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REVIEW

Obesity and the risk and outcome of infection

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The interactions between obesity and infectious diseases have recently received increasing recognition as emerging data have indicated an association between obesity and poor outcome in pandemic H1N1 influenza infection. Obesity is an established risk factor for surgical-site infections, nosocomial infections, periodontitis and skin infections. Several studies indicate that acute pancreatitis is more severe in the obese. Data are controversial and limited as regards the association between obesity and the risk and outcome of community-acquired infections such as pneumonia, bacteremia and sepsis and obesity and the course of HIV infection. As the cause–effect relationship between obesity and infection remains obscure in many infectious diseases, further studies are warranted. The consequences of obesity may have substantial effects on the global burden of infectious diseases.

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INTRODUCTION

The incidence of obesity has increased rapidly during recent decades. More than 30% of Americans are obese, as are more than a quarter of men and women in several European countries.[1] According to the World Health Organization definition, a person is considered overweight if her/his body mass index (BMI) is >25, and obese if BMI is $\geqslant 30$.[2] A recent study on the Framingham Cohort indicated that the number of years lived with obesity is directly associated with the risk of mortality.[3]

Emerging data indicate an association between obesity and infectious diseases.[4] Although the mechanism underlying these findings is not well established, a number of potential factors may be involved (Table 1).[5] Obesity may influence either the risk of getting an infection or the outcome of an infection once it is established. Obesity-related immune system dysregulation, decreased cell-mediated immune responses, obesity-related co-morbidities, respiratory dysfunction and pharmacological issues have been proposed as possible mechanisms.[4,6] In the absence of sufficient scientific evidence, no dosing guidelines of anti-microbials for obesity have been published, although such would be eagerly awaited.[7]

The evidence would appear more substantial regarding the association between nosocomial as opposed to community-acquired infections, except for the recent findings in influenza pandemics. This may be due to the fact that the BMI is recorded routinely only in patients undergoing invasive and surgical procedures, which enables study of this association retrospectively, whereas the BMI is not usually recorded in hospital/health care admissions for other reasons or in the case of community-acquired infections.[4] This may cause bias when evaluating the potential impact of obesity in community-acquired as compared with nosocomial infections.

Studies on the interactions between obesity and infection have used heterogeneous materials and the reporting of methods how BMI data were obtained are variable. Obesity is associated with multiple comorbidities such as type 2 diabetes and hypertension, which may contribute to outcomes.[8] These factors may cause considerable variation between different studies in this field and the composition of multivariate models vary. Large epidemiological studies have studied the potential association between obesity and increased pneumonia risk showing controversial results.[8–10] Kornum and associates documented that adjustment for major chronic diseases eliminated the association between obesity and pneumonia risk documented in an univariate model in one large epidemiological study.[8] One possible bias in pneumonia studies is a misclassification bias due to difficulties in interpreting X-ray photographs of overweight persons.[11] BMI data may be obtained by objective measurement on hospital admission or by inquiry of patient or closest relative. An important factor contributing to our knowledge on the convergence of obesity and infection is that excpecially the earliest studies in this field have used variable BMI cut offs to define obesity.[12,13]

The present article has its emphasis on reviewing current knowledge regarding the association between obesity and the risk and outcome of several infectious diseases. Areas with limited or controversial data are summarized in Table 2. The findings here would indicate that the association between obesity and infections has not been comprehensively established in a wide range of infectious diseases.

THE MECHANISMS OF OBESITY IN INFECTIOUS DISEASES

Obesity has been shown to have substantial effects on immune surveillance.[14] Immune system cells and adipocytes evince similarities in structure and function such as the production of various inflammatory mediators.[14,15] Adipose tissue mediates immune system and adipose tissue interactions by the secretion of adipokines, for example, leptin.[15] The differentiation of macrophages has been shown to be affected by the presence of obesity

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Table 1. Obesity-related factors affecting the risk and outcome of infectious diseases

