

Guidelines on the management of sweating
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Overall objective: To provide guidance on the evidence for the use of various agents in the management of sweating in a specialist palliative care population.

Search Strategy:

Using Medline, Embase and Cinahl databases

Keywords:

Sweating, sweat\$ (or sweat*), diaphoresis, hyperhidrosis, perspiration, hot flushes/flushes, paraneoplastic fever and drug name.

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Mechanisms of sweating

Sweating is an important part of the human thermoregulatory system. Specific thermoreceptors are located in the skin, spinal cord and brainstem which input into the POAH (preoptic and anterior hypothalamus) which acts as a thermoregulatory centre. Thermoregulatory control can be further influenced by higher cortical centres and by various other sites in the brain (e.g. midbrain reticular formation, amygdala, hippocampal formation) which also input into the POAH. Normal thermoregulation is influenced by plasma osmolality, intravascular volume changes and a variety of chemical mediators including catecholamines, acetylcholine and prostaglandin E.

The main thermoregulatory response to temperature changes is mediated through the autonomic nervous system. Sympathetic efferent pathways descend from the hypothalamus through the brainstem to the spinal cord and the preganglionic neurones. From here the fibres exit the cord and enter the sympathetic chain. Postganglionic sympathetic axons containing cholinergic fibres innervate eccrine sweat glands (and blood vessels) in the skin.

Certain areas of the body have a baseline sweat pattern such as the palms and soles of the feet. Sweating in these areas is controlled by inputs from the cerebral neocortex limbic system as well as the hypothalamus. Mental stress and excitement can therefore increase the rate of sweating in these areas and to a lesser extent throughout the whole body. Thermal sweating however tends to affect the body in a uniform pattern.

In a palliative care setting, most patients with abnormal sweat activity complain of hyperhidrosis (excessive sweating) or nocturnal diaphoresis (night sweats). The management of primary hyperhidrosis (due to an inborn error rather than secondary to any pathological process) will not be detailed here. Hyperhidrosis can be further subdivided into localised (usually neurogenic or local causes) or generalised. The latter occurs in patients with various systemic diseases including endocrine disorders, menopause, infections, various cancers and the administration or withdrawal of certain drugs. The mechanism behind the formation of generalised hyperhidrosis is not clearly understood, but may represent an alteration of the thermoregulatory temperature “set point” in the hypothalamus. Symptomatic hyperhidrosis can occur as a response to an area of anhidrosis elsewhere.

A list of therapies used in the management of troublesome sweating is detailed below. Prior management of these patients should include identification of the cause of sweating and any aggravating factors that augment sweating. It is suggested that an up-to-date British National Formulary (BNF) be consulted prior to the commencement of any of the medications listed below.

List of drugs searched

Acupuncture
Aluminium Chloride
Benzodiazepines
Benztropine
Botulinum Toxin
Clonidine
Gabapentin
Medroxyprogesterone
Mirtazepine
Non-steroidal anti-inflammatories
Oestrogens
Propantheline
Selective serotonin reuptake inhibitors
Thalidomide
Thioridazine
Venlafaxine
Vitamins and alternative therapies

No evidence for cimetidine was found in the management of sweating following literature searches for this drug.

ACUPUNCTURE

Evidence

Three case series and one case report in an oncology setting.

Acupuncture in the control of vasomotor symptoms caused by tamoxifen in 12 patients with breast cancer who had previously tried “other pharmacological treatments”. Found SP6 & LR3 for 4 weekly sessions + top-ups provided ‘satisfactory results’. Tolerated well by 10 patients, 8/12 reported reduced severity/duration symptoms. (Towlerton et al, 1999)

26 breast cancer patients on tamoxifen enrolled in study using 5 needle points (Li4, Lr3, Pc6, St36, Sp6). 19/21 ‘responded satisfactorily to treatment’ with statistically significant effect in reducing frequency and intensity of vasomotor symptoms with exception of night sweats. (Cummins & Brunt, 2000)

