Clinical Section

Gerontology

Gerontology 2009;55:13–20
DOI: 10.1159/000173697

Received: July 3, 2008
Accepted: October 7, 2008
Published online: November 12, 2008

Lifestyle Drugs in Old Age – A Mini-Review

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Key Words
Lifestyle drugs · Somatoform disorder · Hypochondria · Body dysmorphic disorder · Botulinum toxin · Isotretinoin

Abstract
Normal aging is no disease. The individual lifestyle may be responsible for a large fraction of the so-called 'age-related' changes. An increasing number of healthy individuals make use of 'lifestyle' drugs, such as nootropics, psychopharmaca, hormones and ecodrugs. In this respect, the fact that many people try to improve their outer appearance, to solve their 'cosmetic problems', to influence their rate of hair growth and to altogether delay, halt or even reverse the natural aging process has become a relevant matter for the practising doctor. Lifestyle drugs are taken in an attempt to increase personal life quality by means of attaining a certain psychosocially defined medical or beauty ideal, rather than to manage a medically identifiable, well-defined disease. Often, patients suffering from somatoform disorders such as hypochondriac disorders, body dysmorphic disorders, somatization disorders or persistent somatoform pain disorders may spontaneously ask physicians to prescribe them lifestyle drugs. Also, when 'healthy' people demand a lifestyle drug, possible side effects and contraindications must be taken into consideration and ruled out.

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Introduction

Lifestyle drugs – also called smart drugs, life-enhancement drugs, vanity drugs and quality-of-life drugs – have become an economically, socially and medically important new group of medications. They are taken in an attempt to increase personal well-being and quality of life. Their intake is influenced by fashion trends and private lifestyle and, more generally, by various socioeconomic factors. Lifestyle drugs are increasingly becoming the subject of articles in lifestyle magazines and of television programs. The amount of information on lifestyle drugs available on the Internet is growing. Likewise, also the number of people requesting to be treated with such drugs in order to increase their sense of well-being is growing [1].

The increasing availability of drugs that may or seem to alter appearance, physical and mental capabilities or even personality in people is changing the social fabric of our culture and represents a difficult challenge to health-care systems. It is also revolutionizing the traditional doctor-patient relationship [2].

Doctor-Patient Relationship

The doctor-patient relationship is obviously undergoing a major change in our times. While in the past patients were seeking a physician's advise and help because

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0304–324X/09/0551–0013$26.00/0

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of symptoms of disease, some medical fields (e.g. aesthetic surgery) are now experiencing pressure from patients to prescribe drugs or perform surgical interventions etc. that are not necessary from the viewpoint of evidence-based medicine. A reverse patient-doctor relationship is also emerging due to the fact that doctors are creating new markets to earn more money! Also, for the first time in history, the goal of medical intervention is not *restitutio ad integrum* or *restitutio ad optimum*, but rather the improvement or enhancement of the human body.

A precise, generally accepted definition of lifestyle drugs is still lacking [2]. Therefore, we propose the following: 'Drugs are to be considered lifestyle drugs whenever they are taken for the sole purpose of increasing personal life quality and of attaining a current psychosocially defined beauty ideal, whereby no medical need for the treatment exists.'

Nootropics, for instance, have been approved for the treatment of specific medical diseases, e.g. psychic or neurological symptoms of cerebral circulatory disturbances of various origins (post-apoplectic, post-traumatic or sclerotic) or also SSRIs (selective serotonin reuptake inhibitors) for depressive disorders. But the same substances could also be improperly used without indication as a lifestyle drug to enhance well-being [3]. Accordingly, a drug can be a lifestyle drug or not depending on its use.

Lifestyle drugs can be divided into two groups [4, 5], namely: (1) drugs approved for a specific 'lifestyle' indication (e.g. finasteride for androgenic alopecia, which is generally not seen as a disease), and (2) drugs approved for specific indications but used for other purposes (off-label use).

