**Supplementary Table 3.** AEs associated with pharmacopuncture solutions

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| --- | --- | --- | --- | --- | --- | --- |
| **Intervention** | **AE** | **CTCAEa** | **Outcomeb** | **BVP-related AE** | | **Reference** |
| **Mueller gradec** | **Treatment decision after AEd** |
| Acupuncture | Mild pain, edema, bruising, itching | 1 | 1 | - | - | Woo et al., 2022 [54] |
| Cough (n=3) and ALT increase (n=1) | 2 | 6 | - | - | Sung et al., 2020 [60] |
| Itching in the low back area (n=2) | 1 | 6 | - | - | Lee et al., 2018 [67] |
| BU mixed with HHT pharmacopuncture | Local pain (n=3 at 1 hr, n=2 at 24 hrs), local redness (n=2 at 1 hr, n=4 at 24 hrs), discomfort (n=2 at 1 hr, n=1 at 24 hrs), pain on activity (n=1 at 1 hr), fatigue (n=5 at 1 hr, n=8 at 24 hrs) | 1 | 6 | - | - | Choi et al., 2003 [218] |
| BU pharmacopuncture | Local pain (n=9 at 1 hr, n=11 at 24 hrs), local redness (n=1 at 1 hr, n=1 at 24 hrs), discomfort (n=4 at 1 hr, n=3 at 24 hrs), pain on activity (n=4 at 1 hr, n=6 at 24 hrs), fatigue (n=4 at 1 hr, n=8 at 24 hrs) | 1 | 6 | - | - | Choi et al., 2003 [218] |
| Whole body pain (n=1), local pain (n=21), redness (n=2), itching (n=2), discomfort (n=8), flushing (n=2), headache (n=1), dizziness (n=3), pain on activity (n=12), fatigue (n=16) | 2 | 6 | - | - | Kim et al., 2003 [219] |
| Whole body pain (n=1), local pain (n=21), redness (n=2), itching (n=2), flushing (n=2), discomfort (n=7), headache (n=1), dizziness (n=1), pain on activity (n=12), fatigue (n=16) | 2 | 6 | - | - | Yook et al., 2000 [226] |
| BUM pharmacopuncture | Local pain (n=17), redness (n=2), itching (n=1), discomfort (n=8), flushing (n=2), headache (n=1), pain on activity (n=5), fatigue (n=4) | 2 | 6 | - | - | Kim et al., 2003 [219] |
| BVP | Rash (n=7), pruritus (n=5), swelling (n=1), vesicles (n=1), erythema (n=1), hives (n=1) | 1,2 | 1 | 1,2 | 1,4 | Lee et al., 2019 [14] |
| Mild itchiness or mild swelling. Mild pain or slight bleeding after acupuncture | 1 | 1 | 0 | 5 | Cho et al., 2018 [15] |
| Mild pain or slight bleeding after acupuncture. Mild redness or mild itchiness | 1 | 1 | 0 | 5 | Doo et al., 2015 [16] |
| Itchiness (n=1) | 2 | 6 | 1 | 1 | Cho et al., 2012 [25] |
| Mild itching and redness at injection sites (n=1) | 1 | 1 | 0 | 4 | Lee et al., 2021 [58] |
| Mild itching and redness at injection sites (n=2) | 1 | 1 | 0 | 4 | Lee et al., 2021 [58] |
| Four drop-outs due to SAEs:  Anaphylactic reaction, pneumonia aspiration, sinus bradycardia, diverticulitis | 3 | 6 | 2,3 | 1 | Conrad et al., 2019 [61] |
| SAEs (n=4), and severe AEs (n=14): Various injection site AEs (swelling (n=15)), discoloration (n=10), pruritus (n=8), erythema (n=7), urticaria (n=5), injection related reaction (n=5), hypersensitivity (n=3), edema (n=3), pain (n=3), injection site reaction (n=3), vesicles (n=3), rash (n=1), hematoma (n=1), irritation (n=1), joint pain (n=1), paresthesia (n=1) | 2 | 6 | 1,2 | 1,5 | Conrad et al., 2019 [61] |