A pilot study of 7 men with prostatic carcinoma on Gn-RH analogues and vasomotor symptoms for 12 weeks, initial needling twice every week then weekly (electroacupuncture included). Statistically significant decrease in number of flushes after 6, 10 and 24 weeks. (Hammar et al, 1999)

Single case report in cancer associated sweating of a 60 year old women inoperable lung cancer. Needle acupuncture reduced sweating. (Hallam & Whale, 2003)

Conclusion

Case reports/series demonstrate some benefit for acupuncture in sweating associated with vasomotor symptoms secondary to tamoxifen in breast cancer, to hormonal treatment in prostate cancer and in malignancy associated sweating. No data to guide frequency of treatments and points to be used.

ALUMINIUM CHLORIDE

Obstructs sweat pores and induces atrophy of the secretory cells in sweat glands.
Made up normally at a concentration of 20% in alcohol.
Available as a roll on applicator.
Initially apply every night to dry skin and wash off residual in the morning.
Use can be decreased to a maintenance level, usually once every 1 – 3 weeks.
Main side effect is irritation of skin, may be less irritant in different vehicles e.g. salicylic acid gel base.

Evidence

No evidence for use for generalised sweating, in cancer patients or in a palliative care setting. Use in focal hyperhidrosis documented with two blinded placebo controlled trials and two non-controlled trials demonstrating effectiveness.

Conclusion

Use in focal hyperhidrosis in localised areas only.

BENZODIAZEPINES

Used as hypnotics, anxiolytics and anti-tussive agents in our patient population.
Potential problems exist with tolerance, dependence and withdrawal phenomena.

Evidence

No data found in palliative care setting or in oncology patients in general.

Two applicable case reports and some data in animal models with palmar hyperhidrosis (not presented).

Two patients given 10mg Diazepam with Paracetamol 1 hour before γ -IFN, prevented rigor, profuse sweating and high fever. Symptoms recurred when diazepam, not paracetamol, omitted. (Beattie & Smyth, 1988)

73 year old woman with three year history of local hyperhidrosis of left face and scalp. No abnormal findings on examination, imaging or biopsy. Successful reversible treatment on 1mg Clonazepam daily. (Takase et al, 1992)

Conclusion

Limited evidence that benzodiazepines might affect normal sweat gland activity.

BENZTROPINE

Anti-muscarinic licensed for use in Parkinson's.
Discontinued orally in 2003.

Evidence

4 Case reports, 2 on use in venlafaxine-induced night sweats and 2 on use in palmar hyperhidrosis and social anxiety. None in our patient cohort.

The 2 Venlafaxine case reports used benztropine 0.5mg nocte – 0.5mg bd, noted immediate effect with recurrence of sweats on stopping, but significant side effect of dry mouth reported. Sweats refractory to treatment after one month, leading to change in anti-depressant. (Pierre & Guze 2000, Gaber & Gregory 1997)

Dose used in sweating due to social anxiety was 2mg od- tds, in combination with relaxation techniques. Improvement in sweating when used in combination with relaxation (better than individual modalities used alone). (Drimmer 1985, Rapp 1979)

Conclusion

Very limited use in non-cancer populations.

BOTULINUM TOXINS

Inhibits release of acetylcholine, principal periglandular neurotransmitter in eccrine sweat glands.

Injected into numerous sites in the axillae or palms (latter requires anaesthetic).

Side effects are cold/flu-like symptoms, perceived increase in non-axillary sweating after axillae treatment and dose dependant transient muscle weakness in the palms after palmar treatment.

Evidence

No evidence for use in palliative care setting, cancer patients or in generalised hyperhidrosis. Randomised placebo controlled trials in palmar and axillary hyperhidrosis demonstrate reduction in sweating for a number of months duration.

Conclusion

Use in focal hyperhidrosis in localised areas only.

CLONIDINE

Centrally active α -agonist that reduces vascular reactivity.

Use as anti-hypertensive, migraine prophylaxis and for menopausal vasomotor symptoms. Side effects include dry mouth, sedation, fluid retention, bradycardia and dizziness.