Phosphodiesterase inhibitors, for example, are indicated for erectile dysfunction, but are also used by healthy subjects to increase sexual performance. Occasionally, men fantasize about a 100% controllable erection. As a consequence, psychosocial causes of erectile dysfunction may be somatized; otherwise 'normal' occasional failures may become a widespread disease: the drug here becomes a lifestyle drug depending on where one draws the line between normal inconveniences of life and real diseases [6–8]. Also, the use of doping agents, particularly anabolic androgenic steroids, has changed from being a problem restricted to sports to one of public health concern, especially with regard to their side effects and long-term consequences. Furthermore, 'anti-aging' medicine has become popular for which there is little or no supporting scientific evidence of either safety or efficiency. Seniors are thought to be at particular risk of physical harm because they often take multiple prescription pharmaceuticals, increasing their risk of possible dangerous supplement drug interactions or adverse effects; they can be harmed indirectly if they take unsubstantiated supplements and forgo needed conventional medical treatment. In addition, the questionable and even harmful effects of anti-aging health products for seniors can also pose a considerable economic burden on the usually poorly informed older segment of the population [3].

The main drugs involved – mostly requiring prescriptions from the physician – are discussed in the following paragraph.

Specific Lifestyle Drugs and Abuse

Nowadays, lifestyle drugs are mostly represented by nootropics, hormones, psychopharmaceuticals and 'eco-drugs' including herbal products, vitamins, minerals and amino acids (table 1) [8].

– Vitamin E and selenium are promising nutrients for the prevention of prostate cancer, and both are currently being tested in a large randomized trial for prostate cancer. A 10-year average intake of supplemental vitamin E was not associated with a reduced prostate cancer risk overall [9]. The amino acid L-arginine is a substrate for nitric oxide synthase which is increasingly used as a health supplement and has the potential to reduce vascular stiffness. In a randomized, double-blind, placebo-controlled trial, L-arginine, when added to standard post-infarction therapies, does not improve vascular stiffness measurements or ejection fraction and may be associated with higher post-infarction mortality [10].

– Overweight represents a major medical problem in our society. Orlistat and sibutramine are used to treat obese patients, but are also used as lifestyle drugs in subjects with normal body weight. They function as inhibitors of gastrointestinal lipid-metabolizing enzymes. Possible side effects are disorders of pigmentation, flatulence, bowel incontinence and rectal pain.

– Antidiabetics like metformin and lipid-lowers (simvastatin, rosuvastatin or cerivastatin) are popular substances, which are also abused as lifestyle drugs for weight reduction or to counterbalance high-fat meals ('the pill after the fat') [11]. Confiding in the alleged safety of these medications, people indulge in uncontrolled eating orgies, bringing their metabolism out of balance and meeting unnecessary side effects.

– Psychopharmaceuticals, especially SSRIs like fluoxetine (USA: Prozac), are also taken as lifestyle drugs to

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Table 1. Presently available lifestyle drugs (modified from Hesselink [8])

Nootropica	Psychopharmaca	Hormones	'Ecodrugs'	Others
Dimethylamino-ethanol (DMAE)	γ-Hydroxybutyrate (GHB)	Dehydroepiandrosterone (DHEA)	Absinth	Dextromethorfane (DXM)
Hydergine	Ketamine	Pregnenolone	Echinacea	Metformin
Piracetam	Fluoxetine	Melatonin	Kava-kava	Propranolol
Pramiracetam	Selegiline	Desmopressin (DDAVP)	Herbal ecstasy	Coenzyme Q
Acetyl-L-carnitine	*S*-Adenosyl-methionine (SAM)	Norethisterone	Ritual spirit	Orlistat
Oxiracetam	Methylphenidate	Contraception drugs	Guarana	Nimodipin
Aniracetam	Adrafinil/modafinil	Growth hormone	Chinese herbs	Centrophenoxin
Vinpocetine	Sibutramine	Anabolic steroids	Rose of Sharon	Clenbuterol
Idebenone	L-Tryptophan	Bremelanotide	Vitamins	NADH
Vincamine	Serotonin		Minerals	Phenytoin
Cyprodenate	Dexfenfluramine		Amino acids	Deprenyl
Yohimbine	Ecstasy (XTC)		*Gingko biloba*	Bupropion
	Ondansetron			
	Parlodel			

