Fortnightly review

Work factors and upper limb disorders

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In 1713, Ramazzini wrote of upper limb problems in professional writers (box).[1] His observations of causative factors (prolonged static postures, highly repetitive work, psychological attributes of the work) and difficulties in treatment and management are still debated today.

Classification and diagnosis

Precise identification of the tissue(s) responsible may be difficult in symptom based conditions. The non-specific soft tissue disorders may involve loss of grip and pinch strength, and nerve dysfunction, and are the source of concern, debate, and, often, litigation. Other disorders of the upper limb may allow a definite diagnosis. The diagnostic criteria used may depend on the setting—for example, sensitive criteria (low false negative rate) may be needed in an occupational setting and more highly specific criteria used in secondary or tertiary care to avoid overdiagnosis. Prospective studies support the relation between physical exposures in the work system and upper limb disorders.[2] Some studies show a relation between increased exposure and increased response.[3 4] There is some conflict between the epidemiological findings and current theory relating to underlying disease and possible mechanisms for the disorders under investigation.[5]

Methods

Current epidemiological evidence is often based on studies with weak designs.[6 7] The consistency in the results, however, strongly supports a relation with factors arising from work. Here, I review evidence on selected disorders that provide insights into the associations and aetiology of this group of disorders.[3]

> The diseases of persons incident to this craft arise from three causes: first constant sitting, second the perpetual motion of the hand in the same manner, and thirdly the attention and application of the mind .... Constant writing also considerably fatigues the hand and whole arm on account of the continual and almost tense tension of the muscles and tendons. I knew a man who, by perpetual writing, began first to complain of an excessive weariness of his whole right arm, which could be removed by no medicines, and which was at last succeeded by a perfect palsy of the whole arm.
>
> Ramazzini (1713)[1]

Summary points

- Occupational and work associations with pain in the shoulder, arm, and hand have been recognised for almost 300 years
- The most important work system factors are prolonged static muscle load; highly repetitive and monotonous work; high force exertions or mechanical compression of tissues, especially at the hands; use of vibrating equipment and tools; and work with many deadlines and little control
- Surprisingly few objective data or epidemiological studies exist on the importance of individual factors (such as age), systemic conditions, and activities outside work
- Management of the conditions is enhanced through early reporting or presentation and liaison in the workplace
- The importance of active surveillance to identify people with symptoms and those at risk should be emphasised to employers
- All studies are hampered by the difficulty in defining diagnostic criteria and the problems of obtaining valid measurements of exposure to risk

Articles were selected for this review from an extensive search of the current literature and computerised searches of Medline and Ergonomic Abstracts (keywords: upper limb, neck, shoulder disorders, work related) along with key review papers published in high quality peer reviewed journals over the past five years.

Carpal tunnel syndrome

Carpal tunnel syndrome has been studied widely. Workers in the garment industry had a threefold increase in risk compared with hospital workers,[8] and oyster and crab packers had a relative risk of 14.8 and meat and poultry industries 13.8 compared with industry wide levels.[9] More specific studies have found odds ratios of 15.5 for workers in jobs requiring high force and high repetition compared with those in low

exposure groups; high repetition on its own had an odds ratio of 5.5.[10] People working with flexed wrists and those working with extended wrists had odds ratios of 8.7 and 5.4 respectively,[11] whereas industrial workers exposed to jobs requiring high force and high repetition had an odds ratio of 4.0 compared with those doing light work.[12] Others have also reported significant findings.[13] Using hand held vibrating tools also increases the risk (different studies have found odds ratios of 4.8 and 7.0), as does repetition of wrist movements (odds ratios 4.6 and 2.0).[14 15] Most of these studies have controlled for age and sex, where feasible.

Although some studies have considered the potential protective effect of work,[16] there is considerable evidence that carpal tunnel syndrome is strongly associated with several factors in the work system. This is consistent with the probable mechanisms leading to the syndrome—namely, the stretching or compression of the median nerve at the wrist, and ischaemia.[3] This, coupled with the increase in pressure in the carpal tunnel when the wrist is in extreme postures, helps clarify the process leading to the syndrome. Individual factors associated with this condition, such as obesity,[17] are considered further below.