Evidence

No studies looking at clonidine in palliative care setting

Studies in breast cancer and prostate cancer patients for sex hormone insufficiency causing hot flashes/flushes.

77 patients with prostate cancer post-orchidectomy (medical or surgical) with a history of >1/12 hot flashes in a randomised double blind cross-over trial (4 weeks treatment; 4 weeks placebo). Transdermal patches used as treatment (equivalent oral dose 0.1 mg/day). 50 patients completed the trial. No significant efficacy difference found between patch and placebo; higher frequency of dry mouth and patch erythema in treatment group ($p = 0.03$). (Loprinzi et al 1993)

A prospective comparison of treatments for symptomatic hot flushes following endocrine therapy for carcinoma of the prostate in 68 patients. Arbitrary allocation to therapy; Phenobarbital and ergotamine (21), Clonidine PO or TD 1mg/day (14), Diethylstilbestrol 0.5 mg/day (16), Megestrol acetate 0.25mg/day (11). Response classified as complete, partial or none. Complete response rate with megestrol or diethylstilbestrol was significantly greater ($p < 0.0001$) than with phenobarbital or clonidine. (Smith 1994)

Randomised, double-blind, placebo-controlled clinical trial of oral clonidine in postmenopausal patients with breast cancer experiencing at least one hot flash per day. 198 patients enrolled, 149 patients completed full 12/52 follow-up. At 8 weeks follow-up, mean decrease in hot flash frequency greater in the clonidine group than placebo 38% vs 24%. Only significant toxicity was difficulty sleeping - 41% with clonidine versus 21% ($p = 0.02$). Mean change in QOL scores; 0.3 clonidine vs 0.2 placebo ($p = 0.02$). (Pandya et al 2000)

Randomised, double-blind, crossover trial of Transdermal Clonidine for ameliorating Tamoxifen-Induced Hot Flushes in breast cancer patients with a least seven hot flashes per week. Double blind randomisation to 4/52 clonidine TD (equivalent to 0.1mg/day) or identical-appearing placebo patches. 116 patients entered study. Significant reduction (20%) in hot flash frequency with clonidine vs placebo ($p < 0.0001$). Significant reduction (10%) in severity ($p = 0.02$). Clonidine therapy associated with significantly increased side effects (dry mouth, constipation and drowsiness). (Goldberg et al 1994)

Conclusion

Only reliable data in cancer patients with hot flashes secondary to sex hormone insufficiency. Benefit demonstrated only in breast not prostate cancer.

GABAPENTIN

Chemical analogue of GABA. Binds to gabapentin-binding protein and interacts with calcium channels in CNS. Increases GABA synthesis and release. Licensed for use in partial seizures and neuropathic pain. Used with caution in patients with psychotic

illness, renal impairment and the elderly. Side effects include drowsiness, dizziness, ataxia, fatigue, nystagmus, tremor and diplopia.

Evidence

No studies in palliative care patients.

Two RCTs, two open label pilot studies, two case series and three case reports.

One randomised, double-blind, placebo-controlled trial in postmenopausal women suffering from 7 or more hot flashes per day. Randomised to either gabapentin 300mg tds or placebo for 12 weeks. 59 patients recruited (54 patients completed), 67% of patients treated with gabapentin had a >50% reduction in hot flash score compared with 38% in the placebo group. (Guttuso et al 2003)

A randomised trial over an eight week period in 420 women with breast cancer found 900mg gabapentin a day reduced the frequency of hot flushes by 26% and the severity by 30% relative to placebo. (Pandya et al 2005)

Open label pilot study of post menopausal women with breast cancer on tamoxifen with >2 hot flashes per day. Gabapentin 300mg tds administered for 4 weeks. 22 patients recruited, 4 patients discontinued due to side effects. 8 patients had a complete response and chose to continue gabapentin. Overall reduction in hot flash frequency (44% reduction), severity (53%) and duration (74%). (Pandya et al 2004)