increase one's psychological drive, to facilitate social contacts, but also to lose weight. More recently, paroxetin has become widely fashionable as the 'pill for the still' in the context of sociophobia. Ritalin or atomoxetin (Strattera), indicated to treat attention-deficiency syndromes, are improperly used as stimulants to increase alertness and improve intellectual performance [12]. In this context, it is important to remind that often benzodiazepines are being widely used without proper indication [13].

– Modafinil (Vigil), registered for the treatment of narcolepsy, is improperly taken to prolong waking periods and alertness [14]. In Germany, the prescription and use of this substance is regulated by the law on narcotics.

– Donepezil is used for the treatment of Alzheimer's disease; currently, students take it as a lifestyle drug to increase cognition, improve learning, global function and memory. But the real efficacy is questionable and possible long-term side effects in the elderly may give rise to serious problems [15].

– Hardly any other medication as sildenafil (Viagra) has raised such a broad public discussion worldwide on private sexual behavior. Sildenafil, a phosphodiesterase inhibitor for therapy of erectile dysfunction, was introduced to the market in 1998. Meanwhile, in addition to sildenafil, new drugs like tadalafil and vardenafil with longer-lasting effects ('weekend pill') are available. Occasionally, sildenafil has been prescribed for women, as it has been to shown to have a (dose-dependent) effect in female sexual arousal disorder (FSAD) [16]. Among the side effects of sildenafil, one should especially be aware of possible cardiovascular complications which may even lead to death [17]. In recent years, additional rare side effects of phosphodiesterase inhibitors have been observed, such as non-arteritic anterior ischemic optic neuropathy (NAION, 50 cases) in the treatment of erectile dysfunction [18].

– Testosterone patches, testosterone transdermal systems and injections have been used for substitution therapy in deficiency syndromes. In the present discussion of the 'aging male syndrome', a decrease of testosterone is held responsible for a decline or loss of libido and other complaints like impairment of general well-being, decrease of muscle power, sleeping disorders, depression and 'nervousness' [19]. However, a scientific correlation of these symptoms to testosterone serum levels has not yet been proven. The new testosterone formulation (testosterone undecanoate) possesses long-term kinetics allowing application only four times a year, and mimics eugonadal testosterone serum levels without supra- or subphysiological serum concentrations [20]. Especially the gel application, available since 2003, is abused as a lifestyle medication in people whose testosterone levels are within the normal range. In a randomized, double-blind placebo-controlled study, the testosterone-patch Intrinsa® improved sexual function and decreased distress in surgically menopausal women, but there is no indication for this drug for similar complaints from the part of the Food and Drug Administration (FDA) [21]. In this context, it is interesting to point out a recent study on bremelanotide (PT-141 nasal spray), a hormone-like synthetic peptide that is a melanocortin analogue of the

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Table 2. Lifestyle drugs in aesthetic medicine (dermatology)

Medication	Indication	Lifestyle abuse
Isotretinoin/tretinoin	Acne vulgaris	Dorian-Gray syndrome (dream of eternal youth), stopping normal seborrhea
Minoxidil, finasteride	Androgenetic alopecia	Body dysmorphic disorder with unremarkable findings
Botulinum toxin, methanthelinium bromide	Hyperhidrosis	Suppression of normal exercise-dependent sweating, body dysmorphic disorder, sociophobia, shame disorder
Sildenafil, tadalafil, phentolamine, apomorphine	Erectile dysfunction	Eternal potency and 100% controllable erection
Testosterone	Testosterone deficiency	Midlife crisis
Somatotropin	Hypophyseal dwarfism	Fountain of youth, doping
Metformin, crestor, simvastatin, orlistat, sibutramine	Adiposity, diabetes, hypercholesterinemia	Anorexia nervosa, Sisi syndrome

