Update on intra-abdominal and post-surgical infections

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The present article is an update of the literature on intra-abdominal infection, which represents a spectrum of diseases with a common pathogenesis. Establishing a prompt diagnosis and avoiding treatment delays are key to achieving the best outcomes. Mortality depends on initiating early appropriate treatment to restore fluid and electrolyte imbalances, supporting the function of vital organs, providing appropriate broad-spectrum antimicrobial therapy, and achieving adequate source control.

A multidisciplinary group of Spanish physicians with an interest in these infections selected the most important papers produced in the field during 2005 and 2006.

One of the members of the group discussed the content of each of the selected papers, with a critical review by other members of the panel.

After a review of the state of the art, papers from the fields of epidemiology, pathophysiology, basic science, causative microorganisms and microbiological diagnosis, main clinical syndromes, principles of therapy, new antibiotics and surgical procedures, preventive measures, recommended antimicrobial regimens and guidelines were discussed by the group. Faculty from this panel have made an interesting contribution to our understanding and management of intra-abdominal infections at present. Their contribution is particularly relevant for clinical practice.

Key words: **Intraabdominal infections. Peritonitis. Pancreatitis. Biliary tract infections. Early post-transplantation infections. Epidemiology. Pathophysiology. Microbiological diagnosis. Organ failure. Source control. Antibiotic therapy. Prevention. Guidelines.**

Actualización sobre infecciones intraabdominales y posquirúrgicas

El presente artículo es una puesta al día de la literatura sobre infecciones intraabdominales, que constituyen una gama de procesos con una patogenia común. Para lograr los mejores resultados tiene una importancia decisiva establecer un diagnóstico precoz y evitar los retrasos en el tratamiento. La reducción de la mortalidad se basa en iniciar precozmente un tratamiento apropiado para restaurar los desequilibrios hidroelectrolíticos, en apoyar la función de los órganos vitales, en proporcionar un tratamiento adecuado con antibióticos de amplio espectro y en controlar correctamente las fuentes de la infección.

Un grupo multidisciplinario de médicos españoles interesados en este campo seleccionó los trabajos más destacados que se han publicado sobre el tema en 2005 y 2006. Cada artículo seleccionado fue analizado por un miembro del panel, y el resto de miembros efectuó una revisión crítica.

Después de revisar el estado del arte, el grupo discutió los trabajos sobre epidemiología, fisiopatología, ciencias básicas, microorganismos causales y diagnóstico bacteriológico, principales síndromes clínicos, fundamentos del tratamiento, nuevos antibióticos y procedimientos quirúrgicos, medidas preventivas, y pautas y normas antimicrobianas recomendadas.

Los miembros de este panel han aportado una interesante contribución a nuestros conocimientos y a la conducta a seguir actualmente ante las infecciones intraabdominales. Su contribución es especialmente relevante para la práctica clínica.

Palabras clave: **Infecciones intraabdominales. Peritonitis. Pancreatitis. Infecciones del tracto biliar. Infecciones precoces postrasplante. Epidemiología. Fisiopatología. Diagnóstico bacteriológico. Fallo orgánico. Control de la fuente. Tratamiento antibiótico. Prevención. Normas.**

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State of the art: intra-abdominal infections (Dr. M. Salavert, Dr. J. Torre-Cisneros)

Intra-abdominal infection (IAI) covers a spectrum of diseases with a common pathogenesis. While the microbiology of these different diseases can be variable, their treatment and outcomes are remarkably similar and are somewhat predictable. IAI can be localized (intra-abdominal abscess) or uncontained (diffuse peritonitis). Although IAI can occur in many forms, surgeons predominantly treat patients with secondary peritonitis, in which case contamination originates from the gastrointestinal tract. It is not uncommon for the exact source of the infection to be indeterminate prior to surgery. A smaller percentage of patients with IAI have tertiary peritonitis, which is usually defined as recurrent infection following secondary peritonitis. Patients with tertiary peritonitis have a more complicated form of infection with a different microbiology and greater mortality.

Although peritonitis has been recognized as a common and complex disease entity since ancient times, surgeons and physicians still do not have a true understanding of its pathophysiology and treatment. The clinical course and outcome of peritonitis is dependent upon the struggle between the quantity and virulence of the pathogen and host's physiologic reserve, including the ensuing inflammatory response. Current multimodality treatment of IAI is based upon the fundamental principles established at in the early 1980s: surgical source control, fluid resuscitation, adequate nutrition, support of failing organ systems, and antibiotic therapy. Although dramatic advances have been made in the pharmacological treatment of IAI, mortality for complicated cases remains high. Consequently, future directions in management of peritonitis may require agents that target specific endotoxin receptors, inflammatory signaling molecules, or immunomodulatory moieties.

Epidemiology

Our current understanding and treatment of peritonitis, a complex disease induced by invasion of microorganisms in the peritoneal cavity with a subsequent host response involving local and systemic inflammation, is the result of a slow evolutionary process. Peritonitis is classified into 3 categories, according to etiology and treatment: primary, secondary, and, more recently, tertiary. Primary peritonitis is the apparent spontaneous onset of bacterial growth in a previously sterile peritoneal environment, with no identified source or cause. This form of peritonitis usually occurs in the setting of hepatic failure and ascites, or in patients with nephrotic syndrome. Medical treatment is the mainstay when managing this form of peritonitis—the role of surgery is minimal. Secondary peritonitis, however, is infection of the peritoneal cavity by microbes from an anatomic breach of the alimentary tract. The cause of this breach can be trauma, surgery, malignancy, inflammation, obstruction, ischemia, or perforation. Treatment for this more common form of peritonitis is the main subject of discussion in this review.

Tertiary peritonitis is defined as persistent or recurrent peritonitis despite appropriate treatment for primary or secondary peritonitis[1]. This clinical syndrome is characterized by multiple organ dysfunction and a state of prolonged systemic inflammation with persistent peritoneal infection by organisms that are normally of low pathogenic potential. The failure of an appropriate host response, therefore, seems to play a major role in this clinical entity, which has yet to be elucidated. Tertiary peritonitis occurs when source control is unsuccessful, antimicrobial therapy is ineffective, or host defenses are inadequate[2]. It has a different microbiology in that gram-positive organisms (particularly enterococci), yeasts, and antibiotic-resistant gram-negative organisms are more commonly present. Thus, obtaining proper cultures of infected peritoneal contents is critical to the selection of antimicrobial therapy, which is often very different from that used for secondary peritonitis. Only 30% to 40% of these patients have signs of intra-abdominal infection on examination, although most have fever and leukocytosis. Abdominal computed tomography (CT) scan is useful can help establish diagnosis and direct treatment. Ninety-five percent of these patients will require additional "source control" as a component of treatment[3].

Pathophysiology

The response to IAI depends on 5 key factors: *a)* inoculum size; *b)* virulence of the contaminating organisms; *c)* the presences of adjuvants within the peritoneal cavity; *d)* adequacy of local, regional, and systemic host defenses, and *e)* the adequacy of initial treatment. The pathophysiology of peritonitis has been studied in numerous animal and cellular models, and can now be applied in clinical practice. Understanding the pathophysiology of peritonitis is crucial to the current multimodality approach to management of IAI.

The important relationship between the degree of contamination and the development of infection has been demonstrated best in experimental models[4]. This interaction is most obvious when host defenses are compromised. Inoculum size can also influence the response to treatment. The virulence of the microorganisms involved in IAI is quite variable. Although more than 300 microbiological species have been identified in the human colon, relatively few of these organisms are involved in the actual disease process. Thus, the virulence of isolated organisms is strongly dependent on local environmental factors such as local oxygen pressure, organism symbiosis or antagonism, duration of exposure, and previous treatment, all of which can affect the growth of organisms involved in IAI. Adjuvant substances such as blood, enteric contents, bile, necrotic tissue, and inert materials are commonly present with secondary peritonitis. These adjuvants can inhibit chemotaxis of bacteria and block lymphatic absorption through the diaphragm. In addition, adjuvants may provide nutrient substrates such as iron that actually encourage bacterial growth[5].

Contamination of the peritoneal cavity by bacteria and other chemical irritants results in activation of multiple, interdependent inflammatory systems at both the local and systemic levels. The host response to IAI involves lo-

cal, regional, and systemic factors. Macrophages are the dominant white blood cell type in the inviolate peritoneal cavity. Once contamination occurs, there is a rapid influx of polymorphonuclear leukocytes, complement, opsonins, and antibodies into the peritoneum. There is also stimulation of local cytokine and chemokine production. The bacteria are opsonized and killed by the white blood cells. These "spent" white blood cells, as well as some viable bacteria, are absorbed through the diaphragm and transported by the thoracic duct to systemic circulation where they are disposed of through the reticuloendothelial system. Systemic cytokine production is initiated and there is pulmonary sequestration of white blood cells, which is regulated by local chemokine production[6]. These factors are responsible for initiating the systemic inflammatory response syndrome (SIRS) and can result in organ failure. The struggle and balance between these forces determines the clinical course of the IAI: resolution, formation of an abscess cavity, or SIRS and multiple organ failure.