Lateral epicondylitis

In two studies of lateral epicondylitis, risk was sixfold greater in exposed groups than controls.[2 18] Exposure in the groups was defined as strenuous work requiring use of the muscle tendon structures of the upper limb. In another study, more strenuous work led to the reporting of more symptoms, but clinical examination showed a similar prevalence in groups doing strenuous and non-strenuous work.[19] Other research, however, did not support a work related aetiology.[20] Unfortunately, none of these studies considered exposure with regard to the extensor muscles of the forearm or cumulative exposure. Though this condition is often known as tennis elbow, there are few studies of the role of tennis in such disorders.[3]

Hand-wrist tendinitis

High risks for hand-wrist tendinitis have been found in groups such as meat processing workers and workers in other manufacturing industries. Large increases in risk (odd ratios 36,[2] 29,[21] 7,[22] and 8[20]) strongly support the association between work exposure and hand-wrist tendinitis. A meta-analysis found the adjusted odds ratio for hand-wrist tendinitis to be 9.1 (95% confidence interval 4.9 to16.2).[23]

Neck and shoulder disorders

Though lacking specificity in outcome measures, many studies have found associations between factors within the work system and disorders of the neck and shoulder.[3 5] Both physical and psychosocial work system factors show significant associations,[24 25] but the strongest associations have been found with physical factors at work.[26] Cumulative exposure also seems to have an effect.[4]

Hand-arm vibration syndrome

Vibration applied to the hand is associated with serious disturbance of the vascular system (Raynaud's disease or vibration white finger). It seems probable that vibration impairs muscle strength, and it may lead to osteoarthritis of the wrist and elbow.[3] Vibration is thought to alter the feedback from the mechanoreceptors in the hand, which may lead to overlarge forces being exerted to operate the tool, and the tonic vibration reflex leads to further muscle load.[3] The use of vibrating tools often requires high forces at the hand because of the intrinsic design of the tools (their weight and size) and the tasks being performed.

Non-specific conditions

Studies of non-specific conditions tend not to have specific outcome measures. Many have used symptom questionnaires, and then used symptoms of pain and discomfort at specific body sites to assess the strength of association to work related factors.[3] Some studies have reflected on the lack of an identifiable pathological basis for these disorders coupled with the uncharacteristic pain patterns.[6] The reported pain may arise from muscle or tendons, and psychological events may be contributing to patterns of pain reporting and subsequent chronic pain.[3]

High relative risks for butchers (11.5), food industry workers (8.8), and packers (7.9) have been recorded.[27] Risk factors reported for these disorders show consistency for highly repetitive work, static or constrained neck and shoulder postures, and high physical loads or forces at the hand as well as for the duration and intensity of exposure. A study of sewing machine operators found that those working only a few hours a day had fewer problems, but this shorter exposure postponed the onset of symptoms only by about six months.[28] Mechanisms for muscle disorders are consistent with this reporting pattern. However, in the absence of detailed clinical histories of these disorders it may be some time before the true underlying pathology is understood. That said, those who currently suggest a predominantly psychological or psychosomatic origin do so with little, if any, supporting evidence. Although personal characteristics and other environmental and psychosocial factors may contribute, most evidence shows that there are several important work related risk factors.[3]

Individual factors

Most epidemiological studies consider age and sex, but it is less clear which additional factors should, or could, be

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Individual factors and upper limb disorders

Factor	Carpal tunnel syndrome	Hand-wrist tendinitis	Epicondylitis
Age	Conflicting evidence	No association	Association
Sex	Women at increased risk, but evidence not consistent	Women at increased risk, but evidence not consistent	Insufficient data
Anthropometric characteristics	Association	Insufficient data	Insufficient data
Anatomical differences	Conflicting evidence	Insufficient data	Insufficient data
Obesity (weight, body mass index)	Association	Insufficient data	Insufficient data
Systemic diseases (inflammatory diseases, arthritis, etc)	Association	Association	Insufficient data
Unaccustomed to work	Insufficient data	Association	Insufficient data
Recreational activity	Insufficient data	Insufficient data	Association

Adapted from E Viikari-Juntura (personal communication).

considered. For example, significant increases in risk for carpal tunnel syndrome associated with obesity (body mass index) have been reported,[17] but few studies have paid equal attention to details of work systems and individual factors. Age has been recognised as having an effect, but findings are not consistent. Other factors such as time in the job and reproductive status (in women) require control before conclusions can be reached.

The table provides an overview of studies that have shown an association between individual factors and various conditions. Though consistent or strong associations have been found,[12] the table is dominated by conflicting results and lack of information. Thus, sex differences may be due to genetic differences or to gender differences in exposures at and away from work. For example, although the incidence of carpal tunnel syndrome seems to be more common in women (male:female ratio of 1:3),[29] studies that have controlled for exposure show no evidence of greater susceptibility to work related carpal tunnel syndrome in women.[9] Differences may be due to differences in anthropometric variables, physical strength, or the tasks performed rather than to sex differences. Studies of physical dimensions (of the carpal canal, for example) have produced conflicting results,[3] and there is little to support the belief that previous trauma increases susceptibility. Although the importance of individual factors must be recognised, and should be studied further, current evidence indicates that exposure to hazards in the work system is important.