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α-melanocyte-stimulating hormone, which acts as an agonist at the melanocortin receptors. Its effects on libido in both females and males are currently being investigated, whereby preliminary evaluations suggest a positive effect on desire and on arousal in women with sexual arousal disorder [22]. The erectogenic potential of bremelanotide and its efficacy in facilitating erections in patients who do not respond adequately to PDE5 inhibitors suggests that PT-141 may provide an alternative treatment for ED [23]. PT-141 was safe and well tolerated in two studies, but the drug is not yet available on the market [22].

– Growth hormones like somatotropin are nowadays gene-technically produced and hence available at low cost. The abuse of somatotropin by athletes is based on its allegedly strong anabolic effects. Furthermore, somatotropin is seen as a 'fountain of youth' in the elderly, a substance rendering those who take it younger and thinner [24]. As a lifestyle drug, this hormone is currently broadly used to strengthen muscles, reduce body fat, decrease wrinkles, increase energy and improve sexual life. Severe side effects, especially induction of diabetes mellitus and malignant neoplasms (or inducing progression of already existing ones), cannot be ruled out [25, 26].

Lifestyle Drugs of Special Interest in Aesthetic Medicine

In cosmetic medicine, lifestyle drugs are probably generally rather harmless and noninvasive compared with surgical procedures, but side effects cannot be ruled out. People request lifestyle drugs for (table 2): (a) cosmetic findings, which are usually a mere result of the natural aging process of the skin, and (b) norm variants (e.g. hyperhidrosis).

The current focus of controlled (prescription-only) lifestyle drugs is on skin rejuvenation, including antiwrinkle therapy, hair loss or sweating. The use of lifestyle drugs reflects the wish that skin and hair reveal youth and beauty at first sight. As a visible organ, the skin allows the patient to observe all physical symptoms in detail, so that the slightest findings are given an exaggerated importance. People who consult a physician often already have a precise idea of the treatment they wish to undergo.

– Vitamins, nutrient supplements, minerals, and skin creams have been aggressively promoted as being able to delay aging and prolong life. Vitamins A, E and C are used in prophylaxis and therapy of skin aging. In vitro investigations suggest positive effects of the vitamins A, C and E as potent antioxidants and partial stimulants of collagen synthesis [27]. However, increased mortality was observed in people who consumed very high amounts of vitamin E (>1,000 IU/day) [28].

– Low-dose isotretinoin medication is used to reduce physiological seborrhea and to prevent a 'shining face'. Possible side effects, like teratogenicity and metabolic impairments, are disproportionally serious if compared to the desired effect of isotretinoin as a lifestyle medication [29].

– Finasteride (Propecia) as a typical lifestyle drug is used to treat androgenetic alopecia, which is no disease in the proper sense. Finasteride is a 4-azasteroid, which inhibits the human type II of 5α-reductase in the hair fol-

licles and blocks the peripheral conversion of testosterone to androgen dihydrotestosterone. Reported side effects include reduced libido, a reduction in the ejaculation volume and erectile dysfunction as well as an increase in breast size. Numerous new market launches can be expected in this area (Dutasterid: 5α-reductase type I and II, Latanoprost) [30].

– Botulinum toxin is the neurotoxin of the anaerobic bacterium *Clostridium botulinum* and is used broadly in cosmetic medicine for wrinkles and sweating. It binds to presynaptic cholinergic nerve terminals and blocks the exocytosis of acetylcholine at the motoric and vegetative nerve ends [31]. Botulinum toxin is the strongest known poison and is responsible for the clinical signs and symptoms of botulism, a type of food poisoning. The use of botulinum toxin in aesthetic medicine is a lifestyle medication par excellence.