Systemic host defenses can be assessed by calculating a physiologic score (usually APACHE II), which accounts for preexisting diseases and the response to the acute attack. The APACHE II and similar scoring systems provide a method to estimate and compare mortality across groups of patients with similar diseases. The mortality of secondary peritonitis can vary between 5 and 40%. A variety of risk factors are associated with mortality and treatment failure. These include increasing age, a greater APACHE II score, vital organ dysfunction, malnutrition, resistant organisms, and delayed surgery. Patients who have IAI related to appendicitis have a lower mortality than those with non-appendiceal sources of infection[7]. Globally, mortality rates for IAI range from less than 5% for simple, uncomplicated peritonitis to as high as 30-40% for the more complex and severe forms. APACHE II score, nutritional status, and age are the most noteworthy factors for predicting survival or death. Other studies have shown that mortality of peritonitis is mainly dependent on the patient's systemic response and premorbid physiologic reserve (estimated by the APACHE-II score)[8,9]. Consequently, investigators also have demonstrated that death from peritonitis occurs not from the IAI, but from the resultant multisystem organ failure or SIRS[10].

Diagnosis

The diagnosis of IAI is generally made on physical examination. Some patients will require abdominal ultrasound or CT scan to establish the diagnosis. Although ultrasound is accurate for the simple detection of an isolated fluid collection, CT is considered the modality of choice for complete evaluation of an abscess because of its unlimited imaging properties[11]. Before abdominal CT was readily available, it was much more difficult to diagnose IAI and diagnosis was often delayed. The modern armamentarium of diagnostic imaging includes CT, ultrasound, magnetic resonance imaging, and radioisotopes, which are capable of diagnosing abscesses in many cases, although CT and ultrasound remain the mainstay for diagnosis. The advantages of ultrasound and CT scan are their almost universal availability, very high accuracy, and ability to guide diagnostic and therapeutic drainage techniques[12]. Only visualization and knowledge of the many pathways of spread or multiple cavities can provide sufficient information to permit appropriate choice, planning, and insertion of the required catheters (number, size, type, catheter irrigant, and suction). The relationship of such fluid collections to intestinal loops, blood vessels, organs, appendix, biliary system, diverticuli, and other structures can reveal the origin of abscesses, which may or may not require surgery.

The definitive diagnosis of an infection in a fluid collection or tissue is only possible by recovery of a sample for microscopic examination and culture. Additional blood culture procedures are mandatory in the presence of fever and sepsis. In a review of patients with bacteremia from Bacteroides, an anaerobe commonly involved in IAI, Fry et al pointed out that 75% of patients with this disorder had a surgically treatable cause of infection[13]. This and a subsequent study of enterococcal bacteremia emphasized the need to search for IAI when patients open either of these organisms in a blood culture. When abdominal CT is unavailable or impractical, peritoneal lavage remains a useful method to diagnose IAI. The positive predictive accuracy of this study is 90% and the negative predictive accuracy is 98% in these circumstances[14].

Source control

Martin Kirschner established "source control" as 1 of the major principles of peritonitis treatment in 1926 when he demonstrated a decrease in overall mortality from 87 to 30% between 1895 and 1926. Kirschner's observations laid the foundation for gradual evolution of the current fundamental principles for surgical treatment of peritonitis as described by Polk in 1979: gastrointestinal decompression, fluid resuscitation, support of failing organ systems, adequate nutrition, systemic antibiotics, and source control of contamination[15]. The current "multimodality" approach to management of secondary peritonitis, therefore, necessarily includes not only surgical control and drainage of the infection, but also supportive and pharmacologic therapeutic measures. The sine qua non of successful treatment is prompt surgical intervention, or "source control," to halt delivery of pathogens into the peritoneal cavity. The term "source control" refers to interventions designed to eliminate the focus of infection, control ongoing contamination, and restore normal anatomy and function. Surgical intervention encompasses a vast array of procedures including resection, anastomosis, exteriorization, drainage, debridement, peritoneal lavage, and simple or multiple laparotomies[16]. The concept of "source control" is well established. However, a consensus regarding the description and details of this procedure and its contribution to the success or failure of treatment for peritonitis does not currently exist. Nevertheless, surgical treatment remains crucial in the overall successful management of IAI. Delays in the operative management of IAI are associated with increased mortality. Therefore, the goals of "source control" are to manage the source of contamination (most often by resection or closure), drain abscesses, débride necrotic tissue, and remove gross debris.

Adequate source control can be achieved during the initial operation in approximately 90% of patients and the

need for reoperation in this group is less than 10%. In contrast, when source control cannot be obtained during the initial operation, the reoperation rate is 30% or more. Patients without organ failure have a better response to repeat attempts at source control. There is a considerable increase in mortality and decreased long-term survival in patients undergoing planned relaparotomy compared to those who have re-laparotomy on demand[17]. Patients with intestinal ischemia, severe advanced tertiary peritonitis, uncontrolled infection (infected ascites), and those who need to have intestinal continuity reestablished should have a planned reoperation.

Pancreatic necrosis is a unique condition that can initiate an inflammatory peritoneal response in the absence of infection. Antimicrobial prophylaxis has been shown to reduce the need for operation in this group of patients, most likely due to a reduction in the incidence of infected necrosis[18], although its contribution to mortality is currently under discussion. This is a marked change in management compared with earlier reports where surgery was more common, even when infection was absent. Recognition and early drainage of intra-abdominal abscesses reduces mortality. Over the last 30 years, interventional radiologic drainage of intra-abdominal abscesses has been shown to be as successful as operative drainage for patients with unilocular abscesses[19]. In contrast, patients with multiple intra-abdominal abscesses, multilocular abscesses, or associated enteric fistulas or tissue necrosis usually have superior results with operative rather than percutaneous drainage[20]. Occasionally, subphrenic or subhepatic abscesses are located in such a way that neither percutaneous methods nor transperitoneal laparotomy is the safest approach to drainage. In these circumstances, a direct approach can be advantageous.

Treatment strategy and antibiotics

The treatment of IAI is based on restoration of normal homeostasis. The principles of treatment include restoration of fluid and electrolyte imbalances, physiologic support of organ systems, control of the source of the infection, and administration of appropriate empiric antimicrobial therapy. Dramatic advances in the development of antibiotics have greatly aided the surgeon's battle against peritonitis. Prompt initiation of broad-spectrum antimicrobial therapy has been established as a major contributor to the multimodal management of peritonitis, and as an important adjunct to other principles of treatment[21,22]. Experimental evidence indicates that among the initial plethora of microbes, the responsible pathogens are reduced to only a few bacteria that have evolved to survive outside their natural milieu: aerobic or facultative anaerobic *Enterobacteriaceae* (*Escherichia coli* and others, responsible for the early bacteremic phase) and obligate anaerobes, especially *Bacteroides fragilis* (contribute to the late abscess phase)[23]. In the early antibiotic era, combination therapy produced better survival rates without recurrent or residual infections when both types of pathogens were targeted. The current practice of early, initial empiric therapy is based on multiple human trials that validate the significance of providing adequate pharmacologic coverage against *Enterobacteriaceae* and anaerobes. Since the era of "triple antibiotics," namely ampicillin, gentamicin, and clindamycin, multiple antibiotics with broader coverage have been introduced, and many clinical trials have been conducted with these newer agents (piperacillin/tazobactam, new fluoroquinolones, ertapenem, tigecycline, new anti-gram–positive agents, etc). There is no demonstrated lower benefit of combination therapy over monotherapy, or viceversa, if the agents used have appropriate activity against most responsible pathogens. When these agents are compared, they are equally effective and no differences in mortality or infectious complications are observed. The few studies that noted differences analyzed mainly surgical site infections and not more serious complications.

The microbiology of secondary peritonitis dictates the need for antimicrobial therapy that is effective against gram-negative enteric pathogens and gram-positive and gram-negative anaerobic bacteria. It is not necessary to routinely treat enterococci, yeasts, or fungi unless the patient has developed IAI after previous surgery or is otherwise at risk for these pathogens. In such circumstances, these and other resistant pathogens are more common. This may also be related to selection of pathogens based on previous therapy.