Obesity
Respiratory tract[22]
Pulmonary restriction
Decreased pulmonary volumes
Ventilation-perfusion mismatching
Obstructive sleep apnea
Risk of pulmonary embolism
Dysregulated immune response in the lung
Skin and soft tissues and bone[23]
Disrupted micro- and macrocirculation
Decreased wound healing
Lymphedema[93]
Immune system[14]
Impaired chemotaxis
Altered differentiation of macrophages
Dysregulated cytokine production
Imbalanced cross-talk between immune system and adipose cells
Obesity-related comorbidities
Diabetes mellitus
Atherosclerosis
Pharmacological issues[7]
Limited or no data on the right dosing of antimicrobials in obesity
Altered protein binding, metabolism and volume of distribution of antimicrobials

Table 2. Infections, the risk or outcome of which have not been associated with obesity or infections on which the data are controversial

No data/controversial or limited data	
Infection risk	*Infection outcome*
Pneumonia[8–11]	Pneumonia[6,115–121]
Helicobacter pylori infection[122–127]	Helicobacter pylori infection (no studies)
Fungal infections (no studies)	Nosocomial and surgical-site infections[86,87]
Tropical infections (no studies)	Periodontitis (no studies)
Tuberculosis[128–130]	Urinary tract infections (no studies)
Influenza (no studies)	Skin infections[99]
Viral hepatitis (no studies)	Influenza viruses other than H1N1[(ref. 37)]
Bacteremia and sepsis[43,57,58,65,74,87,131]	Bacteremia and sepsis.[44,132]
HIV (no studies)	HIV[133–140]
Acute pancreatitis[88]	

and complex interactions take place between immune cells and metabolic cells.[15] Obesity violates the well-balanced system of adipocytes and immune cells, with subsequent disturbance to the immune surveillance system. This leads to dysregulated immune response, impaired chemotaxis and altered macrophage differentiation (Figure 1).[14,15]

The adipocyte derived cytokine leptin is a link between inflammation and metabolic alterations. Circulating leptin levels have been shown to reflect adipose tissue mass and nutritional status in noncritically ill individuals.[16] Serum adiponectin, which also originates from adipose tissue, has been shown to predict mortality in critically ill patients upon admission to the intensive care unit (ICU).[17] Obesity has been shown to be strongly associated with circulating levels of C-reactive protein and fibrinogen, and chronic inflammation has been considered to be one pathophysiological mechanism explaining the increased risk of atherosclerotic disease associated with obesity.[18]

Although obesity involves a risk of complications, prolonged hospitalization and need for mechanical ventilation following major trauma,[19] the development of acute respiratory distress syndrome[20] and constitutes a risk factor for prolonged hospitalization associated with critical illness,[21] the impact of obesity on intensive care-related mortality is controversial.[21] Obesity has been shown to have an effect on pulmonary function[22] and wound healing.[23] It is somewhat surprising, how little is known as to the appropriate dosing of antimicrobials in obesity and there are no antimicrobial treatment guidelines for the obese.[4,7]

INFLUENZA

Interest in the interactions between obesity and infection has been prompted by the influenza H1N1 pandemic, which has shown that obesity affects the disease course and increases the mortality rate in this condition.[24–32] Half of Californians $\geqslant 20$ years of age hospitalized with the 2009 H1N1 infection were obese.[24] One prospective, observational and multicenter study undertaken in 144 ICUs in Spain indicated that obesity was associated with higher ICU resource consumption and longer ICU length of stay in H1N1 influenza.[33] One review of studies originating from the Southern hemisphere indicated that obesity and morbid obesity were more commonly reported as the level of health care increased in patients with H1N1 infection.[29] Interestingly, obesity has been shown to be a particularly significant risk factor among patients <60 years of age.[25] Obesity has also been shown to be a risk factor for mortality in patients with H1N1 infection-related community-acquired bacterial pneumonia.[34] A recent systematic review and meta-analysis including a total of 3059 subjects confirmed findings in individual cohort studies indicating that obesity is associated with higher risks of ICU admission or death in patients with influenza A (H1N1) infection.[35] One recent global study conducted by World Health Organization included 70 000 laboratory confirmed cases with H1N1 from nearly 20 countries indicated a clear association between obesity and poor outcome in H1N1.[36]

Data on the impact of obesity on the outcome of influenza virus infections other than H1N1 are scant. A recent cohort study by Kwong *et al*.[37] over 12 influenza seasons aimed to examine the association between obesity and respiratory hospitalizations during seasonal influenza epidemics. They showed that severely obese patients are at increased risk for respiratory hospitalization during influenza seasons. BMI data in this study were based on self-reported height and weight.