Prospective, single arm, open label pilot study in patients with history of breast cancer with no current active disease and hot flashes at least 14 times per week. Increasing doses of gabapentin on a weekly basis until 300mg TDS achieved. 24 patients recruited, 14 patients were on tamoxifen. Mean reduction in hot flash frequency of 66% and hot flash score of 70% over 4 weeks from baseline. 4 patients stopped due to side effects. 14 patients chose to continue gabapentin when study completed. (Loprinzi et al 2002)

Case series of 6 adult patients (4 pts post hysterectomy/oophorectomy) with Gabapentin doses ranging from 200mg od to 400mg qds. Resulted in decreased frequency of hot flashes within 1-3 days of treatment. (Guttuso 2000)

A cases series involving 11 postmenopausal women where Gabapentin was titrated from 300mg/day up to 1200mg/day. Gabapentin was found to be extremely effective in reducing hot flush activity. (Albertazzi et al 2003)

Case report of 70 year old man with prostate cancer on antiandrogen and GnRH therapy with no response to clonidine, megestrol acetate, diethylstilboestrol and venlafaxine. Gabapentin 600mg/day led to near complete resolution of symptoms. (Jeffery et al 2002)

Case report of 32 year old women post hysterectomy and BSO with severe hot flashes occurring 20-30 times per day. Multiple previous treatments including oestrogen therapy, fluoxetine, paroxetine and sertraline. Gabapentin 300mg tds commenced with reduction in hot flash frequency to 3-4 per day within 3 weeks. (Guttuso 2004)

Conclusion

No evidence in palliative care population.

One RCT in breast cancer patients and one in post menopausal women suggest it is effective in treating hot flashes.

Two pilot studies in patients with breast cancer suggest it is effective for treating hot flashes.

Various case reports and case series suggest it can be used to treat hot flashes and hyperhidrosis of various aetiologies.

GLYCOPYRRONIUM

Most commonly used in the palliative care setting in the management of respiratory secretions. Side effects are the same as for other antimuscarinic medications.

Evidence

No evidence in our patient population. Case reports in Freys syndrome (diabetic gustatory sweating) suggest efficacy of topical glycopyrronium 0.5% for local sweating control. (Urman & Bobrove 1999) Similar case report in treatment of a healthy adult with craniofacial hyperhidrosis. (Luh & Blackwell 2002)

Conclusion

Use for local control measures as an alternative to other anti-cholinergics that may produce more in the way of systemic side effects.

MEDROXYPROGESTERONE (FARLUTAL, PROVERA) / MEGESTROL ACETATE (MEGACE)

Progestogens have a role treating endometrial cancer, less use in breast cancer and renal cell cancer and rarely used in prostatic cancer.

Side effects: often mild, include nausea, fluid retention, wt gain with risk of Cushingoid syndrome at high dose. Caution with fluid retention: epilepsy, hypertension, migraine, asthma, cardiac or renal dysfunction ; risk of thromboembolism ; avoid in liver impairment and monitor co-existent diabetes closely.

Evidence

Few RCTs in control of hot flashes in post menopausal women demonstrating benefit.

Italian case series in 37 patients with prostate carcinoma treated with progestogens, a therapeutic efficacy of 80% was observed following cyproterone acetate and of 70% following medroxyprogesterone acetate (Ronzoni et al 1998).

A double-blind cross-over study performed on 21 patients treated for endometrial carcinomas who had severe menopausal symptoms. Patients were randomized into two groups and received medroxyprogesterone acetate (MPA) 100 mg twice daily for

12 weeks and a placebo for 12 weeks. A significantly better effect on hot flushes and sweating was obtained with MPA than with the placebo. On average the maximum effect was achieved by MPA after 4-6 weeks (Aslaksen et al 1982).