Antimicrobial agents should be selected based on demonstrated efficacy in prospective, randomized clinical trials of IAI and the suspected pathogens should have *in vitro* susceptibility to the chosen drug. Once treatment is initiated, it is imperative to review the culture and sensitivity results when available and to adjust the antibiotic choices accordingly. Patients can be switched to oral therapy once gastrointestinal function has returned and if an appropriate agent is available. The duration of treatment is variable and depends on the type of infection found, the status of the host defenses, and the response to treatment. Patients who have localized peritonitis or an intra-abdominal abscess and who are not immunocompromised can be treated for a relatively brief period (7-10 days), whereas patients with generalized peritonitis and whose condition is more severe require a longer duration of treatment (10-14 days, or more). It may be that the host inflammatory response is sufficient to complete the process of eradicating the infection after antimicrobial agents have assisted in reducing the inoculum of bacteria to a more "manageable" level. However, the host response may be too extravagant and lead to detrimental effects, before ultimately resulting in SIRS. Unless prospective trials are carried out to address this question, the optimal duration of antimicrobial treatment of IAI will remain unknown. Antimicrobial therapy should continue until there are clear signs that the infection has resolved. This includes resolution of fever, return of gastrointestinal tract function, and return of the white blood cell count and biological plasma reactants to normal. When these parameters remain abnormal, persistent IAI or the occurrence of nosocomial infection at another site should be suspected and investigated. The cause of the absence in clinical improvement may be inadequate activity of the antibiotic against resistant pathogens. More likely, however, is the possibility that a problem exists with surgical source control: inadequate drainage, further necrotic tissue from the "penumbra" surrounding the focus of infection, or leakage of anastomosis. Several studies emphasize the high incidence of

relaparotomy rates for adequate infection[24]. Thus, failure of adequate clinical response should prompt the attending physician to reassess the patient with regards to the adequacy of source control and appropriateness of the antibiotic regimen.

The presence of antibiotic-resistant organisms in culture of infected peritoneal fluid is a predictor of treatment failure and increased mortality[25]. Enterococci are isolated more often among patients who are older, have a high APACHE II score, develop postoperative infections particularly from a colonic or small bowel source, or have been institutionalized in a healthcare facility[26]. However, studies comparing therapy that included enterococcal coverage versus those that did not failed to show any difference in clinical outcomes, which suggests enterococcal coverage was not necessary, at least initially.

Yeasts are cultured more often from IAI in patients who have been institutionalized, when there have been delays in treatment, and in patients with tertiary peritonitis. Yeasts should be treated when they are the dominant organism in culture, are identified at another location or in the blood stream, or are found in the immunosuppressed patient.

In addition, the prevalence of methicillin-resistant *S. aureus* (MRSA) and extended-spectrum β-lactamase (ESBL)-producing *E. coli* in both the community and hospitals is substantial and on the rise. "High-risk" patients for these multi-drug resistant pathogens may benefit from initial coverage of MRSA or ESBL-*E. coli*, but "high risk" patients have not been clearly defined.

Special types of abdominal wall infection (mesh infection)

Every year, approximately 1.5 million abdominal hernias are repaired in the United States and Europe. The 2 most commonly used techniques are simple suture of the abdominal wall and repair using mesh. In recent years, several studies have shown that the latter technique is significantly associated with a lower risk of recurrence of the hernia, without a parallel increase in the incidence of surgical wound infection. Therefore, reconstruction of the abdominal wall with a mesh is the technique of choice for most surgeons. The incidence of surgical wound infection of an inguinal hernia is about 2% regardless of the technique used. Nevertheless, it is clear that, when the infection occurs on a foreign body (mesh), it is more difficult to cure. This is mainly because when the microorganisms reach an inert surface, they are capable of forming a biofilm that tends to cover a more or less extensive surface of the implant. Biofilms are defined as a community of bacteria that grow covered in a polysaccharide ("slime") that protects them from the host's defense mechanisms (antibodies, complement, phagocytes) and the action of antibiotics. The infection of any medical device is the result of a microorganism seeding on the implant surface either directly or by hematogenous spread. The most frequent route is direct contamination at the time of surgery and the source of microorganisms can be the patient's skin, the environment of the operating room or the operating room personnel's skin. The time from contamination to the onset of symptoms of infection is variable–most infections are detected during the first 3 months after surgery, although some are diagnosed more than 3 months or even years after hernia repair. The time from surgery to clinical manifestations depends on the type of infecting microorganism. High virulent microorganisms, such as *Staphylococcus aureus*, streptococci, and Gram-negative bacilli are the most commonly isolated agents in early postoperative infections, while coagulase-negative staphylococci predominate in late chronic infections. A hematogenous infection represents the metastatic seeding of the implant from an episode of bacteremia at any time after surgery, and the most common etiologic microorganism is *S. aureus*.

The most important clinical consequence of these events is that, generally, it is necessary to remove the implant in order to cure the infection. In this sense, infection of a reconstruction mesh is not an exception and in most of the cases reported in the literature, the treatment of choice is removal of the mesh, which, on the other hand, can favor relapse of the hernia. In the light of these data, it seems very important to establish the need for antibiotic prophylaxis to reduce the infection rate, to evaluate the impact of antibiotic-coated mesh, and to know the clinical characteristics of this type of infection.

Severe acute pancreatitis and risk infection

Acute pancreatitis (AP) is mainly caused by symptomatic gallstone disease and excessive alcohol intake[27]. Because of improvements in management including better diagnostic and treatment modalities, disease-related mortality has declined during the past 2 decades despite an increase in the overall incidence of AP in many countries[28]. Most AP episodes do not require a particular intervention, since they are mild and self-limiting. In contrast, about one fifth of patients develop a severe form of AP, which is still associated with mortality exceeding 30%[29]. This type of AP is usually accompanied by necrosis of the pancreas and the surrounding tissue (necrotizing pancreatitis [NP]). Such necrosis is best assessed by contrast-enhanced CT[30], and the Balthazar score is the most commonly used score to define the extent of necrosis[31]. Alternatively, magnetic resonance imaging (MRI) can be used, eg, when intravenous CT contrast is contraindicated[32]. According to the Atlanta classification, AP is severe if it is accompanied by single or multiorgan failure, local complications, 3 or more Ranson criteria, or an APACHE II score of ≥ 8 points.

NP is the severe form of human AP[33]. The past decade has seen a considerable increase in our understanding and management of NP. The natural course of severe AP progresses in two phases. The first 14 days are characterized by the SIRS resulting from the release of inflammatory mediators[34]. In patients with NP, organ failure is common and often occurs in the absence of infection. In addition to organ dysfunction, general disorders include hypovolemia, hyperdynamic circulatory regulation, fluid loss from the intravascular space, and increased capillary permeability. The second phase, beginning approximately 2 weeks after the onset of the disease, is dominated by sepsis-related complications resulting from infection of pancreatic necrosis[35]. This is associated with multiple systemic complications, such as pulmonary, renal, and

cardiovascular failure. In the natural course of the disease, pancreatic necrosis occurs in 40 to 70% of patients and it has become the most important risk factor of death from NP[36]. More than two thirds of deaths from AP are due to late septic organ complications[37]. Antibiotic treatment with agents penetrating deep into the pancreas has been shown to prevent infection in severe AP and possibly to lower the mortality rate[38,39]. Still, antibiotic therapy and general treatment principles in NP, particularly the role of surgery, are controversial issues. During the 1980s, 50 to 70% of patients with NP were treated surgically. In 1991, Bradley and Allen[40] introduced the concept of non-surgical management of sterile necrosis by applying early antibiotic treatment. The promising concept of using infection as the main parameter of surgical decision making has so far not been adopted generally[41] and remains a matter for discussion[42], requiring careful examination of established and evolved paradigms of severe AP management[43]. The goal of any consensus statement will be to provide recommendations regarding the management of the critically ill patient with severe AP or NP[44].

Non-operative drainage of intra-abdominal abscesses

Today, abundant literature documents the safety and efficacy of ultrasound- and CT-guided percutaneous drainage of abdominal and extraperitoneal abscesses. The success of percutaneous drainage is generally defined as effective source control with avoidance of surgery. In some instances, success also includes the ability to delay surgery until the acute process and sepsis are resolved and a definitive procedure can be performed under elective circumstances.

Image-guided percutaneous abscess drainage has become a standard method of treatment for most abdominal abscesses. In most cases, it should be considered the treatment of choice, but there are selected areas and circumstances that require specific approaches and methods. Typical abscesses within solid parenchyma organs or those in the peritoneal spaces can be reliably detected and efficiently drained. Abscesses that are multiple or long and circuitous require careful placement of catheters. Management of the drainage catheters includes irrigation with fluid to minimize accumulations of material that may impair egress of fluid. In selected cases, fibrinolytic agents have proved effective in shortening the drainage times and shortening hospital stays. Resolution of splenic abscesses, pancreatic abscesses, echinococcal abscesses, and fungal abscesses should involve careful selection and meticulous technique[45].

When considering primary percutaneous management of intra-abdominal abscesses, clearly establishing the etiology, location, and morphology of the abscess prior to drainage is important; it is necessary to evaluate the presence of ongoing enteric leak or fistula formation. With proper indication, most studies have reported success rates greater than 80% (range 33-100%) for drainage of localized non-loculated abscesses[46]; however, the success rates depend to some degree on the underlying pathology. In these studies, no significant differences were found between operative and primary non-operative management with regard to overall morbidity or length of hospital stay (mean duration of drainage 8.5 d).

