Review

Preoperative alcoholism and postoperative morbidity

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Background: Preoperative risk assessment has become part of daily clinical practice, but preoperative alcohol abuse has not received much attention.
Methods: A Medline search was carried out to identify original papers published from 1967 to 1998. Relevant articles on postoperative morbidity in alcohol abusers were used to evaluate the evidence.
Results: Prospective and retrospective studies demonstrate a twofold to threefold increase in postoperative morbidity in alcohol abusers, the most frequent complications being infections, bleeding and cardiopulmonary insufficiency. Wound complications account for about half of the morbidity. The pathogenic mechanisms include preoperative immune incompetence, subclinical cardiac insufficiency and haemostatic imbalance. In addition, surgical trauma and/or postoperative abstinence result in an exaggerated stress response, which may further contribute to postoperative morbidity.
Conclusion: Alcohol consumption should be included in the preoperative assessment of likely postoperative outcome. Reduction of postoperative morbidity in alcohol abusers may include preoperative alcohol abstinence to improve organ function, or perioperative alcohol administration to avoid the abstinence response.

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Introduction

Preoperative estimation of likely postoperative outcome has become part of the routine when considering surgical intervention. Several scoring systems have been validated to quantify cardiac risk, overall morbidity and mortality[1–3]. However, preoperative chronic alcohol abuse has not received much attention, although it seems to be a potential predictor of impaired postoperative outcome. This article reviews the literature to estimate the potential additional risk of preoperative alcohol abuse, to evaluate possible pathogenic mechanisms, and to outline strategies for prevention.

Definitions

Alcohol abusers are defined by consumption of at least five drinks (more than 60 g ethanol) per day for several months or years[4–11]; one drink contains on average 12 g ethanol. All but two outcome studies[9,10] have excluded abusers with signs of alcohol-related symptomatic illness, which in itself may add to surgical risk. In addition to the dose definition, two studies[8,9] have included alcohol-dependent patients who meet the criteria of the *Diagnostic and Statistical Manual of Mental Disorders* (third edition, revised) (DSM-IIIR) of the American Psychiatric Association[12] or the Michigan alcoholism screening test[13]. Dependent patients have an increased risk of developing the alcohol withdrawal syndrome (AWS), potentially adding to postoperative morbidity. Other patterns of abuse, such as binge drinking *versus* daily intake, life-time *versus* short-lived abuse, female *versus* male, have not been evaluated in relation to surgical outcome. Henceforth the term alcohol abuse is defined as a daily intake of at least 60 g ethanol without signs of alcohol-related illness, unless otherwise stated.

Methods

A formal Medline search was carried out using the keywords postoperative morbidity or complications combined with alcohol* (asterisk denotes use of a truncated word) over the period from 1967 to 1998. A total of 379 citations was found, of which 235 included patients with alcohol-related illness (predominantly cirrhosis). Of the remainder, 57 did not involve surgery and 27 were reviews, case reports or letters; 33 did not differentiate between surgical and non-surgical patients in the study population, evaluating the outcome of a specific diagnosis or trauma rather than

surgical outcome. Thirteen authors did not define alcohol abuse in any terms and/or gave information of the consumption at the time of surgery. Two studies had methodological shortcomings combined with small patient numbers. Of the remaining 12 studies, four were parallel publications in the *Danish Medical Journal* (*Ugeskrift for Laeger*) with permission. The final eight publications are included in this paper[4–11].

The evidence

Several retrospective studies have suggested that alcohol abusers to have a twofold to threefold increased rate of morbidity compared with matched patients who have no more than two drinks daily. The evidence comes from different types of procedure, major and minor, elective and acute (*Fig. 1*)[4–7]. The abusers had on average a 50 per cent longer hospital stay, from 3 to 9 days depending on the type of operation[4–6], and required significantly more secondary surgery, probably as a consequence of the increased postoperative morbidity after the primary operation[4–7]. The long-term outcome after 3 months also seemed poorer than that of non-abusers[5–7]. Recently, prospective comparative studies have confirmed the increased postoperative morbidity of alcohol abusers (*Fig. 2*)[8–11]. The high incidence of complications in alcohol abusers is not explained by hepatitis or cirrhosis[8].