Megestrol acetate was found to be effective after 2 – 3 weeks of treatment in a double-blind placebo-controlled crossover study in 97 women with a history of breast cancer and 66 men receiving androgen ablation therapy for prostate cancer. Patients receiving Megestrol acetate (20 mg BD) experienced a 75 – 80% reduction in hot flashes compared to a 20 – 25 % reduction in those taking placebo. (Loprinzi et al 1994)

A 3-year follow up of this cohort revealed that 45% were continuing to use megestrol acetate having titrated their dose to the lowest possible to control their hot flushes. (Quella et al 1998)

Conclusion

Beneficial effect in hormone-related cancer induced sweats (breast, prostate and endometrial cancer populations).

MIRTAZEPINE

A pre-synaptic α antagonist which increases central noradrenergic and serotonergic neurotransmission, indicated in the treatment of depressive illness. It has few anti-muscarinic effects unlike similar drugs but can cause sedation particularly in the first week of treatment.

Evidence

One prospective single arm pilot clinical trial involving 22 women with hot flashes demonstrated a 53% median reduction in daily hot flashes (16 patients completed the study) involving doses of Mirtazepine ranging from 7.5mg to 30mg. (Perez et al 2004)

Conclusion

Some benefit shown in a non-palliative care setting.

NSAIDS

Naproxen in particular has been used in the differential diagnosis of neoplastic fever. It may work in a different way to other anti-inflammatories, but is typically used in the management of arthritis and gout. Side effects are similar to other NSAIDs (intermediate risk of gastrointestinal side effects, renal impairment, bronchospasm, fluid retention, reduced platelet activity etc.).

Evidence

Chang et al (1984) looked at 21 patients with neoplastic fever in a non controlled study which showed a good response in fever to 250mg BD of naproxen. After starting treatment there may have been an excessive period of sweating

Chang et al (1995) again headed a retrospective case note review of 39 patients with neoplastic fever and showed naproxen to be superior to steroids in 12 of the patients 36/39 had a response to naproxen.

Two separate case reports (n=4, n=5) suggest Cox II drugs may be effective in the management of sweating (Chang et al 1998, Kathula et al 2002).

The only prospective randomised trial was by Tsavaris et al (1990) of 48 patients with neoplastic fever. They were randomly allocated to naproxen 250mg bd, diclofenac 25mg tds, or indomethacin 25mg tds. There was no difference in the level of effectiveness of the three drugs. There was also no difference in the duration of apyrexia. If fever returned trying a different NSAID was effective.

Conclusion

There is minimal evidence and larger trials are needed but for a difficult problem NSAIDs may have a role in controlling neoplastic fever.

OESTROGENS

Widely accepted in treatment of menopausal hot flushes. Not used in general paraneoplastic sweats. All evidence in cancer patients is in sweats due to hormone deficiency (prostate cancer, breast cancer). Use of oestrogens in breast cancer remains a controversial area and results from an ongoing RCT are awaited. Side effects include headache, gastrointestinal disturbances, weight changes, risk of thromboembolus and hormone dependent cancers.

Evidence

915 patients randomised to parenteral oestrogen or androgen ablation (medical or surgical) demonstrated a lower incidence of hot flushes ($p < 0.001$) and associated distress ($p < 0.001$) in the oestrogen group, but a higher incidence of gynaecomastia ($p < 0.01$). (Spetz et al 2001)

12 men treated with leuprolide injections who had moderate to severe hot flushes in a cross-over study comparing different doses (0.05mg and 0.1mg) had a significant reduction in flush severity in both high and low dose groups, but significant reduction in frequency only in the high dose group. Mild breast swelling and tenderness only side effects. 8 opted to continue with the treatment and were given high dose patches. (Gerber et al 2000)

68 men with prostate cancer with bone mets or soft tissue mets outside the pelvis having had medical or surgical castration and hot flushes in a non-randomised study involving 4 treatment groups {Phenobarbital and ergotamine (21), Clonidine (20), Megestrol acetate (11) and Diethylstilbestrol 0.25-0.5mg po od (16)}. In oestrogen

arm, 11 patients (70%) had elimination of hot flushes and 3 had partial response. Complete response superior to phenobarbital / ergotamine and clonidine groups ($p < 0.0001$) equal to Megace, however most oestrogen patients had tender gynaecomastia. (Smith 1994)

Conclusion

Worth trying in prostate cancer but megestrol acetate has fewer side effects so should be tried first. Patches probably best because less thromboembolic risk. Always try other treatments first in breast cancer but could consider HRT if symptoms very severe and other measures fail. Do not use with aromatase inhibitors.