Common reasons for failure of primary non-operative management include enteric fistula (eg, anastomotic dehiscence), pancreatic involvement, infected clot, and multiple or multiloculated abscesses. Significant procedure-related complications are reported to occur in less than 10% of cases (range 5-27%) with a less than 1% attributable mortality rate in the case of experienced physicians. In peritoneal abscess formation caused by subacute bowel perforation (eg, diverticulitis, Crohn disease, appendicitis), primary percutaneous management with percutaneous drainage was successful in most patients. Patients with Crohn disease whose abscesses were drained percutaneously had significantly fewer associated fistulae[47]. Failure in these patients was related to preexisting fistulization and extensive stricture formation. Concerns regarding the transgression of small or large bowel with drainage catheters in deep abscesses or ileus have been addressed in animal studies, which have found no increase in abscess formation, independently of whether catheters remained for 5 days or longer. Similar data are not available for human patients.

In summary, percutaneous and surgical drainage should not be considered competitive, but complementary. If an abscess is accessible to percutaneous drainage and the underlying visceral organ pathology does not clearly require surgery, percutaneous drainage can be used safely and effectively as the primary treatment modality. Closely monitoring the clinical progress of these patients is important. Improvement should be observed in less than 24-48 hours. If there is no improvement, patients must be reevaluated aggressively (eg, repeat CT scan) and the therapeutic strategy should be altered accordingly. Successful treatment is most likely to be achieved with candid consultation between the various clinical services.

Below, a group of Spanish physicians with an interest in the field of IAI discusses the most remarkable papers produced in this area during the last 2 years. The following are the publications selected for discussion.

Basic investigation-pathogenesis

Kimura F, Shimizu H, Yoshidome H, et al. Increased plasma levels of IL-6 and IL-8 are associated with surgical site infection after pancreaticoduodenectomy. Pancreas. 2006;32:178-85.

This study examined the relationship between plasma levels of cytokines and chemokines and the postoperative infectious complications observed after duodenopancreatectomy (DP). The authors studied 60 consecutive patients who underwent surgery during the period 2001-2003. Of these, 27 presented surgical wound infection (SWI). The IL-6 and IL-8 values measured at days 0 and 1 were significantly greater in patients with SWI. Linear regression analysis revealed a significant correlation between IL-6 on day 1 and the duration of surgery and pancreatic flow.

Comments

The authors propose that this disproportionate inflammatory response could lead to inhibition of the immune re-

sponse and, consequently, greater predisposition to postoperative intra-abdominal infection. Nevertheless, in order to demonstrate a cause-effect relationship, it would have been necessary to carry out tests *in vitro* or *in vivo* to reveal an inadequate immune response. Therefore, we can conclude that this study correctly evaluates the inflammatory response (IL-6, IL-8, MCP-1) and the mechanisms of regulation (IL-10) that appear after major surgery. However, problems defining SWI and the lack of biological and clinical parameters mean that the relationship between findings and onset of SWI is not very consistent.

Delikoukos S, Tzovaras G, Liakou P, Mantzos F, Hatzitheofilou C. Late-onset deep mesh infection after inguinal hernia repair. Hernia. 2007;11:15-7.

Delikoukos et al aimed to describe the clinical characteristics and outcome of 5 patients with late-onset deep mesh infection. Between 1988 and 2005, 1452 patients underwent groin hernioplasty using various types of mesh. Five patients (0.35%) appeared with late mesh infection. The patients' records were retrospectively reviewed. Two patients were admitted to hospital because of acute local inflammatory signs and 3 because of groin mass. The time from surgery ranged from 2 to 4.5 years. In all cases, ultrasound or CT showed abscesses around the mesh. The patients were operated on through the same groin incision. Pus was found in 3 patients and the meshes were removed. The cultures were positive in only 1 case and the microorganism isolated was *S. aureus*. The immediate postoperative period was uneventful and the patients were followed up for a median of 22 months (range: 6-44 months) postoperatively. There was no recurrence of hernia and/or chronic groin pain.

Comments

The incidence of late-infections after hernia repair using mesh is very low. Mesh removal and antibiotic therapy is the treatment of choice and it was associated with good outcome in the 5 cases presented here. The clinical characteristics (acute infections) and the etiology (*S. aureus* in 1 case) suggest that the infections reported in the present article were due to hematogenous seeding from a distal origin. As in the case of other implants (such as joint prosthesis), the incidence of acute hematogenous infections in mesh used for abdominal wall repair is extremely low. An animal experimental model showed that the risk of hematogenous infection of a foreign device decreases dramatically 3 weeks after implantation. Further studies are necessary to evaluate the incidence rate of late chronic mesh infections, which could sometimes be misdiagnosed due to the absence of typical symptoms of infection.

Harrell AG, Novitsky YW, Kercher KW, Foster M, Burns JM, Kuwada TS, et al. *In vitro* infectability of prosthetic mesh by methicillin-resistant *Staphylococcus aureus*. Hernia. 2006;10:120-4.

The aim of this study was to evaluate the ability of various common chlorhexidine/silver-coated and non-coated hernia biomaterials to resist adherence of methicillin-resistant *S. aureus* (MRSA). The prosthetic biomaterials tested were polypropylene, expanded polytetrafluoroethylene with and without silver/chlorhexidine coating, composite meshes, and lightweight polypropylene meshes. In this *in vitro* study, 15 samples (8 mm diameter) of each mesh type were placed individually into a sterile glass tube and inoculated with 108 MRSA. After incubating the glass tubes at 37 °C for 1 h, the mesh pieces were then removed and the broth supernatant saved for subsequent analysis. Each mesh piece was vortex-washed 5 times in phosphate buffered saline. All the washes were pooled for subsequent quantitative analysis. The adherent bacteria were determined by taking the initial inoculum and subtracting both the broth and the wash counts. This number was divided by the initial inoculum to give the percentage of adherent bacteria. The meshes were also examined using a scanning electron microscope. The mesh coated with chlorhexidine/silver had no detectable MRSA in the broth or the pooled wash samples, whereas it was detected in all the other type of mesh. Scanning electron microscopy demonstrated bacterial adherence to all mesh types except the coated mesh.

Comments

The mesh coated with chlorhexidine/silver demonstrated bactericidal activity against MRSA. In the future, it will be necessary to evaluate the impact of this type of implant on the infection rate. Bacterial attachment and proliferation on the surface of biomaterials is a key step in acute and delayed mesh infections. The ability of a biomaterial to resist infection may be a reasonable approach to reducing wound and prosthetic infections. The most common antiseptics used for coating biomaterials are chlorhexidine and sulfadiazine. In fact, previous clinical experience with central venous catheters coated with different antibiotics or antiseptics have demonstrated a reduction in catheter-related bloodstream infections.

Risk factors for infection

Gil P, Fernández Guerrero ML, Bayona JF, et al. Infections of implantable cardioverter-defibrillators: frequency, predisposing factors and clinical significance. Clin Microbiol Infect. 2006;12:533-7.

These authors studied the incidence of infection in 423 defibrillators implanted in 278 patients attended during the period 1988-2001. Infection was classified as early if it occurred during the first 4 weeks after surgery and late if it presented beyond 4 weeks. Onset of fever during the immediate postoperative period was quite common (13.7%), as was development of hematoma in the generator pocket (5.8%). The prevalence of infection was 2.4% in all cases (10/423) and 2.8% in all patients (8/273: 1 patient had 3 infectious episodes). Four cases were early and 6 late with a mean time to presentation of 14 days (5-21 days) and 26 months (1.5-84 months), respectively.

The following were associated with a greater risk of infection: (i) carrying out the procedure in 2 parts (OR 21.7; 95% CI, 4.73-99.48; $P < .01$); (ii) subcostal instead of subclavicular insertion (OR 6.62; 95% CI, 1.39-31.45; $P < .01$);

and (iii) implantation of the generator in the abdomen rather than in the subpectoral region (OR 5.03; 95% CI, 1.32-19.16; $P < .04$). In all cases, attempts were made to save the implant with antibiotic therapy. This was achieved in 3 of the 4 cases of early infection and in none of the cases of late infection (the material had to be removed in all the cases of late infection and in 1 of the cases of early infection).

Comments

The limitations of a retrospective study and the design of this study–evaluating cases instead of patients and analyzing each case as a patient–mean that the infection rate reported by the authors is surprising, although it can be explained by the long study period. Two-part surgery should be avoided, as should the subcostal approach and abdominal implantation. The authors do not clarify whether the patients had bacteremia, which increases the risk of implant infection. Neither do they comment on the use of transesophageal echocardiography to decide whether to remove the material, since the absence of involvement of the cables is associated with a high probability of cure with antibiotics. We must not forget that current recommendations advise early removal of all the material in the management of infections affecting implantable cardiac devices (pacemakers or defibrillators).

Epidemiology

Asensio A, Cantón R, Vaque J, et al. Nosocomial and community-acquired methicillin-resistant *Staphylococcus aureus* infections in hospitalized patients (Spain, 1993-2003). J Hosp Infect. 2006;63:465-71.