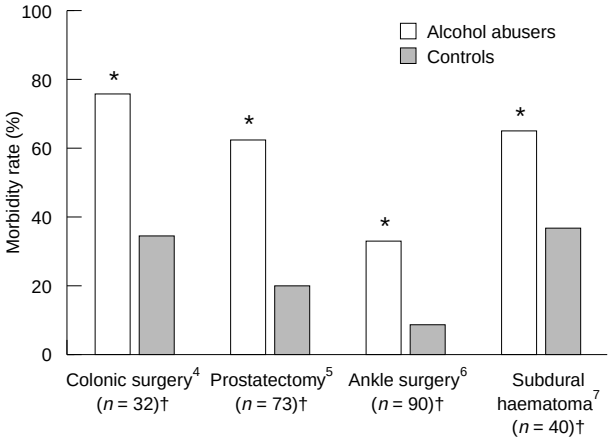

Fig. 1 Retrospective studies[4–7] of postoperative morbidity in alcohol abusers and controls. *$P < 0{\cdot}05$ *versus* controls; †number of alcohol abusers

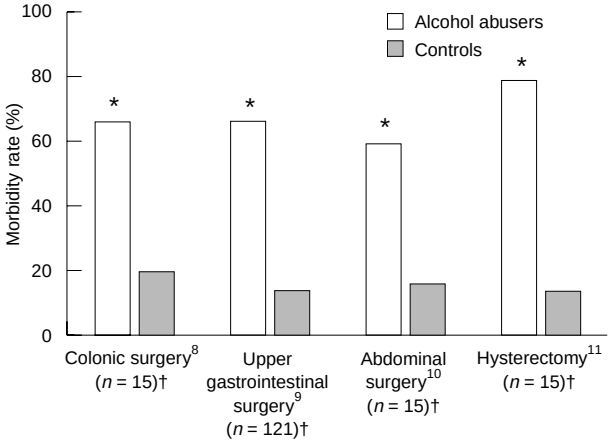

Fig. 2 Prospective studies[8–11] of postoperative morbidity in alcohol abusers and controls. *$P < 0{\cdot}05$ *versus* controls; †number of alcohol abusers

In both retrospective and prospective studies, the most frequent complication was infection, followed by bleeding problems and cardiopulmonary insufficiency requiring intensive care. Infections included superficial and deep abscesses, pneumonia, urological infections and bacteraemia. About half the complications consisted of wound infection, haematoma or wound rupture, all requiring therapeutic intervention.

All alcohol abusers developed AWS in one study[9], while 0–25 per cent of the abusers in the other studies developed AWS after operation[4–8,10,11]. The postoperative mortality rate was increased threefold in abusers after major surgery (7–35 per cent), but increased significantly in only two studies[7,9]. This evidence is based on a relatively small number of alcohol abusers, but preliminary results from an ongoing study of 341 patients support the importance of alcohol abuse as a predictor of postoperative morbidity; this is also true after controlling for confounders[14].

Pathogenic mechanisms

The mechanism of the increased surgical risk in alcohol abusers is probably multifactorial and includes preoperative alcohol-induced dysfunction of several organ systems, an exaggerated surgical stress response and/or abstinence-induced organic dysfunction.

Immune incompetence

Chronic alcohol abuse leads to immune incompetence with an increased risk of infection and cancer[15,16]. Ethanol suppresses a variety of T cell-dependent processes involving lymphocyte migration, cell to cell adhesion and activity of membrane-bound enzymes, thus altering the signal transduction across the membrane followed by a change in immune capacity[17]. Furthermore, the mobilization and phagocytic capability of monocytes, macrophages and neutrophils are reduced[18]. Finally, chronic alcohol abuse

may decrease the activation and proliferation of T lymphocytes, the production of free oxygen radicals and cytotoxic activity, and the production of interleukin (IL) 1, IL-2, IL-6 and tumour necrosis factor after stimulation[18]. As a consequence, delayed-type hypersensitivity (DTH) is suppressed[19]. Impairment of the DTH response may have clinical relevance since it is related to increased risk of postoperative infection[20]. Conflicting results have been reported with regard to impairment of natural killer cell activity, which seems to be related more to associated liver disease than to alcohol consumption[21].