The mechanisms underlying these findings have not been fully established. Excessive proinflammatory cytokine release is a key determinant in severe H1N1 infection,[38] and the pathogenesis of severe influenza infection shares properties similar to those in sepsis syndrome. One recent study has shown that the obese evince more intense interleukin-8 release in H1N1 infection as compared with normal-weight individuals.[38] Sheridan *et al*.[39] have shown that obesity is associated with impaired immune response to influenza vaccination in humans. In animal studies diet induced obese mice have been shown to be more susceptible to morbidity and mortality during influenza infection than lean mice due to altered innate immune responses characterized by minimal induction of interferon-alpha/beta, delayed expression of proinflammatory cytokines and chemokines, impaired natural killer cytotoxicity and impaired dendritic cell presentation. Thus, obesity interferes with cellular responses during influenza infection, leading to alterations in the T-cell population that ultimately may be detrimental to the host.[40]

The impact of obesity on infection susceptibility in H1N1 infection has not been established. As most patients with

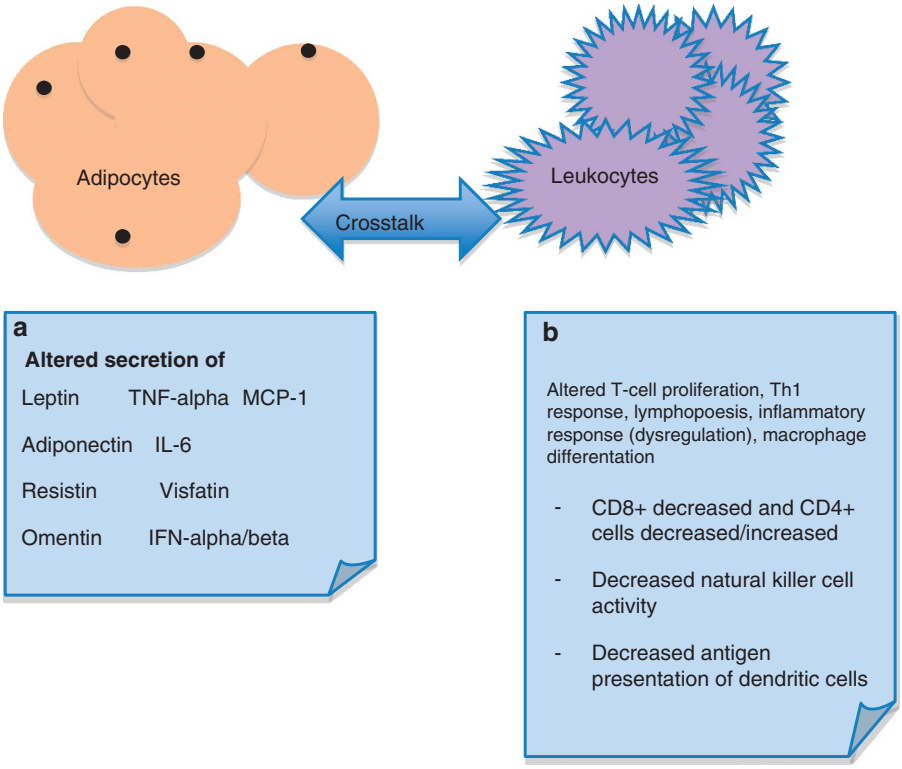

Figure 1. Interactions between adipocytes and leukocytes are complex. Obesity affects cross-talk between these cells resulting in dysregulation of immune system. Central adipokines and cytokines involved are given in box a and central leukocyte functions associated with this cross-talk in box b. IL, interleukin; MCP-1, monocyte chemoattractant protein-1; Th, T-helper, TNF, tumor necrosis factor.

influenza have mild-to-moderate disease with no need for hospitalization or contact with health care, the effect of obesity on the susceptibility to influenza has been difficult to assess. Influenza pandemic has shown that BMI is not a measure routinely recorded on patients admitted to hospital or health care institutions.