The Use of Lifestyle Drugs

Lifestyle drugs have become more and more a part of our daily life due to their widespread presence on the Internet, in commercials, on television and medical demands. Vitamin and mineral supplements are among the most commonly used drugs in the USA. In a study of 77,738 men and women, aged 50–76 years, in western Washington State, 66% used multivitamins, 46% used individual vitamin C, 47% used individual vitamin E, and 46% used calcium [32].

The use of lifestyle drugs in Germany is shown in one representative nationwide survey (n = 2,455): psychotropic drugs 7.3% (12.4% women 45–54 years, 6.8% women 65–74 years), weight reduction 5.3% (13.6% women 25–34 years, 2.1% women 65–74 years), hair growth 2.4% (8.0% men 45–54 years, 3.2% men 65–74 years), erectile dysfunction (3.7% men 65–74 years) [33].

Among 1,802 visitors of 113 fitness centers in Germany, 13.5% confessed to having used anabolic ergogenic substances at some point in time [34]. Besides health-threatening cardiovascular, hepatotoxic and psychiatric long-term side effects, acne occurs in about 50% as an important clinical indicator of anabolic substance abuse.

In 2006 alone, 24,237 cosmetic (anti-wrinkle) procedures with botulinum toxin were performed by the members of the German Society of Aesthetic Surgery [35]. Sildenafil was discussed in 0.5% (68/13,394) of consultations in general practice in London (Great Britain) and orlistat in 0.3% (42/13,394).

Nearly 20% of general practitioners thought such prescriptions were inappropriate [36]. Informed by the physician and the package inserts, users of lifestyle drugs in the majority of cases are well aware of the established and frequent side effects – e.g. cardiovascular complications with sildenafil – but nevertheless, they are ready to take them into account.

Also, the application of a polypill, which has as its ingredients a statin, an antihypertonic drug, folic acid, and aspirin, for subjects beyond 55 years of age for secondary prevention and without medical control cannot be justified. In all drugs, side effects and interactions are possible; pharmaceuticals are only labeled for specific indications, and with missing efficacy there could be a negative risk-benefit relation [37].

Meanwhile, nearly every lifestyle drug praised as 'medication for healthy people' can be purchased without medical control on the black market, especially via Internet or special shops, from worldwide distribution systems [8]. Until today, this black market for anti-aging and other lifestyle drugs certainly results in a vastly underestimated number of reported cases that by far exceeds the official numbers, as is for example evident from the worldwide market for human growth hormone that amounts to several billion dollars, i.e. much more than would be needed for treatment of dwarfs and cachectic and/or elderly patients.

Lifestyle Drugs and Emotional Disorders

Massive emotions like anger and rage may arise in the doctor-patient relationship when 'healthy' people – sometimes aggressively – demand a lifestyle drug belonging to a prescription-only group, and the doctor refuses because of contraindications or possible side effects [6]. Initially the patient idealizes the physician, but as soon as his expectations are not met, he instigates a conflict with the physician who then becomes an object of anger ('celebrity killer' behavior) [38]. Thus, the patient can liberate himself from the role of the putative passive sufferer.

But the group of lifestyle drug users also encompasses a considerable number of people suffering from emotional disturbances. The question of using or not using a lifestyle drug without medical need is to an extent that is not matched in other fields of medicine dependent on conscious or unconscious emotional motivations of the patient, and thus the psychosocial context must also be assessed and taken into account by physicians who are con-

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fronted with a request for a lifestyle drug. Hair loss for example, and especially the common androgenetic alopecia in men, is a frequent reason for consulting a dermatologist. With the introduction of the new lifestyle drug finasteride (Propecia) in January 1999, there has been a simultaneous increase in consultations of patients with a somatoform disorder – in particular with body dysmorphic disorder (BDD) – and regular scalp hair or with the wish of a preventive prescription of this lifestyle drug [39]. Patients with BDD worry about a non-existing defect in their appearance or heavily overrate a minimal, actually existing defect. The preoccupation causes clinically significant distress or impairment in social and occupational areas, or other important areas of functioning.