Although most of these immunological changes have been demonstrated to be related to alcohol, other factors, such as malnutrition and cigarette smoking, may contribute to the increased susceptibility to infection in alcohol abusers. In addition, surgical trauma *per se* may induce immune suppression[22]. In the alcohol-abusing patient a more pronounced perioperative suppression of DTH has been demonstrated after colorectal resection compared with that in non-abusers, concomitant with an increased surgical stress response[8].

The immune suppression is reversible during abstinence from alcohol in non-surgical patients. The depressed myelopoiesis characterized by primitive blasts in the bone marrow improves about 2 days after ethanol withdrawal[23]. However, functional reversibility is much slower; 2 weeks of abstinence is necessary to improve DTH, with normalization after 2 months[19].

Alcoholic cardiomyopathy

Although minor alcohol intake of a few drinks per day may prevent ischaemic cardiac morbidity and mortality, long-term abuse predisposes to congestive cardiomyopathy, characterized by a dilated left ventricle and reduced ejection fraction[24]. More discrete changes induced by alcohol are subclinical myocardial damage and dysrhythmias in the absence of overt congestive heart failure or hypertension[24]. As a result of a direct toxic effect of alcohol on the ultrastructure and function of mitochondria, alterations of the cardiac electromechanical coupling and dysfunction of contractility develop before the hypertrophy[24]. About one-third of chronic abusers may have evidence of preclinical cardiomyopathy with lowered ejection fraction[25].

During major surgery, cardiac work increases with haemodynamic changes and higher pulmonary resistance due to sympathetic stimulation. The preoperative subclinical dysfunction (reduced ejection fraction) in alcohol abusers may predispose to postoperative cardiac complications, such as dysrhythmias[8] and cardiac failure[4]. Alcohol-induced cardiac dysfunction is usually reversible after 1 month of withdrawal among symptom-free abusers[26], and symptomatic alcoholic cardiomyopathy is improved in about half of patients after 3–6 months of abstinence[27].

Haemostatic imbalance

Alcohol consumption alters haemostatic function by modifying coagulation and fibrinolysis. Platelet count and mean volume are reduced in chronic abusers, because alcohol suppresses thrombopoiesis at the level of megakaryocyte maturation[28]. Platelet aggregation in response to collagen, adrenaline, arachidonic acid, platelet-activating factor and adenosine diphospate is also reduced, and the release of thromboxane A_2 and B_2 is inhibited[29]. Experimentally, ethanol administration inhibits the activity of phospholipase A_2, thus reducing the synthesis of arachidonic acid metabolites[30]. The defective haemostatic function in alcohol abusers is demonstrated by a prolonged bleeding time[28,31].

Moderate drinking reduces the fibrinogen level[32], and an inverse correlation between fibrinogen and coagulation factors VII and VIII with alcohol use has been reported in women, but not in men[33]. Alcohol increases fibrinolytic activity by promoting release of plasminogen activators and reducing inhibitors[34]. A possible mechanism involves a direct effect of alcohol on the fibrinolytic protein components localized on the cell surface[35]. The exact role of alcohol on coagulation has not been evaluated; severe coagulation defects in alcohol abusers may be caused by secondary liver disease.

Surgical intervention *per se* causes activation of both coagulation and fibrinolysis, followed by depression of fibrinolysis, thereby increasing the risk of thromboembolism[36]. Alcohol-abusing surgical patients have a significantly prolonged bleeding time before, during and after operation[8], which may account for the increased risk of bleeding complications[4–8,11]. The risk of postoperative thromboembolic complications in abusers seems to be comparable to that in non-abusers, but the small size of study populations does not allow final conclusions to be drawn[4–8,11]. During withdrawal, platelet count and thromboxane formation increase, and the prolonged bleeding time decreases after 1 week[37]. However, limited data do not allow any conclusions relevant to surgical patients.