| Other AEs:  Headache (n=24), back pain (n=13), nasopharyngitis (n=11), upper respiratory tract infection (n=11), pain in extremity (n=10), arthralgia (n=8), diarrhea (n=10) | 1,2 | 6 | 0,1 | 1,5 | Conrad et al., 2019 [61] |
| Minimal itching sensation (n=4), headache (n=1) generalized myalgia (n=1) | 1 | 1 | 1 | 1 | Seo et al., 2017 [69] |
| Drop-out due to hypersensitivity:  Hypopressure and whole body itching) (n=1) | 2 | 6 | 2 | 1 | Lee et al., 2014 [78] |
| Pain at injection (n=3) | 2 | 6 | 0 | 1 | Lee et al., 2014 [78] |
| Swelling, rash, itching (n=22) | 1 | 1 | 0 | 1 | Lee et al., 2014 [79] |
| Drop-out due to itching (n=1) | 2 | 6 | 1 | 1 | Cho et al., 2013 [80] |
| Slight pruritus, local swelling, redness (under 20 mm in diameter) (n=30) | 1 | 1 | 0,1 | 5 | Koh et al., 2013 [82] |
| Drop-out due to mild, generalized swelling and aching (n=1) | 2 | 6 | 2 | 1 | Koh et al., 2013 [82] |
| Mild local redness and itching (1.0 cm in diameter) (n=1) | 1 | 1 | 0 | 1 | Park et al., 2013 [84] |
| Drop-out due to hypersensitive reaction:  Systematic pain (n=5), headache (n=5), dizziness (n=5), fatigue (n=5) | 2 | 6 | 2 | 1 | Lee et al., 2012 [92] |
| Drop-out due to hypersensitive reaction:  Systematic pain (n=3), headache (n=3), dizziness (n=3), fatigue (n=3) | 2 | 6 | 2 | 1 | Lee et al., 2012 [92] |
| Drop-out due to hypersensitive reaction:  Systematic pain (n=4), headache (n=4), dizziness (n=4), fatigue (n=4) | 2 | 6 | 2 | 1 | Lee et al., 2012 [92] |
| Drop-out due to itchiness (n=1) | 2 | 6 | 1 | 1 | Shin et al., 2012 [96] |
| Pruritus (n=15), skin flare (n=5), edema (n=4), skin rash (n=2) | 1 | 1 | 1 | 4 | Shin et al., 2012 [96] |
| Drop-out due to pruritus (n=1) | 2 | 6 | 1 | 1 | Gwak et al., 2009 [114] |
| Pruritus (n=2), swelling (n=1), pain (n=1) | 1 | 6 | 0 | 4 | Kim et al., 2008 [120] |
| Pruritus (n=4), swelling (n=1) | 1 | 6 | 0 | 4 | Kim et al., 2008 [120] |
| Severe swelling, redness, itching of 12-24 hr or 24-48 hr duration (n=7), local pain of 6-24 hr duration | 2 | 1 | 1 | 5 | Kim et al., 2008 [122] |
| Localized edema, localized itching | 1 | 1 | 0 | 4 | Lee et al., 2008 [124] |
| Pruritus (n=8), burning sensation (n=3), pain (n=2) | 1 | 6 | 0 | 4 | Ko et al., 2007 [130] |
| Local pain 24-48 hr duration, severe swelling (n=3), redness (n=3), moderate swelling, redness, moderate itching of 24-48 hr duration | 2 | 1 | 1 | 5 | Na et al., 2007 [133] |
| Drop-out due to infection (n=1), fracture (n=2) | 2,3 | 6 | - | 1 | Seo et al., 2006 [147] |
| Drop-out due to severe itching (n=1) | 2 | 6 | 1 | 1 | Song, 2005 [157] |
| Local itching, redness from scratching (n=2), common cold (n=2) | 2 | 1 | 0 | 2,4 | Yin et al., 2004 [165] |
| Drop-out due to vesicle (n=1), urticaria (n=1) | 2 | 6 | 1 | 1 | Won et al., 1999 [181] |