PROPANTHELINE

An agent with anti-cholinergic activity used in the management of smooth muscle spasm and gustatory sweating. It has a relatively high incidence of anti-muscarinic side effects compared to other drugs in its class.

Evidence

Mostly from review articles where propantheline is mentioned in general for management of sweats, otherwise only case reports. No evidence in oncology setting.

2 case reports in patients following a cervical cord injury. Propantheline 15mg reduced sweating after 24 hours of use in these individuals. Topically applied propantheline in 20 healthy volunteers shown to be more efficacious than aluminium chloride, best results for localised sweating shown with these two topical agents in combination. (Canaday & Stanford 1995, Puschmann 1980)

Conclusion

Of limited use only in management of localised hyperhidrosis.

SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRI'S)

Used in the treatment of depression, particularly when there is a risk of deliberate overdosing. Side effects include gastrointestinal disturbances, hypersensitivity reactions, bleeding disorders, sedation and antimuscarinic activity. Use is contraindicated for 2 weeks post cessation of a MAOI.

Evidence

No specific evidence in palliative care setting.

Pilot trial of 13 women experiencing hot flashes who had chemotherapy for breast cancer within last 6 months. Open label study; paroxetine 10mg nocte for 3 nights, then 20mg nocte for a month. 11 women still experienced hot flashes, but severity decreased from 100% to 38% - secondary outcomes of improved sleep quality and reduced fatigue. (Weitzner, 2002)

Open label study of 10mg paroxetine daily for 7 days, then 20mg daily for 4 weeks in 30 women (27 completed) with a history of breast cancer with 14 or more hot flashes per week. Mean reduction in frequency was 67% (67% reported >50% reduction in frequency). Mean reduction in severity of hot flashes was 75% (73% reported >50% reduction in severity). Unable to assess differences in response between natural and induced menopause. Improvements in sleep, anxiety, depression, QoL as secondary outcome measures (Stearns, 2000)

A double-blinded, randomised, two-period crossover trial of fluoxetine 20mg OD versus placebo. 81 women with inclusion criteria >13 hot flashes per week, 77 completed the study. Hot flash scores (frequency x average severity) decreased 50% in fluoxetine arm versus 36% in the placebo arm (p=0.02) (Loprinzi, 2002)

Conclusion

Both fluoxetine and paroxetine appear to have a role in the management of vasomotor symptoms in postmenopausal women and may also be effective in women who experience a 'premature menopause' as a result of surgery and/or chemotherapy. There is no consensus as to the influence that simultaneous treatment of depressive symptoms has on the experience of vasomotor symptoms.

THALIDOMIDE

Synthetic derivative of glutamic acid – R & S enantiomers. Undergoes non-enzymatic hydrolysis in plasma. Prescribed widely in 1950's as a sedative / hypnotic and antiemetic. Withdrawn in early 1960's due to its potent teratogenic effects resulting in severe limb deformity. Hypnosedative, anti-angiogenic, anti-inflammatory and immunomodulatory properties. Side effects include peripheral neuropathy, constipation, headache, skin rashes and sedation.

Access to thalidomide is now strictly controlled. The prescription must be written by a registered physician and dispensed by a registered pharmacy to a registered patient as a 28 day supply. Oral and written information about adverse effects must be given. If the patient is not competent or able to sign a consent form they are excluded.