Wound healing

It has recently been reported[38] that alcohol abuse has a more significant relationship with surgical wound infection than either wound contamination or duration of operation greater than 2 h. Examination of wound healing in otherwise healthy alcohol abusers has revealed a significantly poorer accumulation of protein[39]. In addition, the

surgical insult is associated with a reduced accumulation of collagen[40]. The demonstrated increased risk of wound complications is probably due to a combination of suppressed immune function, impaired haemostasis and reduced wound healing. Eight weeks of abstinence in non-surgical abusers may improve wound healing[39].

Stress

Acute alcohol intake activates the hypothalamic–pituitary–adrenal (HPA) axis with a dose-related increase in adrenocorticotrophic hormone (ACTH) in experimental and clinical studies[41,42]. During prolonged abuse, the HPA axis may remain activated and the hyperactivity may even cause a pseudo-Cushing syndrome[43], although habituation often takes place. The mechanisms include alcohol-induced release of corticotrophin-releasing factor and ACTH secretion and/or a direct effect of alcohol on the adrenal cortex[43].

Surgical trauma increases HPA axis and sympathetic activity, more so in chronic abusers than in non-abusers[8]. Similarly, experimental haemorrhage in alcohol abusers is followed by a higher noradrenaline response, but with a delay in the upregulation of blood pressure[44]. Experimental studies suggest that impairment of the cardiovascular response in such circumstances is related to a protracted metabolic acidosis during the posthaemorrhagic phase[45]. The enhanced surgical stress response in abusers may contribute to immune suppression, poor haemostatic function and increased demands on the heart, which together may all increase the risk of postoperative morbidity.

Alcohol withdrawal induces an endocrine and metabolic stress response, and the resulting increase in plasma noradrenaline concentration correlates with the severity of symptoms of abstinence[46]. The catecholamine response reverses after 2–7 weeks, and the ACTH concentration normalizes within 1–4 weeks of abstinence[47], although hypercortisolaemia is still measurable after 4 weeks[47]. The stress response may be more pronounced in patients who develop significant AWS, which is associated with hallucinations, seizures and cognitive disorders[48]. Patients with AWS seem to have increased postoperative morbidity and mortality compared to alcohol abusers without AWS[9].

Clinical implications

The apparent pronounced increase in postoperative morbidity in alcohol abusers has widespread physical, psychological and economic consequences. The order of magnitude involved compares with that of the most common predictors of surgical morbidity, but alcohol abuse has not been included as a risk factor in such indices[1–3]. Hypothetically, the first step in reducing postoperative morbidity should be preoperative withdrawal from alcohol, which may improve the preoperative alcohol-induced organic dysfunction. Reversal of immunosuppression, cardiac dysfunction, haemostatic imbalance and increased endocrine activity may occur within 1 week to 3 months of abstinence. Unfortunately, no conclusive data are available to demonstrate the effect of such a prophylactic intervention on postoperative morbidity. Preliminary observations suggest that 4 weeks of preoperative abstinence in alcohol abusers may reduce postoperative morbidity after colonic surgery[49].

For emergency procedures and subacute operations for which preoperative withdrawal is impossible, prevention of the abstinence response, which may have detrimental consequences when superimposed on surgical stress, is logical. However, a single dose of preoperative ethanol does not reduce the endocrine response to surgery[50]. Postoperative infusion of a large dose of ethanol, along with chlormethiazole, clonidine and benzodiazepines, may prevent alcoholic withdrawal symptoms[51,52]. However, no data are available on the effect of prophylactic perioperative ethanol infusion on postoperative morbidity in alcohol abusers. Finally, alcohol-abusing surgical patients seem likely to benefit from multimodal intervention with a focus on early rehabilitation[53].

In conclusion, alcohol-abusing surgical patients have significantly increased postoperative morbidity, prolonged hospital stay and requirement for secondary surgery. Therefore, alcohol consumption should be included in any preoperative assessment. Interventional studies on preoperative alcohol abstinence and/or prophylactic alcohol administration to avoid the acute withdrawal response are much needed.

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