In conclusion, obesity has been shown to be associated with adverse outcome in pandemic H1N1 infection. There are no data on the association between obesity and the risk of influenza virus infection.

URINARY TRACT INFECTIONS

Several studies have studied the risk of urinary tract infection (UTI) in obese. The earliest study in this field did not indicate an association between obesity and increased risk of UTI; a large epidemiological study conducted in the 1980s of 17 032 women taking part in the Oxford Family Planning Association contraceptive study indicated that obesity was associated with a decreased risk of UTI.[13] Vessey *et al.*[13] used BMI $\geqslant 24$ as an obesity definition, which differs from the current obesity definition. Recent studies have consistently shown that obesity increases the risk of UTI. A recent cohort study by Semins *et al.*[41] with a total of 95 598 subjects indicated that obesity is a risk factor for UTI. As regards pyelonephritis, the obese were nearly five times more likely to be diagnosed than were the nonobese; females were at particularly higher risk.[41] Obesity proved to be a risk factor for UTI in a cohort study of male patients with diabetes mellitus[42] has been shown to predispose to UTI after traumatic injury[43] and ICU-acquired UTIs.[44] Obesity has been shown to be a risk factor for UTI in pregnant woman[45] and during the postpartum period.[46] A retrospective review and analysis of adult postoperative complications after noncardiac moderate or major surgery indicated that obesity confers a risk factor for UTI in these patients.[47] In conclusion, several recent studies have shown an association between obesity and an increased risk of UTI. One large epidemiological study conducted in the 1980s showed opposing results, which may originate from methodological differences. There are no data on the effect of obesity on the outcome of UTI.

PERIODONTITIS

Obesity has been shown to be associated with an increased risk of periodontitis,[48] having been shown to predict it independently of smoking.[48] A recent meta-analysis has likewise indicated a statistically significant positive association between overweight and obesity and the risk of periodontitis.[49] One other recent meta-analysis also indicated a consistently positive association with obesity in the development of periodontal disease. The authors concede that with few high-quality longitudinal studies it is not possible to distinguish the temporal order of events, this limiting the evidence that obesity is a risk factor for periodontal disease or in conversely, that periodontitis might increase the risk of weight gain.[50]

Interestingly, in animal models (for example, rats) chronic administration of lipopolysaccharide and proteases induces periodontal inflammation and hepatic steatosis,[51] and one cohort study has indicated that the severity of periodontal disease is associated with the development of glucose intolerance in non-diabetics.[52]

NOSOCOMIAL INFECTIONS AND SURGICAL INFECTIONS

Nosocomial infections incur substantial clinical and economic costs.[53] Cohort studies indicate an association between obesity and the risk of nosocomial infections.[12,54] A recent retrospective case–control study has shown obesity to be an independent predictor of nosocomial bloodstream infection in older adults.[54]

ICU AND TRAUMA PATIENTS

In retrospective and prospective studies, obesity has been shown to be an independent risk factor for infection after trauma.[43,55,56] Obese patients had a more than twofold increase in the risk of acquiring a bloodstream, urinary tract or respiratory infection in a prospective cohort study of critically ill trauma patients.[43]

Obesity has been shown in several cohort studies to have an impact on the infection risk in critically ill ICU patients.[43,57–59] Obesity has been shown to be an independent risk factor for ICU-acquired catheter and blood stream infections in one prospective observational study.[57] The authors concluded that one reason for this observation may be explained by the relative difficulty in obtaining venous access in these patients.[57] A large multicenter prospective study of nearly 200 ICUs in 24 European countries showed that obese and very obese patients more frequently developed ICU-acquired infections than patients in lower BMI categories.[58] In this study by Sakr *et al*.[58] BMI was prospectively measured at admission to the study ICU. One risk-adjusted matched cohort study indicated that obesity was associated with an increased risk of ICU-associated infections such as septic shock and ventilator-associated pneumonia.[59] However, obesity was not associated with any increased risk of infection-related case fatality in these patients.[59] One prospective multicenter matched epidemiologic study, again, indicated no association between obesity and the risk of catheter-related infection or ventilator associated pneumonia.[60] However, the study in question compared severely obese (BMI $\geqslant 35$) with nonobese (BMI < 30) leaving the group of those with BMI $\geqslant 30$ to < 35 out of the study. In this study, patients were weighed at ICU admission (lift bed scale).