Evidence

Case report of 59 year old man with a diagnosis of mesothelioma. Main symptoms were profuse night sweats necessitating up to five changes of pyjamas per night. Trial of thalidomide 200 mg nocté lasted for 14 days. After 3 days the night sweats stopped completely, only needed to change pyjamas once in 10 days. At end of trial sweats returned within 24 hours. Again they resolved with re-challenge with Thalidomide (100mg). (Deaner 1998)

Case series of 7 patients with advanced malignancy (a total of 10 approached from a total patient pool of over 1200). 10 day course of thalidomide, starting dose 100 mg nocté. 4 patients completed the trial with a reduction in "distress scores". 2 patients withdrew due to side effects. (Deaner 2000)

One study regarding the use of Thalidomide to manage anorexia and weight loss in cancer cachexia found that a patient with metastatic adenocarcinoma of the colon had a significant reduction in night sweats following Thalidomide administration (100mg/day) within 2 days of initial dosing. (Calder & Bruera 2000)

Conclusion

Thalidomide may have a place in the management of distressing sweating in terminal malignant disease.

Short courses and low doses, the benefits outweigh the risks.

THIORIDAZINE

Anti-muscarinic used under specialist supervision in the second line treatment of schizophrenia in adults.

Thioridazine is associated with QT-interval prolongation and increased risk of ventricular arrhythmias. It is therefore contraindicated in significant cardiac disease, history of ventricular arrhythmia or concomitant use with other drugs known to prolong the QT interval. Cautious use with concomitant use of drugs that inhibit or are metabolised by cytochrome P450 2D6.

Evidence

No randomised controlled trials, three case-series only:

17 patients with advanced local or metastatic solid tumours with “sweating sufficiently severe to affect their quality of life”. Starting dose 10mg thioridazine orally at night increased if necessary to 30mg. 15 patients reported an improvement in sweats (Regnard 1996)

20 patients with breast, prostate or lung cancer and a diagnosis of cancer related sweating. Dose 10mg-25mg daily. 8 patients demonstrated a definite improvement, 2 patients partial improvement. 2 patients withdrawn due to side effects (confusion predominantly). (Cowap & Hardy 1998)

10 patients with advanced malignancy in a palliative care setting with troublesome sweating. Dose 10mg-25mg at night. 7 patients reported a significant improvement (Abbas 2004)

Conclusion

Evidence of improvement in cancer related sweating in 32 out of 47 patients in a palliative care setting. Use may be restricted due to its potential adverse effect on cardiac function.

VENLAFAXINE

A serotonin and noradrenaline reuptake inhibitor (SNRI) licensed for the treatment of depressive illness and generalised anxiety disorder. Side effects include gastrointestinal disturbance, hypertension and skin reactions but is meant to lack the sedative and anti-muscarinic effects of tricyclics.

Evidence

Pilot evaluation of venlafaxine hydrochloride (12.5mg BD) for the therapy of hot flashes in women with history of breast cancer (23 patients) and men (5 patients) with history of androgen deprivation therapy. Demonstrated a 50% reduction in hot flash frequency in 54% patients (mean decrease from 6.6 to 4.3 flashes per day). Incidence of severe hot flashes fell from mean of 1.4 to 0.1 per day ($p < 0.0002$). Most of effect overall seen in first week of therapy. (Loprinzi et al 1998)

Compared with other placebo-controlled studies: hot flash scores reduced by 30% with vitamin E or clonidine, 55% with venlafaxine, 85% with megestrol acetate and 20% with placebo. Adverse effects included 2 patients withdrew; 1 due to impaired cognition, 1 due to depression, nausea, dry mouth, fatigue and sleepiness. 64% wished to continue taking it after the study.