This study included 8,302 infections caused by *S. aureus* from a sample of more than 580000 patients from 296 Spanish hospitals representing more than half of the hospitalized population in Spain. The prevalence of methicillin-resistant *S. aureus* (MRSA) in hospitalized patients grew during the period 1993-2003 from 22 to 41% for nosocomial infections and from 7 to 28% for community-acquired infections. Geographic variations are observed, with higher rates of resistance in the center of Spain and the lowest in the south. The prevalence of MRSA increases linearly with age (10% in children under 10 to 32% in patients aged over 80). The highest rates by service were in intensive care (34%) with intermediate rates in medical and surgical services (25 and 22%, respectively). The percentage of MRSA is higher in ICU patients (34%), with the lowest in pediatric and obstetrics-gynecology patients. Baseline risk of patients and the number of intrinsic risk factors are linearly associated with the proportion of MRSA. The nosocomial origin of the infection and its site are also associated with the percentage of MRSA–this was lowest in the case of bacteremia (25%) and highest in respiratory and cutaneous infections (40 and 38%, respectively).

Comments

The study shows a progressive increase in nosocomial infections caused by MRSA. It is noteworthy that the areas of the body most exposed to external contamination, such as the respiratory tract or the skin, are the sites with the greatest percentage of infections by MRSA (unlike bloodstream infections).

Martínez JA, Aguilar J, Almela M, et al. Prior use of carbapenems may be a significant risk factor for extended-spectrum {beta}-lactamase-producing *Escherichia coli* or *Klebsiella* spp. in patients with bacteraemia. J Antimicrob Chemother. 2006;58: 1082-5.

This was a retrospective observational study of hospitalized patients with nosocomial clinical bacteremia caused by *Escherichia coli* or *Klebsiella* spp. The authors studied 2,172 episodes of nosocomial bacteremia. In the multivariate analysis, the following were associated with ESBL-producing *Enterobacteriaceae*: previous isolation of these microorganisms, severe comorbidity, renal transplantation, urinary origin, shock, and previous use of cephalosporins, carbapenems, and glycopeptides (the latter as a protective factor).

Comments

The authors found that previous use of carbapenems was a risk factor. This could be explained by 2 hypotheses: First, it would be related with a lower *in vitro* activity of carbapenems against ESBL-producing *Enterobacteriaceae*. The second and more plausible explanation, based on mathematical models, shows that, after using 2 antibiotics in 1 institution, exposure to the second drug for which there is no resistance behaves on an individual level. As a risk factor this is important, even if it reduces the prevalence of resistance to the first drug. As many patients carrying sensitive *Enterobacteriaceae* are admitted, treatment with carbapenems would eliminate these bacteria from experienced patients; therefore, they are more likely to be recolonized by the resistant strain that is endemic in the hospital.

Mannien J, Wille JC, Snoeren RL, van den Hof S, et al. Impact of postdischarge surveillance on surgical site infection rates for several surgical procedures: results from the nosocomial surveillance network in The Netherlands. Infect Control Hosp Epidemiol. 2006;27:809-16.

This study is based on the voluntary Dutch surgical infection surveillance system (PREZIES). The recommended active post-discharge surveillance (PDS) was by the use of a registration card for the patient's outpatient history on which the surgeon records an infection. Other forms of PDS that were not recommended included patient questionnaires, surgeon questionnaires, and telephone interviews with patients. In addition to these active methods, passive PDS included accidental identification of SWI. A total of 141321 operations carried out between 1996 and 2004 were analyzed. PDS was carried out in accordance with some of the methods recommended in 31134 operations (24%), in accordance with another active method in 32589 operations (25%), and using passive surveillance in

68075 operations (52%). PDS helped identify 31% of all SWI. More deep infections than superficial infections were identified after discharge (52 vs. 48%). The percentage of SWI identified after discharge was greater when the recommended method was used.

Comments

The main objective of monitoring nosocomial infections is to obtain reliable estimations of the risk of developing infection that can be compared with other reference estimations to identify risk situations or problems against which action must be taken. Therefore, the system must be highly sensitive, ie, able to identify most of the infections that arise. As hospital stays tend to be shorter, more infections tend to appear after discharge. This is particularly important for infections that take longer to appear or be identified (eg, deep infections associated with prosthetic implants). Monitoring with PDS provides more correct infection rates, especially for surgical procedures involving a short stay and/or when many of the SWI appear after discharge.

Activity of antimicrobials–resistance

Goldstein EJ, Citron DM, Warren YA, Tyrrell KL, Merriam CV, Fernández H. *In vitro* activity of moxifloxacin against 923 anaerobes isolated from human intra-abdominal infections. Antimicrob Agents Chemother. 2006;50:148-55.

This was a comparative antimicrobial sensitivity study involving:

– Strains: 923 anaerobes collected from 2001 to April 2004 from intra-abdominal infections before starting antibiotic therapy.
– Antimicrobials (cutoff point in µg/mL): moxifloxacin (2), levofloxacin (4), clindamycin (4), cefoxitin (32), ampicillin-sulbactam (16), and metronidazole (16).
– Sensitivity testing: agar dilution method as described in CLSI M11-A-6.

Of all the strains studied, 83% were sensitive to moxifloxacin at concentrations of 2 µg/ml or less. The most resistant species were *Bacteroides uniformis*, *B. vulgatus*, *Clostridium clostridiiforme* and *C. symbiosum*. If these species were not taken into consideration, 86% of the strains of other *Bacteroides* and 94% of other species of anaerobes were sensitive. Moxifloxacin was twice as active as levofloxacin. With the exception of the most aerotolerant species (*Actinomyces* and *Lactobacillus*) and of some isolates of *Peptostreptococcus* micros, *P. anaerobius* and the D*ialister-Suterella* group, 100% of strains were sensitive to metronidazole. In general, except for the occasional species, the activity of clindamycin, and particularly of cefoxitin and ampicillin-sulbactam, was superior. All the strains inhibited by metronidazole were also inhibited at a lower cutoff point (8 mg/mL).

Comments

The greatest limitation to using moxifloxacin alone in intra-abdominal infections stems from the high rate of resistance of *E. coli*, which is the facultative microorganism most commonly associated with anaerobes.

Betriu C, Rodríguez-Avial I, Gómez M, et al. Antimicrobial activity of tigecycline against clinical isolates from Spanish medical centers. Second multicenter study. Diagn Microbiol Infect Dis. 2006;56: 437-44.

This study examines the activity of tigecycline and other antimicrobial drugs against different groups of bacteria collected in Spain in 2005 and compares them with those of another multicenter study carried out in 2001. A total of 1102 bacterial isolates were processed: 915 were aerobes and 187 were anaerobes. Tigecycline, with an MIC90 of 0.06 µg/mL, was the most active of the antimicrobial drugs studied against *S. pneumoniae* with resistance to penicillin and macrolides. Linezolid, vancomycin, and teicoplanin were uniformly active against all the staphylococci studied. Tigecycline was the most active agent against MRSA, with an MIC90 of 0.125 µg/mL. The activity of tigecycline against coagulase-negative staphylococci was 8 times greater than that of vancomycin. For *E. faecium*, resistance to vancomycin was 6%, for ampicillin it was 79%, and for quinupristin-dalfopristin it was 29%. Tigecycline showed good activity against *E. faecium*, with an MIC90 of 0.06 µg/mL and was 16 times more active than linezolid, vancomycin, and teicoplanin. All the isolates of *E. faecalis* were sensitive to tigecycline, vancomycin, and ampicillin, but the MICs of tigecycline were lower (0.06-0.125 µg/mL). Tigecycline showed excellent activity against enterobacteria, inhibiting 90% of strains between 0.125 and 1 µg/mL, including 12% of ESBL-producing *E. coli* and *Kebsiella* spp. The most active agent against *A. baumannii* was polymyxin B, which inhibited all isolates at 1 µg/mL, whereas tigecycline (MIC50 4 µg/mL and MIC90 8 µg/mL) was 4 dilutions more active than imipenem and cefepime. Although most strains of *S. maltophilia* were resistant to several antibiotics, tigecycline showed good activity by inhibiting all strains at 4 µg/mL. On the contrary, tigecycline showed poor activity against *P. aeruginosa* (MIC90 16 µg/mL).