In conclusion, several studies indicate an association between obesity and the risk of ICU-related or posttraumatic infections, but not all have confirmed this. One potential bias in studies of this field is the challenges in obtaining BMI data in critically ill patients, and weight measured at admission may not reflect patients' real weight because of vascular fluid volume depletion.

SURGICAL INFECTIONS

Prospective and retrospective cohort studies have indicated that obesity is associated with a significantly increased risk of skin and soft-tissue infection (SSI) after surgery.[61–64]

INFECTIONS FOLLOWING GASTROSURGERY

Overweight and obesity have been shown to be a risk factor for infection after pancreatoduodenectomy in cohort studies.[65,66] Obesity has been shown to be associated with a higher risk of post-operative pelvic abscesses after cancer surgery[67] and a predictor for surgical-site infection after hepatic resection.[68] In laparoscopic bariatric procedures, the super obese group proved to have a significantly greater incidence of postoperative complications, including superficial and deep wound infections, sepsis, septic shock and 30-day mortality.[69] One study of patients undergoing colectomy has shown that morbidly obese patients had a higher risk of surgical-site infection as compared with normal-weight subjects, whereas the occurrence of pneumonia, UTI or 30-day mortality did not differ significantly by BMI.[70] Gervaz *et al*.[71] have shown that obesity was strongly associated with postoperative SSI after colon or rectum surgery and a simple clinical score based on four preoperative variables including obesity data was clinically useful in predicting the risk of SSI in these patients.[71]

INFECTIONS FOLLOWING VASCULAR AND CARDIAC SURGERY

Obesity has been in one large cohort study shown to almost double the risk of postoperative SSI after lower extremity bypass.[72] However, the risk of sepsis or septic shock was not affected by obesity.[72] Several cohort studies indicate an association between obesity and the risk of sternal wound infection, mediastinitis and bacteremia after cardiac surgery.[73–77] In one retrospective cohort study, obese diabetic patients had a 7.7-fold increased risk of deep chest infections after controlling for confounders and an independent risk factor for superficial surgical-site infections.[78] A recent nested case–control study indicated that obesity is a risk factor for SSI after central venous catheter-related infection in cardiac surgery.[79] Several cohort studies have identified as an independent risk factor for leg-harvest-site infection.[80,81]

INFECTIONS FOLLOWING ORTHOPEDIC SURGERY

Morbid obesity and obesity combined with diabetes are risk factors for periprosthetic infection after total knee arthroplasty.[82] Cohort and case–control studies indicate that obesity increases the risk of prosthetic hip infection.[83,84] In a case–control study of pediatric patients undergoing spinal surgery, obesity was a risk factor for SSI.[85]

In conclusion, several studies indicate that obesity increases the risk of surgical infections. The association seems to be most evident in vascular, cardiac and orthopedic surgery.

OBESITY AND THE OUTCOME OF NOSOCOMIAL AND SURGICAL INFECTIONS

The impact of obesity on the outcome of various surgical or nosocomial infections remains obscure. One retrospective cohort study in appendicitis patients indicated that the outcome of appendicitis pre- or postoperatively did not differ between obese and non-obese subjects. Only the length of stay in hospital in those with perforation was adversely affected by obesity.[86]

One recent study on patients with durable mechanical support at a single institution from January 2000 to December 2008 showed that obese patients, as compared with the non-obese, had higher incidence rates of sepsis (64.5% vs 34.7%, respectively, $P = 0.006$) and reoperation for infectious complications (34.2% vs 13.3%, respectively, $P = 0.014$).[87]

PANCREATITIS

Data on the potential effect of obesity on the risk of acute pancreatitis are scant. One large epidemiological study has indicated that obesity is a risk factor for gallstones, gallbladder disease and pancreatitis.[88]