Pilot evaluation of venlafaxine (12.5mg BD) for the treatment of hot flashes in 21 men undergoing androgen ablation therapy for prostate cancer. 16 patients evaluated, 3 withdrew due to nausea (most common side effect). In 10 patients the hot flash score fell by at least 50%. Mean daily incidence of severe and very severe hot flashes fell from 2.3 to 0.6 ($p = 0.003$). (Quella et al 1999)

A randomised controlled trial of Venlafaxine in management of hot flashes in survivors of breast cancer. Three treatment groups (Venlafaxine 37.5mg per day, 75mg and 150 mg per day) and one placebo group; 191 patients in total. Significant reduction in hot flash score ($p < 0.0001$) in all treatment groups after four weeks versus placebo. Also statistically significant difference between 37.5mg and 75mg treatment groups ($p = 0.01$) but not seen for the 2 highest dose treatment groups. Higher level of side effects observed for highest dose (150mg) group. Concluded that patients should start on 37.5mg then be titrated to a maximum of 75mg per day after one week. A longitudinal continuation study as an extension of this trial in 102 patients over 13 weeks demonstrated a maintenance of the reduction of the hot flash score seen after initial titration. (Loprinzi et al 2000, Barton et al 2002)

Conclusion

Evidence that Venlafaxine is beneficial in patients with hormone-related sweats (breast and prostate cancer). It should be noted that Venlafaxine may itself induced sweating.

VITAMINS AND ALTERNATIVE THERAPIES

Vitamin E

125 women with history breast cancer in an 8 week double blind crossover trial of 400IU b.d. vitamin E. No significant adverse effects but no patient preference. (Barton et al 1998) Conclusion: mainly placebo effect

Evening primrose oil

Oil extracted from seeds of the evening primrose and contains Linoleic acid, (Gamma) linoleic acid or gamolenic acid and Vitamin E. Linoleic acid is a precursor of prostaglandin E which may have a role in release of gonadotrophins.

Randomised, double blind trial in 56 menopausal women of 2g evening primrose oil and 10mg Vitamin E. No evidence of benefit over placebo. (Chennoy et al 1994)

Soy Products

Phytoestrogens derived from soy products - structurally & functionally similar to oestradiol.

177 patients with history breast cancer in a randomised double blind 8 week trial of soy tablets and randomised double blind 12 week trial in 123 patients with history of breast cancer demonstrated that soy was no more effective than placebo. (Van Patten et al 2002)

Black Cohosh

Indigenous North American plant with Oestrogen-like activity.

A randomized, double blind trial in 69 patients with a history of breast cancer. No significant difference in reported frequency of hot flashes but significant reduction in sweating in cohosh group. (Jacobsen et al 2001)

Dong Quai

A herb native to China / East Asia and ginseng have not demonstrated any benefit over placebo in previous trials in post-menopausal women. (Hang et al 2002, Kronenberg et al 2002)

Conclusion

1. Evening primrose oil & vitamin E (no evidence but benign treatment)
2. Dietary supplementation of soy products
3. Possible benefit from Black Cohosh

Overall Conclusion

Given the evidence provided above, treatment of sweating will be sub-divided into those therapies shown to have an effect in the management of hot flashes/flushes in hormone related malignancies (breast and prostate), those used to treat localised areas of sweating and those used in the management of generalised sweating. It should also be noted that there is very little evidence overall as to the effective management of sweating in general and these guidelines may therefore also reflect current practice within the Yorkshire area.

Management of sweating in hormone-related malignancies

Breast cancer:	Megestrol acetate 20mg BD Venlafaxine (37.5mg increasing to 75mg BD) Gabapentin 300mg TDS Paroxetine 20mg OD Acupuncture Clonidine
Prostate cancer:	Medroxyprogesterone acetate 100mg BD / Megestrol acetate 20mg BD Diethylstilboestrol 0.5mg OD Venlafaxine 12.5mg BD Acupuncture
Endometrial cancer:	Medroxyprogesterone acetate 100mg BD

Management of localised sweating

Aluminium chloride
Proprantheline
Botulinum toxin

Management of generalised sweating

In the absence of any good evidence in the management of generalised sweating per se, a suggested strategy is below:

1. Trial of NSAID, particularly if there is a suspicion of tumour related pyrexia
2. Gabapentin or the antidepressants paroxetine, fluoxetine or venlafaxine may be useful although their evidence is based generally on hormone related hot flashes
3. Thalidomide 100mg ON
4. Thioridazine 10mg increasing to 30mg
5. Acupuncture

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Acupuncture

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