Behaviour of the worker is an additional factor in determining the modification of exposure. For example, some workers may feel more able to take short rest pauses and thus alleviate potential fatigue than do others. Similarly, highly motivated workers may exceed normal thresholds and cause "damage" in much the same way that people participating in active sports may injure themselves through overexertion.

Checklist for surveillance of risk factors

- Awkward postures (eg deviated wrist)
- High static muscle load (eg neck, shoulder girdle)
- High force exertion at hands
- Sudden applications of force
- Work with short cycle times
- Little task variety
- Frequent tight deadlines
- Inadequate rest or recovery periods
- High cognitive demands
- Little scope for control over work
- Cold work environment
- Exposed to vibrating equipment
- Localised mechanical stresses on tissues
- Poor social support

Factors outside work

Little is known of the contribution of factors outside of work to the development of disorders of the upper limbs. Some sporting activities are commonly thought to have an association, but there is little epidemiological evidence to support these beliefs. The same is true of hobbies such as knitting. The role of soft tissue mechanisms of trauma and injury to the soft tissues of the upper limbs has been reviewed extensively elsewhere.[3]

Developments in the understanding of muscle pain and injury would seem to be particularly relevant to the non-specific disorders.[30] If the pattern of pain and resultant behaviour is to be fully understood the mechanisms by which skeletal muscle can become damaged (physical trauma, eccentric exercise, metabolic depletion, etc) must be seen in the context of the system as a whole (pressure on nerve tracts, stresses on articulating surfaces, etc) rather than as discrete entities. Low level continuous contractions and static load on the musculoskeletal system may produce changes in the muscle that lead to chronic muscle pain.[3] The role of intramuscular pressure is important but has yet to be fully explained.[31] Small amounts of shoulder abduction or flexion can cause large increases in intramuscular pressure. The occluded and impaired blood flow may lead to chronic muscle damage.[32]

Although most reports of muscle disorders seem to be of those in the shoulder and neck, other examination procedures enable reporting of muscle disorders of the wrist, and in particular the extensors.[33] Static load on nerve tissue (for example, constant hydrostatic pressure) may be critical at relatively low pressure, for example 4000-8000 Pa[34]; pressure in the carpal tunnel with the wrist flexed and extended may approach these values.[35] The recruitment patterns of motor units in specific muscles suggest that units may become overloaded even at very low levels of static loading during contractions of long duration.[36] Changes in slow motor units in patients with chronic muscle pain have been shown.[32 37] Pain may increase muscle activation, which in turn contributes to the chronicity of muscle pain in the neck and shoulder muscles. The relation between acute and chronic pain is important in understanding the course of these disorders and the relation between specific activities and the reoccurrence of pain.[38] The relation between fatigue, pain, and disorder requires further research.

Cold may affect the development of upper limb disorders directly and also indirectly from the use of protective equipment (gloves). The muscles must exert greater force to overcome the restrictions of the protec-

tive clothing and as a result of difficulties in coordinating and applying the appropriate strength at the hand.

Preventing and managing disorders

The need for early intervention in the workplace is well recognised.[3] Prevention of upper limb disorders may be facilitated by surveillance of hazardous exposures, people at risk, and early symptoms (box). Experience from other musculoskeletal disorders (back pain, for example) suggests that the mislabelling of patients and mismanagement at the early stage of presentation may well have an effect on the subsequent course of the disorder. On the basis of the current evidence, treatment and management must consider whether the condition might be related to work. General treatment regimens have been reviewed and summarised elsewhere.[26 39]

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Lesson of the week

Oxybutynin and cognitive dysfunction

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Anticholinergic drugs have been used since the 19th century, when belladonna alkaloids were first given for treatment of Parkinson's disease. Their use declined because they were poorly tolerated, particularly by elderly patients. Recently, anticholinergic drugs have started to be used again for treating detrusor instability and hyperreflexia. Oxybutynin is an antimuscarinic used for this purpose, and its efficacy and adverse effects have been described.[1 2] We report four cases of cognitive dysfunction in association with oxybutynin treatment.

