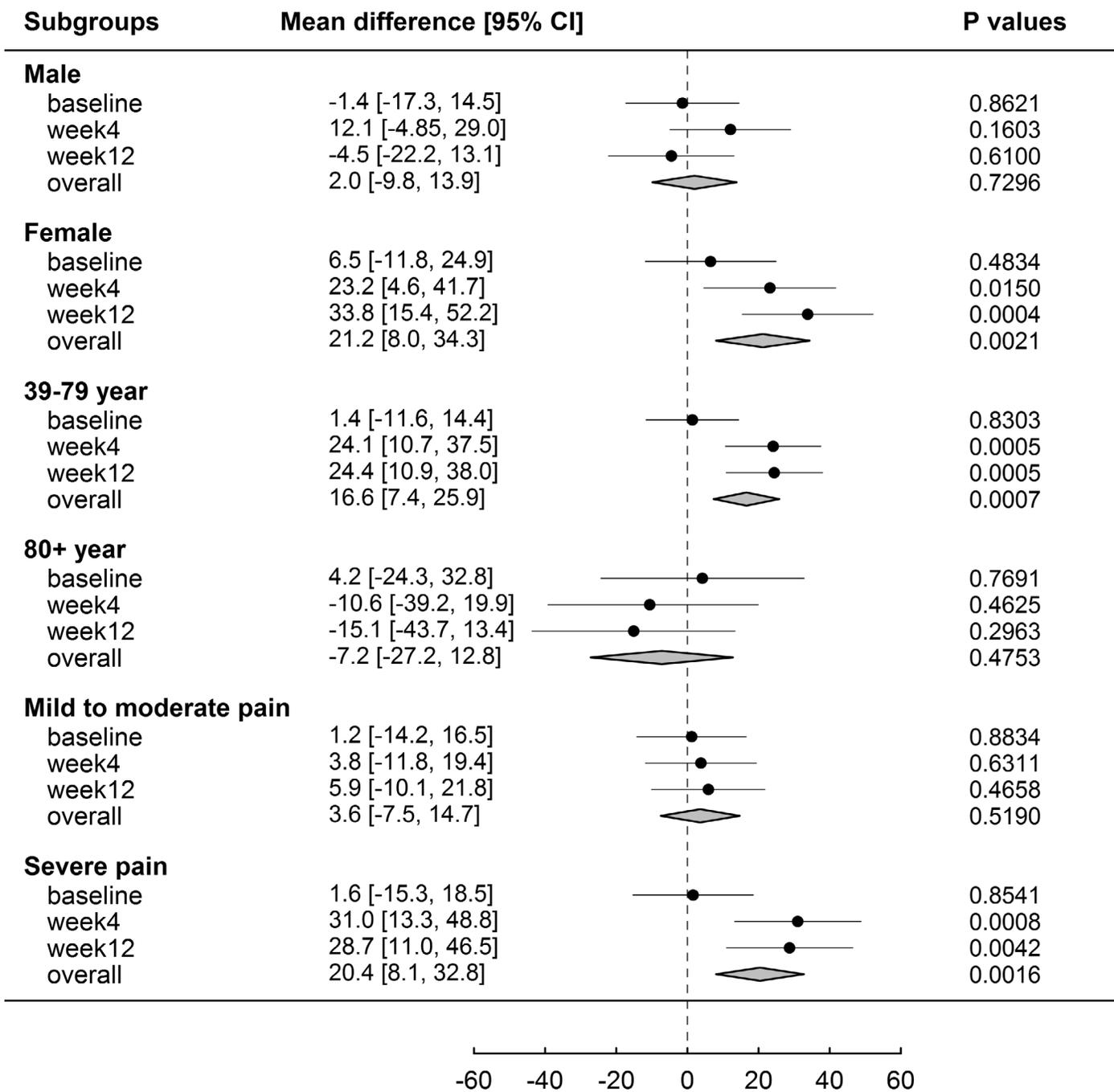


Figure 2. Subgroup analysis treatment effects.

Discussion

The author’s randomised controlled trial³ concluded that SSNB is an effective intervention for hemiplegic shoulder pain. Subgroup analyses suggests that this intervention is most effective in patients aged <80 or with severe baseline pain.

There have been no previous published placebo-controlled randomised controlled trials of SSNB in a stroke population. As such, this subgroup analysis provides a first suggestion of participant variables which may increase the likelihood of a positive response. Similar analyses in non-stroke populations were not found, but subgroup analyses on stroke patients with hemiplegic shoulder pain have been reported in the context of

intra-articular steroid injection [14]. The authors [14] reported that subgroup analyses supported the hypothesis that patients with neglect, visual field deficit and sensory deficits had higher risk of shoulder injury and subsequent capsulitis, and thus less likely to respond to intra-articular injection. Comparison to this study is not possible, as SSNB is effective in adhesive capsulitis [15] and the studies do not use comparable exclusion criteria or outcome measures.

It is important to consider these findings in context of clinical plausibility. Subgroup variables were selected within a clinical framework where interactions were conceivable. Statistically significant interactions were suggested for females, those aged <80, and patients with severe baseline pain. Whilst there is evidence suggesting sex differences in pain experience and analgesic response [16], the finding in the current paper reflects reduced placebo response in females (Figure 1). Previous research has observed reduced placebo responses in females [17,18], with hypothesised explanations including biochemical differences and absence of stress relief in females receiving placebo. Whilst this sex difference is biologically plausible in a placebo controlled trial, this finding should not influence the decision for administration of an active intervention. Age >80 was associated with poor intervention response, whilst participants aged <80 demonstrated increased likelihood of favourable response. Additional underlying pathologies may affect response in older people, and shoulder imaging may play a more important role in guiding treatment in a more complex presentation of hemiplegic shoulder pain. Greater response in those with severe baseline pain is consistent with previously documented effectiveness of SSNB in severe pain [19], and supports the role of this intervention in cases non-responsive to simple analgesics and conservative therapies.

Not all subgroups analysed demonstrated significant interactions, including spasticity and degree of motor deficit. P values on separated analyses of spasticity data indicated interaction, but overall interaction analysis suggest lack of heterogeneity of treatment effect. It has been postulated that patients with significant spasticity may achieve optimal response if the spasticity is treated [20] but we were unable to find any suggestion that the level of spasticity was associated with pain or response to treatment.

Findings of subgroup analyses are observational and have inherent limitations. The post hoc nature of our analyses impacts on the reliability of results. This is a small trial and we performed only seven 'within study' analyses.

Summary and Conclusion

Shoulder pain following stroke is a common problem with limited treatment options. SSNB is a promising treatment and our findings suggest its effects are not confined to one stroke sub-

type. Greatest response occurs in patients aged <80 and those with high reported baseline pain. Whilst no definitive conclusions should be drawn from this analysis, the results generate interesting hypotheses for consideration in larger powered future studies.

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