Comments

The results of the present article confirm the excellent activity of tigecycline against gram-positive and gram-negative microorganisms, including multiresistant strains. The MICs of tigecycline against all the gram-positive aerobes varied from 0.015 to 0.25 µg/mL and against Enterobacteriaceae they ranged from 0.03 to 4 µg/mL. The cutoff points defined by the FDA to determine the sensitivity to tigecycline are 2 µg/mL for *Enterobacteriaceae*, 0.5 µg/mL for *S. aureus*, 0.25 µg/mL for *E. faecalis* and *Streptococcus* spp. other than *S. pneumoniae* and 4 µg/mL for anaerobes. According to these criteria, all the isolates of MRSA, *E. faecalis*, and *C. difficile* in this study were sensitive to tigecycline, as were 99% of enterobacteria and 90% of *B. fragilis*. The activity of tigecycline against *Enterobacteriaceae* was not affected by the presence of ESBL. Tigecycline was not active against *P. aeruginosa*, agreeing with the results of previous studies. A limitation of this study is the non-inclusion of strains of *Proteus mirabilis*,

whose MICs for tigecycline (4 µg/mL) are higher than those of other enterobacteria owing to the presence in this species of an active AcrAB efflux pump for several antibiotics. The fact that all the MICs of tigecycline in this study are 1 to 2 dilutions lower than those published elsewhere may be due to the fact that the agar dilution method was used with plates prepared the same day as the inoculation.

Scheetz MH, Qi C, Noskin GA, Warren JR, et al. The clinical impact of linezolid susceptibility reporting in patients with vancomycin-resistant enterococci. Diagn Microbiol Infect Dis. 2006;56:407-13.

A retrospective paired case-control study was carried out to determine the impact of sensitivity to linezolid on clinical outcome. The study was based on a cohort of 20 cases with isolates of vancomycin-resistant enterococci (VRE) resistant or intermediate to linezolid (LRIVRE) during the period January to August 2004. For each case, 3 controls were included with linezolid-sensitive vancomycin-resistant enterococci (LSVRE) that had the same site of infection and species of VRE. Identification and the antibiotic sensitivity study of all the isolates with VRE were carried out using the Vitek 2 system (Vitek Systems, bioMérieux), with exception of linezolid. Initial sensitivity to linezolid was studied using the Kirby–Bauer disk diffusion method following the recommendations of the National Committee for Clinical Laboratory Standards or the E-test method. To confirm the initial results, the linezolid sensitivity test was repeated for all the LRIVRE isolates and in a selection of LSVRE, using disk diffusion, E-test, and agar dilution. Incorrect sensitivity to linezolid was defined as those isolates which were initially reported as intermediate or resistant, but which were sensitive to linezolid by agar dilution. All the LRIVRE isolates were studied by PCR to confirm whether mutation G2576T was present, and they were all typed using pulsed field gel electrophoresis (PFGE). The clinical investigation was based on a review of the patient's clinical history and the pharmacy and microbiology databases. Thirty-two independent variables were analyzed.

During the study period, 20 VRE isolates (1 per patient) were reported as LRIVRE. Of these, 14 were *E. faecium* and 6 *E. faecalis*. In 19 LRIVRE isolates, sensitivity to linezolid was initially studied by E-test and in 1 by disk diffusion. Of the 11 *E. faecium* isolates that were initially reported as having linezolid-intermediate sensitivity, 9 were sensitive when the E-test was repeated, 1 was sensitive in 2 of the 3 E-tests carried out, and only 1 remained intermediate by the E-test (carried out in triplicate). Of the 3 *E. faecium* that were initially reported as linezolid-resistant, 2 were intermediate by the E-test in triplicate and 1 was sensitive. The 5 isolates of *E. faecalis* initially reported as linezolid-intermediate were sensitive when the E-test was repeated, whereas 1 *E. faecalis* initially reported as resistant was intermediate by the E-test in triplicate. When the study was carried out using disk diffusion, the 14 strains of *E. faecium* and 6 of *E. faecalis* were sensitive. Agar dilution revealed that, except for 2 isolates (1 *E. faecalis* and 1 *E. faecium*), all the others were sensitive to linezolid. In agar dilution, these results correlated perfectly with the PCR study of 20 LRIVRE isolates, in which only these 2 strains (1 *E. faecalis* and 1 *E. faecium*) presented the mutation G2576T. Genotypic analysis by PFGE showed that the 20 LRIVRE isolates were genotypically different. As for the clinical characteristics, patients with LRIVRE developed more nosocomial infections, had more central lines, and underwent computed tomography more often than patients with infection by VRE. The multivariate analysis revealed an increase in the surgical procedures related to VRE infection (P = .008), an increase in the use of linezolid during hospital stay (P = .03), and a delay in the availability of culture and antibiotic sensitivity results, when cases and controls with LSVRE were compared (P = .006).

Comments

Given the results of this study, it seems necessary that, before issuing a report of an isolation of linezolid-resistant enterococci detected by disk-diffusion or E-test, this resistance must be confirmed by more accurate methods, such as agar dilution and PCR. This article shows that incorrect reports of linezolid-resistant enterococci are associated with increased morbidity and in expenditure on hospital resources. This study has a series of limitations, ie, causality could not be proven and data was collected retrospectively by 1 investigator. This may have skewed the collection of subjective variables.

Seguin P, Laviolle B, Chanavaz C, et al. Factors associated with multidrug-resistant bacteria in secondary peritonitis: impact on antibiotic therapy. Clin Microbiol Infect. 2006;12:980-5.

This is a prospective study of 93 consecutive adult patients with secondary peritonitis collected over an 11-month period. In 44 cases, the infection was community-acquired and in 49 it was nosocomial (35 of which were surgical). Patients with a pancreatic or gynecological cause were excluded. Fifteen multiresistant bacteria were isolated in 14 patients. In the multivariate analysis, duration of presurgical admission (5 days or more) and pre-intervention antibiotic therapy were associated with multiresistance.

Comments

The authors point out the limitations of the study: it involves only 1 hospital and center-specific microflora could affect the results of investigation. The importance of this study lies in the simplicity of its application.

Antibiotic therapy and trials

Bare M, Castells X, García A, Riu M, Comas M, Egea MJ. Importance of appropriateness of empiric antibiotic therapy on clinical outcomes in intra-abdominal infections. Int J Technol Assess Health Care. 2006;22:242-8.

Retrospective, descriptive and multicenter trial carried out in patients with community-acquired intra-abdominal infection to determine the frequency of inadequate empiric antibiotic therapy and its possible influence on cure. Clinical cure was classified according to resolution of the

infection by initial therapy, using second-line antibiotics, after reoperation, or when the patient died. The study enrolled 376 cases. Inadequate antibiotic therapy was observed in 51 patients (13.6%) and the relationship with the need for second-line therapy was statistically significant. The relationship with reoperation, mortality, and length of stay was not statistically significant.

Wilson SE, Turpin RS, Hu XH, Sullivan E, Mansley EC, Ma L. Does initial choice of antimicrobial therapy affect length of stay for patients with complicated intra-abdominal infections? Am Surg. 2005;71:816-20.

This was a retrospective study carried out using a commercial clinical database to investigate how the choice of initial empirical antibiotic affects hospital stay. The study analyzed 2150 patients with complicated abdominal infection on first-line therapy (ampicillin-sulbactam, ceftriaxone, ertapenem, levofloxacin, or piperacillin-tazobactam). With a crude analysis and taking into account other factors that affect hospital stay (type of infection, number of comorbidities, and length of stay in the ICU), patients treated with ampicillin-sulbactam and ertapenem had a shorter hospital stay than those who received ceftriaxone, levofloxacin, and piperacillin-tazobactam. This result could be explained by the fact that surgeons classified patients by severity and prescribed ampicillin and ertapenem for less complicated infections not requiring admission to the ICU.

Lau WK, Mercer D, Itani KM, et al. A randomized, open-Label, comparative study of piperacillin/tazobactam administered by continuous infusion vs. intermittent infusion for the treatment of hospitalized patients with complicated intra-abdominal infection. Antimicrob Agents Chemother. 2006;50:3556-61.

This was a randomized, open-label and multicenter study to compare the efficacy of piperacillin-tazobactam in a standard infusion (SI) (3/0.375 g/6 h administered over 30 minutes) with a continuous infusion (CI) over 24 hours (12/1.5 g) in complicated intra-abdominal infections. The duration of treatment ranged from 4 to 14 days. A total of 167 patients were analyzed: 86.4% of the CI group and 88.4% of the SI group were cured or improved (P = .817). No differences were observed in microbiological eradication (83.9% in CI and 87.9% in SI; P = .597); the same held true when the analysis was by pathogen. Defervescence and disappearance of leukocytosis occurred during the first 3 days of treatment in most cases and was similar in both groups. The adverse effects were comparable in the treatment groups.

Matthaiou DK, Peppas G, Bliziotis IA, Falagas ME. Ciprofloxacin/metronidazole versus beta-lactam-based treatment of intra-abdominal infections: a meta-analysis of comparative trials. Int J Antimicrob Agents. 2006;28:159-65.

This meta-analysis of comparative studies of ciprofloxacin + metronidazole and a betalactam alone or in combination with metronidazole in intra-abdominal infection evaluated clinical efficacy and mortality. Five studies obtained from a review of the PubMed database were reviewed: 4 were randomized (ceftriaxone + metronidazole, piperacillin-tazobactam, imipenem, amoxicillin-clavulanate + metronidazole) and 1 was not (cefotaxime + gentamicin + metronidazole), and the total number of patients was 1431. With respect to cure, there was a statistically significant difference in favor of ciprofloxacin + metronidazole (OR = 1.69; 95% IC, 1.20-2.39), although this was not detected when each was analyzed separately. These differences were not appreciated in crude mortality or in infection-related mortality.