Case reports

Case 1—A 79 year old man with Parkinson's disease, chronic obstructive pulmonary disease, peptic ulcer disease, and irritable bladder was seen regularly in the clinic for Parkinson's disease at this hospital. He was taking selegiline, co-beneldopa, ranitidine, theophylline, intermittent courses of prednisolone, and inhaled beclomethasone dipropionate and salbutamol. In May 1994 he developed mild cognitive impairment. Selegiline was

Oxybutynin may cause acute confusional states in elderly patients with pre-existing cognitive impairment

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discontinued; this resulted in a noticeable improvement. His score in the abbreviated mental test was 9/10. Later that year he started taking oxybutynin (2.5 mg three times a day) for his urinary symptoms. His nocturnal confusion worsened, with symptoms including hallucinations, behavioural disturbance, anxiety, and paranoia. Oxybutynin was discontinued and he rapidly returned to his previous mental state, again scoring 9/10 in the abbreviated mental test.

Case 2—An 80 year old man with Parkinson's disease, ischaemic heart disease, congestive cardiac failure, cerebrovascular disease, mild cognitive impairment, prostatism, and temporal arteritis attended the clinic. He was taking isosorbide mononitrate, frusemide, amiloride, naftidrofuryl oxalate, prednisolone, and co-beneldopa. Between 1987 and 1996 his cognitive function declined, resulting in severe dementia secondary to multiple cerebral infarction. He had several episodes of acute deterioration of a chronic confusional state due to pneumonia, depression, and a flare up of his temporal arteritis. All of these episodes resolved after treatment of the underlying cause. In April 1996 he began taking oxybutynin (2.5 mg three times a day) for detrusor instability. Within a few days he developed a florid confusional state with hallucinations and paranoia. On withdrawal of oxybutynin he quickly returned to his previous mental state.

Case 3—A 79 year old man with Parkinson's disease, mild cognitive impairment, and urinary incontinence resulting from transurethral resection of the prostate was seen in the clinic. He was taking co-beneldopa and selegiline. He began taking oxybutynin (2.5 mg twice a day) for detrusor instability in June 1995. Five months later the dose was increased to 5 mg twice a day. The patient became so confused that he was admitted to hospital. On withdrawal of oxybutynin his confusional state subsided.

Case 4—An 85 year old patient with a history of Parkinson's disease, hiatus hernia, Raynaud's disease, and severe dementia (abbreviated mental test score 0/10) attended the clinic. He was taking co-beneldopa, bromocriptine, selegiline, ranitidine, diltiazem, and chlormethiazole. In November 1995 he began taking oxybutynin (2.5 mg twice a day) for urgency of micturation and incontinence. One week later the dose was increased to 5 mg twice a day. This led to acute psychosis with hallucinations and behavioural disturbance. Selegiline and oxybutynin were discontinued and his mental state slowly settled.

Discussion

Oxybutynin has a dual action in reducing detrusor motor instability and hyperreflexia. Its primary action is musculotrophic—acting directly on the bladder muscle as an antispasmodic agent. Its secondary action is neurotrophic—acting on muscarinic receptors.[3] The predominant stimulus to bladder contraction is parasympathetic, cholinergically mediated innervation. Oxybutynin produces systemic cholinergic effects, most commonly dry mouth, blurred vision, and constipation (Smith and Nephew, datasheet on oxybutynin).

Anticholinergic drugs have been associated with cognitive changes when used for treating Parkinson's disease.[4] Changes in mental state secondary to oxybutynin have not been described in the literature and are not referred to in the *British National Formulary*.[5] The Committee on Safety of Medicines has received reports of 73 psychiatric adverse reactions to oxybutynin; these include 13 of confusion, 1 of paranoia, and 13 of hallucinations (Committee on Safety of Medicines, personal communication).

Research suggests that acetylcholine has a role in cognition. The deficit in acetylcholine in patients who have Alzheimer's disease is due to loss of forebrain neurones that innervate the cortex.[6] Several studies have shown reduced activity of acetylcholine transferase (a marker of cholinergic innervation) in the frontal cortex in Parkinson's disease.[7] Atrophy of Meynert's nucleus, which is the source of cholinergic innervation of the cortex, has been found in Alzheimer's and Parkinson's disease.[8] Changes in muscarinic receptor density, sensitivity, and binding in the frontal cortex have also been described.[9–11]

Oxybutynin crosses the blood-brain barrier and may cause electroencephalographic abnormalities in healthy volunteers.[12] Muscarinic receptors are widespread in the central nervous system, especially postsynaptic M1 and M2 receptors.[13] Oxybutynin acts primarily on M1 receptors; hence unwanted central nervous system side effects should be expected.

Studies on the pharmacokinetics and clinical effects of oxybutynin in elderly patients have not described mental changes.[3] Our cases show that this drug may precipitate acute confusional states in elderly patients with Parkinson's disease who are cognitively impaired. Caution should be used when administering this drug to elderly patients, particularly when they have cognitive impairment and are receiving multiple drug treatment.

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