Several studies indicate an association between obesity and severe pancreatitis. Obesity has been shown to predispose to local complications of pancreatitis such as pancreatic pseudocysts, abscess and necrosis.[89,90] Visceral obesity and adipose tissue have proved particularly important as underlying factors in the pathophysiology of severe diseases. It has been shown that adipokines secreted from adipose tissues enhance and maintain systemic inflammation in acute pancreatitis.[91,92] The severity of acute pancreatitis in obese patients and in patients with central fat distribution seems to be related to the amplification of systemic inflammatory reaction.[91] A meta-analysis published in 2004 indicated that severe acute pancreatitis is significantly more common in the obese, and that obesity is associated with systemic and local complications.[89] However, mortality was not significantly higher in obese than in non-obese subjects.[89] On the other hand, an updated meta-analysis of the same group in 2006 indicated that obesity was significantly associated with increased mortality in acute pancreatitis.[90] In conclusion, obesity is a risk factor for severe pancreatitis but data on the potential effect of obesity on the risk of acute pancreatitis are limited.

SKIN INFECTIONS AND CELLULITIS

Obesity causes changes in skin barrier function, the lymph system, collagen structure and function, and wound healing. Evidence suggests that the vascular supply is impaired in obese persons and obesity affects both macro- and microcirculation. Obesity is associated with a wide range of skin diseases.[23]

Case–control studies indicate an increased risk of cellulitis and skin infections in the overweight[93] and obese.[94,95] Björnsdottir *et al*.[96] in a prospective case–control study showed obesity to constitute a risk factor for cellulitis in a univariate model, but in a multivariate model the finding no longer persisted after controlling for other factors. However, several studies have indicated that obesity predisposes to erysipelas independently of potential confounders.[93,94] One prospective cross-sectional study has indicated that obesity is a frequent disease in patients with erysipelas.[97] Data indicate that obesity predisposes to a significantly increased risk of recurrent soft-tissue infections.[94,98]

Data on the association between obesity and the outcome of skin infections are limited. A prospective cohort study has indicated the outcome of cellulitis to be worse in the morbidly obese as compared with non-obese subjects.[99]

To summarize, several well-conducted case–control studies indicate an association between obesity and the risk of cellulitis, but the data on the association between obesity and the outcome of skin infections are limited.

VIRAL HEPATITIS

Cohort studies have shown obesity to be related to an increased risk of hepatic steatosis and fibrosis in non-diabetic patients with chronic hepatitis C infection.[100,101] Overweight has been observed to have an adverse effect on the progression of chronic HCV liver disease, with diminished response to antiviral therapy.[100,101] Interestingly, significant changes in insulin resistance and adipocytokines have been noted to occur under viral treatment, irrespective of virological outcome.[100] Experimental and clinical evidence has proved the contribution of HCV in the development of insulin resistance and diabetes in human HCV infection.[102,103] A recent cohort study has indicated that compared with subjects with seroprotective titers from hepatitis B vaccination, those without protective titers of anti-HBs after vaccination or those with natural infection with hepatitis B have a higher risk of metabolic syndrome.[104] The study in question was limited by the cross-sectional design and did not answer the causal relationship between the status of hepatitis B immunity and metabolic syndrome.[104] In conclusion, obesity is associated with an increased risk of hepatic steatosis in patients with chronic hepatitis C infection.

ANTIMICROBIAL DOSING IN OBESITY

The data on right dosing of antimicrobials in obesity are limited. Whereas there are clear recommendations for antimicrobial dosing in children, no such data are available for obese patients.[7] A correct understanding of the influence of obesity on antimicrobial drug dosing is crucial to achieve maximum safety and effectiveness in therapy. Changes in the pharmacodynamics of drugs in obese are highly variable and depend on multiple factors, including degree of obesity, organ function and on drug characteristics.[105] Obesity affects volume of distribution (V_d) of drugs and thus increases the V_d of lipophilic drugs (for example, fluoroquinolones) and decreases the V_d of hydrophilic drugs (for example, amikacin and tobramycin).[105] Several studies indicate that physicians frequently underdose antimicrobials in obese patients.[106,107]