Malangoni MA, Song J, Herrington J, Choudhri S, Pertel P. Randomized controlled trial of moxifloxacin compared with piperacillin-tazobactam and amoxicillin-clavulanate for the treatment of complicated intra-abdominal infections. Ann Surg. 2006;244:204-11.

This prospective, randomized, double-blind phase III trial compared the efficacy and safety of intravenous-oral sequential moxifloxacin (400 mg/24 h) with intravenous piperacillin-tazobactam (3/0.375 g/6 h) followed by oral amoxicillin-clavulanate (800/114 mg/12 h) in complicated abdominal infections classified according to APACHE II. Duration of treatment was 5-14 days and cure was evaluated between days 25 and 50. There were no statistically significant differences in the global cure rate, microbiological eradication, or in the adverse effects observed. The main weakness of the study is that APACHE II was not very high and many patients had complicated appendicitis.

Ferrer J, Fondevila C, Bombuy E, et al. Controlled, open, parallel-group study of the clinical and microbiological efficacy of piperacillin-tazobactam versus metronidazole + gentamicin in urgent colorectal surgery. Cir Esp. 2006;79:365-9.

This prospective, randomized, open-label trial compared the clinical and microbiological efficacy of piperacillin-tazobactam (4.5 g/8 h iv) with the combination of metronidazole (500 mg/8 h iv) and gentamicin (5 mg/kg/24 h iv). The study included 183 patients requiring emergency abdominal surgery because of colon involvement and/or severe acute appendicitis. The incidence of surgical wound infection was significantly lower in the patients who received piperacillin-tazobactam. In the appendicitis group, the incidence of intra-abdominal abscess was also lower. *E. coli* was the most predominant microorganism in culture.

Comments

Incorrect initial empiric treatment is quite common (14%), thus making it necessary to use second-line antibiotic therapy, although this does not affect mortality or hospital stay. Patients treated with ampicillin-sulbactam or ertapenem had lower hospital stays than those who received ceftriaxone, levofloxacin, or piperacillin-tazobac-

tam. This may be due to the fact that surgeons classify patients by severity and treat the less complicated cases with ampicillin-sulbactam and ertapenem. Clinical trials highlight that piperacillin-tazobactam has proven to be more efficacious than gentamicin + metronidazole in preventing surgical wound infection in emergency colon surgery. When piperacillin-tazobactam administered intermittently (every 6 hours) is compared with continuous infusion over 24 hours, no differences in efficacy or tolerance are observed. Finally, sequential moxifloxacin (intravenous/oral) is as efficacious as piperacillin-tazobactam followed by amoxicillin-clavulanate. A meta-analysis shows that ciprofloxacin + metronidazole is more efficacious than a betalactam alone or in combination with metronidazole.

Surgical technique and complications of intra-abdominal infections

Thompson DA, Makary MA, Dorman T, Pronovost PJ. Clinical and economic outcomes of hospital acquired pneumonia in intra-abdominal surgery patients. Ann Surg. 2006;243:547-52.

The objectives of this study were to evaluate the characteristics of patients who develop nosocomial pneumonia and to analyze the impact of this infection on costs and mortality. Patients were identified from the "2000 Nationwide Inpatient Sample" (NIS), 13292 (10.7%) of whom had pneumonia during the post-operative period. Of all the variables studied, those that showed independent predictive power for developing nosocomial pneumonia were female sex (OR 1.95: 95% CI, –1.87 to 2.03) and belonging to a minority race (OR 4.42: 95% CI, 3.26-6.01). The impact of nosocomial pneumonia on mortality, need for medical attention at discharge, mean stay, and cost for patients who underwent abdominal surgery is shown in the following table 1.

Comments

The study has important limitations stemming from its methodology, which is based on admissions data and on the discharge report. The authors assume that pneumonia is post-surgical, that the diagnosis of nosocomial pneumonia is correct (the chest X-ray of patients who underwent abdominal surgery is often difficult to evaluate). Furthermore, the study does not differentiate between certain factors associated with nosocomial pneumonia such as the need for mechanical ventilation, aspiration pneumonia, and comorbidity. The greatest incidence of pneumonia in patients who underwent gastrostomy was seen in those who had advanced neurological disease, cachexia, and a greater risk of bronchopulmonary aspiration. The greater risk among patients belonging to a racial minority was due to lower income.

Despite these limitations, the size of the sample is sufficiently large and representative to highlight the importance of nosocomial pneumonia after abdominal surgery.

Aufenacker TJ, Koelemay MJ, Gouma DJ, Simons MP. Systematic review and meta-analysis of the effectiveness of antibiotic prophylaxis in prevention of wound infection after mesh repair of abdominal wall hernia. Br J Surg. 2006;93:5-10.

All studies published between 1966 and 2005 appearing in international databases (Medline, Cochrane) were selected by introducing the keywords "hernia" and "antibiotic prophylaxis". Only randomized and placebo-controlled studies were included. Each study was evaluated by 3 reviewers. The statistical methodology applied was that of a meta-analysis. The risk of surgical wound infection was analyzed, as was deep infection, although separately. A total of 6 studies were selected and these included patients who underwent surgery for inguinal hernia by standard placement of mesh. Most studies excluded patients with a high risk of infection (eg, patients with diabetes mellitus). In 3 studies, prophylaxis was with cefazolin (in 2 with 1 g and in 1 with 2 g) and in the other 3 with 1.5 g of cefuroxime, 1.5 g of ampicillin-sulbactam, and 2 g of amoxicillin-clavulanate, respectively. The total number of patients analyzed in the placebo group and antibiotic group was 1230 and 1277, respectively. The global rate of infection was 3% in the placebo group and 1.5% in the antibiotic prophylaxis group, whereas the rate of deep infection was 0.6% and 0.3% for the placebo group and the prophylaxis group. The odds ratio for surgical wound infection when the patient received antibiotic prophylaxis was 0.5 (95% CI, 0.24-1.21).

Comments

The data presented do not recommend routine administration of antibiotic prophylaxis in patients undergoing surgery for inguinal hernia who have mesh fitted. However, we must stress that in 2 studies with a higher infection rate and a greater mean duration of surgery antibiotic prophylaxis significantly reduced the risk of infection. Therefore, the authors should have stressed, as previous studies show, that when the duration of the intervention is above the usual mean duration, a dose of antibiotic prophylaxis should be administered. On the other hand, the low number of patients in randomized studies means that the results do not enable us to draw firm conclusions in any sense. In fact, with a prevalence of infection of 3% in the placebo group and 1.5% in the prophylaxis group, and taking a 5% alfa error and a power of 90%, it would be

TABLE 1

	Patients with pneumonia	Patients without pneumonia	Adjusted OR (95% CI)
Mortality	1421 (10.7%)	7217 (1.2%)	8.50 (7.94-9.09)
Care at discharge	4461 (38%)	48785 (8.1%	4.13 (3.94-4.34)
Mean stay (days)	17.1 ± 18.7	6.07 ± 5.4	10.95 (10.83-11.07)
Cost ($)	52.099 ± 61.779	21.046 ± 27.536	28.160 (27.543-28.778)

necessary to include 2183 patients per arm to find significant differences. Therefore, we understand that the most appropriate message is that antibiotic prophylaxis reduces surgical wound infection (3% to 1.5%) but does not reach statistical significance; therefore, there are not sufficient data to conclude with any certainty that it is necessary to use mesh, although when the duration is extended for any reason, it is necessary to administer a dose of antibiotic during surgery.

Pasqualotto AC, Denning DW. Post-operative aspergillosis. Clin Microbiol Infect. 2006;12:1060-76.

This was a scientific literature review to identify published cases of aspergillosis after surgery and not after dissemination of an infection or previous known colonization by *Aspergillus* spp. MEDLINE, LILACS, and EMBASE were used to search for articles, using the keywords "*Aspergillus*", "surgery," and others referring to organs or specific surgical procedures. Congress abstracts were reviewed using the address: http://www.aspergillus.man.ac.uk. To be accepted as post-surgical aspergillosis, cases had to have microbiological confirmation of *Aspergillus* spp. by culture, histology, or microscopy. A diagnosis of surgical wound aspergillosis was accepted if the skin or subcutaneous cell tissue at the surgical site was involved, if *Aspergillus* spp grew at the surgical site, if antibiotic therapy did not cure the infection, and if no other pathogens were observed or were found in small quantities. More than 500 patients with aspergillosis were selected after several surgical interventions.