Men with muscle dysmorphia (the term indicates a pathological preoccupation with muscularity) have been shown to be significantly more likely to have abused anabolic-androgenic steroids (21.4%) [40]. In one study of individuals with BDD, 48.9% (n = 86/176) had a lifetime substance use disorder [41]. A pathological body image is associated with illicit use of anabolic-androgenic steroids. Patients with BDD may also seek costly treatments with botulinum toxin. The term 'botulinophilia' was inaugurated as a new diagnosis to designate a BDD of patients with a subjectively experienced hyperhidrosis that objectively cannot be confirmed by objective assessment [31].

When addressing physicians, patients with BDD often request some sort of cosmetic treatment. In a study on 289 patients with BDD disorder, 45.2% of adults had already undergone some dermatologic treatment without any improvement of their BDD symptoms [42].

As these examples demonstrate, lifestyle issues in medicine may be associated with somatoform disorders, the somatization of norm variants and the desire for somatic therapy of psychosomatic disorders.

Somatoform disorders (International Classification of Diseases: ICD-10: F45) are defined as repeatedly occurring presentations of physical symptoms associated with persistent requests for medical investigations, in spite of repeated negative findings and reassurances by doctors that the symptoms have no physical basis [41]. As a matter of fact, about 18.5% of the dermatology patients in a routine university outpatient clinic present with somatoform disorders, whereby BDD turns out to be especially predominant [43]. The prevalence of BDD is very high and estimated at circa 1.7% of the German population [44].

A special form of BDD is the wish of patients to stay young forever, termed the 'Dorian Gray syndrome', after the well-known 1891 novel by Oscar Wilde, *The Picture of Dorian Gray* [7]. The Dorian Gray syndrome is associated with narcissistic regression, sociophobia and the strong desire to remain young. Indeed, lifestyle medicaments are often used with the intention to stop or reverse the natural aging process.

Further differential diagnoses in cosmetic medicine include primary mental disorders (dysmorphic delusion, affective/bipolar disorder), personality disorder, acute stress reaction, secondary mental disorders and comorbidities [6].

Management of Patients Requesting Lifestyle Drugs

Physicians should consider the possibility of facing a patient suffering from a psychosocial impairment if the patient requests a prescription of a lifestyle drug. In these cases, an uncritical, straightforward prescription of the lifestyle drug may lead to chronification of unrecognized emotional disorders.

Patients with somatoform disorders will usually strictly deny a psychosocial relationship to the complaints reported [45]. A major resistance to a psychosomatic interpretation of a complaint is generally accompanied by the expectation of a purely somatic treatment. Thus, the desire for therapy with lifestyle drugs is often an attempt to achieve an emotional balance with the help of a drug, thus attaining a 'pseudosolution' of an unconscious emotional conflict at the organic level. Medicalization of physiological life is expected to solve psychosocial problems, but the treatment is bound to fail if the causally significant emotional disorder behind the symptoms is ignored.

The question as to when psychotherapy is indicated depends on coexisting diseases and conflicts as well as on the motivation of the patient. There are studies supporting the efficacy of behavioral cognitive therapy with cognitive restructuring in BDD [46].

The indication for psychopharmaceutical therapy generally depends on the emotional disorder in the foreground and the primary target symptoms. One randomized placebo-controlled study showed the efficacy and safety of fluoxetine both in delusional and non-delusional BDD patients [47].

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Conclusion

The use of lifestyle medications in an uncritical manner is contraindicated. Lifestyle drugs need a precise indication and physicians must be aware of possible abuse, long-term risks, complications and side effects. Patients with psychological disturbances sometimes willingly ignore possible risks and complications or deny side effects. Psychosomatic disorders must be excluded in the entire area of lifestyle medicine in any patient.

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