| Local itching with duration of 2-3 wks (n=60), chills (n=49), local pain (n=36), edema (n=25), muscle pain (n=16), headache (n=14), fever (n=13), nausea (n=4), sweating (n=3), fatigue (n=3), vertigo (n=3), vomiting (n=1), abdominal pain (n=1) | 1,2 | 6 | 0,1,2 | 5 | Won et al., 1999 [181] |
| Whole body pain (n=1), local pain (n=14), redness (n=5), itching (n=11), discomfort (n=5), swelling (n=1), flushing (n=6), headache (n=4), dizziness (n=5), pain on activity (n=7), fatigue (n=10), nausea (n=4) | 1 | 6 | 1,2 | 5 | Kim et al., 2003 [219] |
| Whole body pain (n=1), local pain (n=14), redness (n=5), itching (n=11), discomfort (n=5), swelling (n=1), flushing (n=6), headache (n=4), dizziness (n=5), pain on activity (n=7), fatigue (n=10), lethargy (n=1), nausea (n=4) | 1 | 6 | 1,2 | 5 | Yook et al., 2001 [225] |
| Histamine phosphate intradermal acupoint injection | SAEs (n=4), and severe AEs (n=10): Pruritus (n=2), erythema (n=1), urticaria (n=1), rash (n=1) | 2 | 6 | 0,1,2 | 1,5 | Conrad et al., 2019 [61] |
| Other AEs:  Headache (n=17), back pain (n=9), nasopharyngitis (n=7), upper respiratory tract infection (n=4), pain in extremity (n=4), arthralgia (n=4), diarrhea (n=1) in (B)) | 1,2 | 6 | 0,1 | 1,5 | Conrad et al., 2019 [61] |
| Raw BVP | Localized edema, pain, erythema (n=1), | 2 | 1 | 0 | 1 | Ahn et al., 2016 [189] |
| Chest discomfort, nausea, generalized pruritus, urticaria, erythema, fever (n=1) | 2 | 1 | 2 | 1 | Ahn et al., 2016 [189] |
| Sweet BVP | Hypersensitivity (itchiness) (n=1) | 2 | 6 | 1 | 1 | Ku et al., 2010 [31] |
| Local redness; no other immediate hypersensitivity or delayed hypersensitivity reaction | 1 | 6 | 0 | 4 | Park et al., 2011 [106] |
| Mild swelling (n=2), redness (n=2), mild itching of 2-3 hr duration (n=2), local pain of 1-6 hr duration | 1 | 1 | 0 | 4 | Kim et al., 2008 [122] |
| Local pain 4-6 hr duration, mild swelling and redness (n=3-4), mild itching of 2-3h duration | 1 | 1 | 0 | 4 | Na et al., 2007 [133] |
| De-qi sensation along Large Intestine meridian (n=8), dizziness, lethargy, fatigue, whole body heat (n=7) | 1,2 | 6 | 1 | 5 | Lim et al., 2008 [206] |
| Capsicum frutescens L. pharmacopuncture | Pain over 2 hrs (n=1), nausea after anesthesia with EMLA cream (n=1), continued dull sensation for 5-7 hrs after anesthesia with EMLA cream (n=3), itching (n=1), tingling when breathing in (n=1), fatigue (n=1) | 2 | 1 | - | - | Kim, 2011 [5] |
| Cervi Pantotrichum Cornu pharmacopuncture | Unpleasant (n=18), itching (n=12), drowsy (n=1), headache (n=3), dizziness (n=3) | 1,2 | 6 | - | - | Seo and Xue, 2008 [209] |
| CS pharmacopuncture | Injection-site pain (n=2), ecchymosis (n=2) | 1 | 6 | - | - | Park et al., 2011 [30] |
| Ecchymosis, pain during injection, redness | 1 | 1 | - | - | Park et al., 2008 [50] |
| Bleeding, mild pain, local itching | 1 | 1 | - | - | Lee, 2006 [143] |
| CF pharmacopuncture | Local pain (n=11), redness (n=2), itching (n=1), discomfort (n=3), flushing (n=2), headache (n=2), dizziness (n=1), pain on activity (n=2), fatigue (n=2) | 1 | 6 | - | - | Kim et al., 2003 [219] |