Choosing appropriate antibiotic dosages is extremely challenging when treating obese patients with severe, deep-seated infections and multiple organ failure.[108] Previous data indicate that the penetration process of antimicrobials into the interstitial space fluid is impaired in obese subjects.[109] There are some data on the appropriate dosing of antimicrobials, which require drug concentration monitoring such as vancomycin and aminoglycosides, but the right dosing of most antimicrobials is unclear.[7] Data indicate inadequate plasma concentrations for obese patients, when standard treatment doses of vancomycin are used.[107] A recent multicenter study indicated that vancomycin concentration in obese subjects was $<30\%$ of optimal therapeutic concentrations when a standard dosing (2 g per day) was used.[107] One recent report by Pea *et al*.[108] introduced the use of real-time therapeutic drug monitoring by high-performance liquid chromatography system and showed that this approach would be invaluable in ensuring rapid clinical response and preventing drug-related toxicity in a morbidly obese patient with life-threatening cellulitis and organ failure treated with high-dose daptomycin plus continuous infusion meropenem. The authors stressed the point that in considering dosing strategies for hydrophilic antimicrobials in obese patients, clinicians should bear in mind that standard methods of estimating renal function are inaccurate.[108] Rapid and easy methods for bedside monitoring of drug concentrations and toxicity in the case of obese patients are eagerly awaited. Some data indicate that plasma drug concentrations may not predict tissue concentrations and that therefore dosing on the basis of weight-correction factors may potentially result in subtherapeutic concentrations of the drug in tissues.[109] Morbid obesity has been shown to affect the blood and tissue levels of prophylactic antimicrobials.[110]

After the association between obesity and poor outcome in H1N1 infection became evident, one study has investigated the appropriate dosing of oseltamivir in obesity. The OPTIMO trial was a single-center, non-randomized, open-label pharmacokinetic study of single-dose and steady-state oral oseltamivir phosphate and its carboxylate metabolite in healthy, morbidly obese and healthy, non-obese subjects. With single and multiple dosing, the systemic exposure to oseltamivir was decreased but that of oseltamivir carboxylate was largely unchanged. The authors concluded that an oseltamivir dose adjustment for body weight would not be needed in morbidly obese individuals.[111] Studies that correlate clinical outcomes with plasma concentrations of oseltamivir and viral susceptibility are needed in the future.

One recent study investigated the pharmacokinetics of intravenous levofloxacin administered at 750 mg in obese adults. The peak concentrations of levofloxacin were comparable to those seen with normal-weight individuals. However, the area under the concentration–time curve and clearance were quite variable.[112] Another recent study showed that obese patients with severe infections caused by high-minimal inhibitory concentration may require greater ciprofloxacin dosages.[113]

Many Gram-negative bacteria, such as *Pseudomonas aeruginosa* and *Stenotrophomonas maltophila* survive with inadequate blood antimicrobial drug concentrations and may develop antimicrobial resistance. Thus, some authors recommend using more frequent dosing intervals in obese patients in the treatment of organisms with high minimal inhibitory concentration.[7,114] However, these recommendations are based on single patient cases and no randomized studies have been conducted to make firm conclusions on this topic.

In conclusion, obesity has been shown to alter the pharmacokinetics and pharmacodynamics of antimicrobials, and several studies indicate that underdosing antimicrobials is common in the treatment of obese patients with infection. However, there are no guidelines or randomized studies on this topic. Further studies should focus on the use of antimicrobials in obesity.

CONCLUSIONS

The recent pandemic influenza epidemic and studies on several other infectious diseases have drawn our attention to the

association between the obesity epidemic and infectious diseases. However, the associations have not been assessed in a wide range of infectious conditions. The exact mechanisms underlying obesity-related changes in the course of infectious diseases are not established. Multiple factors may be involved, for example, obesity-related comorbidities, immunological effects and pharmacological issues. As the cause–effect relationship between obesity and infection remains obscure in many infectious diseases, further studies are warranted. Current data indicate that obesity has adverse effects on the disease course of pancreatitis and H1N1 infection, and increases the risk of postsurgical and nosocomial infections. With increasing rates of obesity, we may expect the mortality and morbidity in infectious diseases to increase. Routine measurement of BMI in patients visiting outpatient clinics and in hospitalized patients would potentially increase research possibilities in this area. As the systematic evaluation of drug pharmacokinetics and pharmacodynamics in obese patients are limited, this should be incorporated into the drug development process.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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