| Local pain (n=11), redness (n=2), itching (n=1), flushing (n=2), discomfort (n=3), headache (n=2), dizziness (n=3), pain on activity (n=2), fatigue (n=2) | 1 | 6 | - | - | Yook et al., 2000 [226] |
| Dioscoreae Rhizoma pharmacopuncture | Itching sense (n=3), burning sense (n=1), edema (n=1), dizziness (n=2), numbness (n=1), headache (n=4), insomnia (n=4) | 2 | 6 | - | - | Sung et al., 2012 [28] |
| Itching sense (n=1) | 2 | 6 | - | - | Sung et al., 2012 [28] |
| Skin flare (n=6), itching sensation (n=2), burning sensation (n=3), edema (n=1), subcutaneous bleeding (n=6), discoloration (n=1), induration (n=6), pain upon injection (n=54), pain after injection (n=39), dizziness (n=2), headache insomnia (n=4) | 2 | 6 | - | - | Ko and Hong, 2013 [194] |
| Skin flare (n=8), itching sensation (n=1), burning sensation (n=5), edema (n=6), subcutaneous bleeding (n=6), induration (n=10), pain upon injection (n=66), pain after injection (n=64), cold sweat (n=2),  chest discomfort (n=1), palpitation (n=1) | 2 | 6 | - | - | Ko and Hong, 2013 [194] |
| Non-Dioscoreae Rhizoma pharmacopuncture | Itching sense (n=2), dizziness (n=2) | 2 | 6 | - | - | Sung et al., 2012 [28] |
| HPP | Bruise (n=8), AST/ALT elevation (n=2), back pain (n=1), cervical sprain (n=1), pudendal itching (n=1), left ankle ligament injury (n=1), left flank urticaria (n=1), acute gastroenteritis (n=1), nausea (n=1), painful throat (n=1) | 1,2 | 1 | - | - | Choi et al., 2022 [182] |
| Local pain (n=11), redness (n=8), itching (n=6), discomfort (n=8), flushing (n=4), swelling (n=4), headache (n=1). dizziness (n=3), pain on activity (n=1), fatigue (n=2) | 1 | 6 | - | - | Kim et al., 2003 [219] |
| Jungsongouhyul pharmacopuncture | Pantalgia (n=1) | 2 | 1 | - | - | Seo et al., 2013 [85] |
| Mahuang and green tea pharmacopuncture | Scratch by injection lasting over 1 wk (n=1), itching (n=1), subcutaneous hemorrhage (bruise) lasting over 1 wk (n=1) | 2 | 1 | - | - | Song et al., 2007 [8] |
| NSAIDs | Skin urticaria (n=1), abdominal pain (n=1), nausea (n=1), low back pain due to lumbar sprain (n=1) | 1 | 6 | - | - | Lee et al., 2021 [58] |
| NSP | Pain not burning but severe (n=1), easily overheated with a slight movement (n=1) | 2 | 1 | - | - | Kim, 2011 [5] |
| Scratch by injection lasting over 1 wk (n=1), subcutaneous hemorrhage (bruise) lasting over 1 wk (n=1) | 2 | 1 | - | - | Song et al., 2007 [8] |
| Injection-site pain (n=3) | 1 | 6 | - | - | Park et al., 2011 [30] |
| Moderate pain during injection | 1 | 1 | - | - | Park et al., 2008 [50] |
| Headache (n=2) and dizziness (n=2) | 2 | 6 | - | - | Seo et al., 2017 [69] |
| Slight redness (n=3), pruritus (n=3) | 1 | 1 | - | - | Koh et al., 2013 [82] |
| transient local site pain (n=1), fatigue (n=1) | 1 | 1 | - | - | Seo et al., 2013 [85] |
| Skin rash (n=1), headache (n=1), hand-foot tingling (n=1) | 1 | 1 | - | - | Shin et al., 2012 [96] |
| Slight dizziness (n=1) | 1 | 1 | - | - | Kim et al., 2010 [113] |
| Pruritus (n=2), burning sensation (n=1), pain (n=3) | 1 | 6 | - | - | Ko et al., 2007 [130] |
| Bruise (n=2), cold (n=1), cystitis (n=1), enterocolitis (n=1) | 1,2 | 1 | - | - | Choi et al., 2022 [182] |
| Subcutaneous bleeding (n=4), discoloration (n=8), pain upon injection (n=28), pain after injection (n=29), dizziness (n=1) | 1,2 | 1 | - | - | Ko and Hong, 2013 [194] |
| De-qi sensation along Large Intestine meridian (n=2), dizziness, lethargy, fatigue, whole body heat (n=4) | 1,2 | 6 | - | - | Lim et al., 2008 [206] |
| Unpleasant (n=8), itching (n=5), drowsy (n=3), chest pain (n=1), dizziness (n=1), shortness of breath (n=1) | 1,2 | 6 | - | - | Seo and Xue, 2008 [209] |
| Local pain (n=5), redness (n=2), itching (n=2), discomfort (n=1), flushing (n=1), pain on activity (n=3), fatigue (n=2) | 1 | 6 | - | - | Kim et al., 2003 [219] |
| Local pain (n=5), redness (n=2), itching (n=2), flushing (n=1), pain on activity (n=2), fatigue (n=2) | 1 | 6 | - | - | Yook et al., 2000 [226] |
| PT (HP, ICT) | Stiffness (n=1), pain (n=1), mild AEs not related to intervention (n=2) | 1 | 1,6 | - | - | Kim et al., 2021 [56] |
| SAEs not related to intervention (n=1) | 2 | 6 | - | - | Kim et al., 2021 [56] |
| Shinbaro pharmacopuncture | Localized itching (n=2) | 1 | 1 | - | - | Park et al., 2011 [107] |
| Sumsu (Bufonis venenum) pharmacopuncture | Pain (n=3), itching (n=3), dizziness (n=3) | 2 | 6 | - | - | Seo et al., 2015 [21] |
| TEA + HPP | Local Blood stasis spot (n=17), local pain (n=21), swelling (n=19) | 2 | 1 | - | - | Lee et al., 2021 [12] |
| TEA | Minor bruises from the thread embedding | 1 | 1 | - | - | Park et al., 2020 [13] |
| Sore throat (n=1), cervicalgia (n=1), dysuria (n=1), common cold (n=6), red eye (n=1) | 1,2 | 1 | - | - | Goo et al., 2022 [53] |
| Mild pain, edema, bruising, itching | 1 | 1 | - | - | Woo et al., 2022 [54] |
| Iatrogenic pneumothorax (n=1) | 3 | 1 | - | - | Kim et al., 2021 [56] |
| Stiffness (n=3), bruise (n=6), pain (n=2), edema (n=1), pricking (n=1), irritation (n=1), mild AEs not related to intervention (n=4) | 1 | 1 | - | - | Kim et al., 2021 [56] |
| SAEs not related to intervention (n=2) | 2 | 6 | - | - | Kim et al., 2021 [56] |
| Cystitis (n=1), allergic rhinitis (n=1), BUN increase (n=1), type II diabetes (n=1) | 2 | 6 | - | - | Sung et al., 2020 [60] |
| Temporary stiffness (n=10), bruise (n=2), irritation caused by the thread (n=2), skin flare (n=1), pruritus (n=1), thread sticking out from the skin (n=1) | 1 | 6 | - | - | Kim et al., 2019 [62] |
| Other AEs not related to intervention:  Ccoughing, other musculoskeletal pain, dyspepsia, headache, insomnia | 1 | 6 | - | - | Kim et al., 2019 [62] |
| Pain (n=23), stiffness (n=22), foreign body sensation (n=7), bruise (n=2) | 1 | 1 | - | - | Kim, 2017 [68] |
| AEs not associated with intervention:  Back pain (n=3), cold (n=2), headache (n=2), ophthalmitis (n=2), allergic rhinitis (n=2), dyspepsia (n=1), dry eye (n=1), tinnitus (n=1),  cystitis (n=1), tonsillitis (n=1), HNP of L-spine pain (n=1) | 2 | 1 | - | - | Kim, 2017 [68] |
| Sham TEA | Common cold (n=4), cystitis (n=1), dental problems caused by implants (n=1), laryngitis (n=1), dyspepsia (n=1), headache (n=2), dizziness (n=1), chest discomfort (n=1), red eye (n=1), onychomycosis (n=1), herpes simplex (n=1), contact dermatitis (n=1), otitis media (n=1), allergic rhinitis (n=1) | 1,2 | 1,3 | - | - | Goo et al., 2022 [53] |
| Pain (n=1), stiffness (n=2) | 1 | 1 | - | - | Kim, 2017 [68] |
| UDP pharmacopuncture | Nausea (n=1), itching (n=1) | 1 | 1 | - | - | Kim et al., 2010 [113] |

aAE severity grade was quantified using the CTCAE scale: 1 = mild, with asymptomatic or mild symptoms, intervention not indicated, clinical or diagnostic observations only; 2 = moderate, with local, minimal, or noninvasive intervention indicated, limiting instrumental activities of daily living; 3 = severe or significant, disabling, but not immediately life-threatening, hospitalization or prolonged hospitalization indicated, limiting self-care activities of daily living; 4 = life-threatening consequences, with urgent intervention indicated; and 5 = AE-related death.

bOutcomes were classified into 6 categories: 1 = complete resolution leaving no sequelae; 2 = resolution with sequelae; 3 = in progress; 4 = permanent damage; and 5 = death; and 6 = unknown.

cBVP-related AE severity grade was quantified using the Mueller grade: 0 = Local swelling with > 10 cm diameter and > 24 hr duration; I = Generalized urticaria, itching, anxiety, or malaise; II = Any of the above plus 2 of the following: angioedema, chest constriction, abdominal pain, nausea, vomiting, diarrhea, dizziness; III = Any of the above plus 2+ of the following: dyspnea, wheezing, stridor, hoarseness, dysarthria, dysphagia, weakness, confusion, fear of death; and IV = Any of the above plus 2+ of the following: reduction in blood pressure, loss of consciousness, collapse, urine or stool incontinence, cyanosis.

dThe treatment decision after an AE was categorized into 5 responses: 1 = discontinued, 2 = reduced, 3 = increased, 4 = no change, and 5 = unknown.

A: acupuncture; AE: adverse event; BU: Calculus Bovis · Fel Ursi; BUM: Calculus Bovis · Fel Ursi · Moschus; BUN: blood urea nitrogen; BVP: bee venom pharmacopuncture; CF: Carthami Flos; CS: Carthami Semen; CTCAE: Common Terminology Criteria for Adverse Events; HHT: Hwangryunhaedok-tang; HP: hot pack; HPP: Hominis Placenta pharmacopuncture; ICT: interferential current therapy; n.r.: not reported; NSAID: non-steroidal anti-inflammatory drug; NSP: normal saline pharmacopuncture; PT: physical therapy; SAE: serious adverse event; TEA: thread embedding acupuncture; UDP: Ulmus davidiana Planch.