Comments

The authors stress the risk of severe aspergillosis in immunocompetent patients undergoing habitual surgery, probably associated with environmental contamination of the air in the operating room, surgical material, or grafts. Occasionally, the origin of the infection was found in a neighboring tissue (paranasal sinuses, bronchopulmonary tree) and was not known before surgery. The study does not show the real incidence of aspergillosis after surgery. Furthermore, the article points out the complexity involved in diagnosing this form of aspergillosis, since its course is often indolent and its diagnosis late, sometimes quite a few months after surgery.

Plikaitis CM, Molnar JA. Subatmospheric pressure wound therapy and the vacuum-assisted closure device: basic science and current clinical successes. Expert Rev Med Devices. 2006;3:175-84.

The main clinical uses of the VAC (vacuum-assisted closure device) are described as traumatic wounds and orthopedic conditions, sternal wounds, abdominal wounds, enterocutaneous fistulas, burns, skin grafts and dermal substitutes, and myoglobinuria. There are very few contraindications for VAC, although it must be stressed that it is first necessary to débride the wound well before use. Lastly, the 2 most frequent complications are pain caused by the device and possible bleeding.

Comments

This is a magnificent review of the mechanisms involved in the effects of subatmospheric pressure and of the different scenarios in which this technique can be used. We must stress how this system can be used in almost all circumstances, as it is safe and efficacious. So that the reader is not left with a false impression, we also state that osteomyelitis and infected tissue are contraindications. The authors of the review affirm the contrary by referring to a report of toxic shock in a patient with other characteristics and in which the authors, instead of considering that VAC may not be the ideal option, recommend suitable follow-up (patient with discharge colostomy, stomal necrosis, and dehiscence after reoperation was sent home with VAC and follow-up by outpatient nursing) with early treatment in the case of suspected infection.

Intra-abdominal abscess

Kumar RR, Kim JT, Haukoos JS, et al. Factors affecting the successful management of intra-abdominal abscesses with antibiotics and the need for percutaneous drainage. Dis Colon Rectum. 2006; 49: 183-9.

This study aimed to evaluate the cure rate of IA by medical treatment only and identify the possible factors related to failure and the need for percutaneous drainage. A total of 114 patients were included. Sixty-one cases (54%) were treated with antibiotics only. Of these, 3 cases (5%) had a relapse and 22 (36%) underwent a second operation electively. Fifty patients (44%) required percutaneous drainage due to failure of medical treatment. The median temperature and diameter of these abscesses (6.5 cm) was significantly greater than those of the antibiotic-only group. There were no relapses in the drainage group, but in 7 cases (14%) symptoms persisted and surgery was necessary.

Comments

The literature shows that there is a high percentage of success with hepatic abscesses measuring less than 5 cm and in patients receiving medical treatment only. Similarly, a high percentage of abscesses due to acute diverticulitis are resolved with bowel rest and antibiotics. The authors conclude that, in their experience, 91% of IA can be treated with antibiotics and percutaneous drainage only and that a temperature on admission of > 38.5 °C or abscesses > 6.5 cm are associated with failure of antibiotic therapy. In these cases they recommend percutaneous drainage. This study has serious limitations. Most of the patients included were young with appendicitis and there are no reports of comorbidity or of the criteria used to differentiate between periappendiceal/pericolonic edema and abscess collection.

Kim YJ, Han JK, Lee JM, et al. Percutaneous drainage of postoperative abdominal abscess with limited accessibility: preexisting surgical drains as alternative access route. Radiology. 2006;239:591-8.

The authors of this study report their experience with percutaneous drainage of abscesses with limited accessi-

bility using a pre-existing surgical drain as an access route. This was a retrospective study analyzing 92 patients. The diameter of the abscesses ranged from 2.5 to 13.5 cm with an aspiration volume of between 5 and 1000 mL. The catheter was correctly fitted in 95% of cases. In 27 patients, the surgical drainage catheter was badly fitted, although in 25 it was still possible to obtain adequate drainage. Of the 87 patients with whom the technique was successful, clinical treatment was successful in 75 (86%) without the need for surgery. No complications were recorded during the procedure. In the multivariate analysis, only the presence of a fistula was associated with clinical failure (OR 4.3; 95% CI, 1.1-17).

Comments

The authors describe a new technique of percutaneous access with a high percentage of success and no procedure-associated morbidity. Nevertheless, 24% of cases required fresh handling of the catheter. The search for factors associated with failure is somewhat artificial given their low number, thus preventing correct analysis of the subgroups.

Bile duct: cholangitis-cholecystitis

Lee JK, Ryu JK, Park JK, et al. Risk factors of acute cholecystitis after endoscopic common bile duct stone removal. World J Gastroenterol. 2006;12:956-60.

This retrospective study enrolled 100 patients who underwent endoscopic retrograde cholangiopancreatography (ERCP) to eliminate stones from the common bile duct. Prophylactic cholecystectomy was not carried out. The exclusion criteria were development of acute cholecystitis during ERCP, and presence of a tumor. During the study period, 1986 patients underwent ERCP. The authors only studied 100 patients who fulfilled the inclusion criteria. During a mean follow-up of 18 months, 28 (28%) patients had biliary symptoms: 17 (17%) due to acute cholecystitis and 13 (13%) due to recurrence of stones in the common bile duct. In the multiple regression analysis, the risk factors for cholecystitis were total bilirubin < 1.3 mg/dL and a common bile duct diameter of < 11 mm.

Comments

The basic limitation of this study is that it is retrospective. The results indicate that we should consider prophylactic cholecystectomy to avoid acute cholecystitis in those patients with stones in the gall bladder who undergo ERCP for the removal of stones in the common bile duct and who present a total bilirubin level of < 1.3 mg/dl and a common bile duct diameter < 11 mm. A randomized prospective study should be carried out to confirm these data.

Vracko J, Markovic S, Wiechel KL. Conservative treatment versus endoscopic sphincterotomy in the initial management of acute cholecystitis in elderly patients at high surgical risk. Endoscopy. 2006;38: 773-8.

This prospective study evaluated whether endoscopic sphincterotomy can improve clinical outcome in high surgical risk elderly patients with acute cholecystitis in whom emergency cholecystectomy is not performed. The study included 105 patients over 65 years of age with acute cholecystitis. Patients were randomized to receive conservative treatment (n = 53) or endoscopic sphincterotomy by ERCP (n = 52). The main study parameter was the need to perform emergency cholecystectomy during the first week of admission. The most relevant results of the study were that 15 patients (28%) of the group assigned to receive conservative therapy developed biliary sepsis requiring emergency cholecystectomy, whereas in the sphincterotomy group, no patient needed emergency surgery ($P < .001$); 1 patient presented biliary sepsis requiring surgery 12 days after the sphincterotomy. Three patients who underwent endoscopic sphincterotomy had iatrogenic complications and 1 required surgery. Clinical outcome was favorable by avoiding urgent cholecystectomy and other procedures in 48 patients in whom endoscopic sphincterotomy was performed and in 36 patients who received conservative treatment ($P < .01$). Finally, cholecystectomy was performed in 44 patients treated conservatively: 15 emergency patients, 28 elective patients 3-5 days after completing the preoperative study and 1 patient 3 months later; of the patients assigned to the sphincterotomy group, 38 required elective cholecystectomy at 3 weeks, after all the patients had been discharged.

Comments

According to the authors, acute cholecystitis caused by bile duct obstruction stems initially from a sterile inflammation of the bile duct owing to a reflux of pancreatic enzymes. This is followed by bacterial invasion and biliary sepsis. The removal of stones and, therefore, the obstruction and pancreatic reflux would avoid the development of biliary sepsis and the need for emergency surgery. The results of this study suggest that endoscopic sphincterotomy is an alternative in patients suffering from acute cholecystitis who present a high surgical risk and in whom emergency surgery increases the risk of morbidity and mortality. Sphincterotomy removes the need for emergency surgery in patients with acute cholecystitis. However, other very efficacious and less dangerous techniques must be taken into consideration, such as percutaneous puncture and drainage with guided cholecystostomy.

Pancreatitis

Mazaki T, Ishii Y, Takayama T. Meta-analysis of prophylactic antibiotic use in acute necrotizing pancreatitis. Br J Surg. 2006;93:674-84.

The authors selected studies containing the following information: certain diagnosis, antibiotics used in prophylaxis, control group therapy, infected necrosis rate, mortality, rate of non-pancreatic infections, need for surgery, and hospital stay. The global selection criteria for the articles are explained, as are the reasons for exclusion, until the 6 reference studies are selected. The characteristics of each study are resumed. These show that the trials were carried out with different antibiotics. Furthermore, the low methodological quality of the studies is pointed out (small sample, standard treatment not indi-

cated–both affect the results of the meta-analysis). A total of 329 patients were included, 167 of whom received antibiotics and 162 control patients.

Primary objectives:

– Infected necrosis: use of prophylactic antibiotics does not reduce mortality. RR 0.77 (95% CI, 0.54-1.12; *P* = .173).

– Mortality: no reduction in mortality is shown with the use of antibiotics. RR 0.78 (95% CI, 0.44-1.39; *P* = .404).

Secondary objectives:

– Extrapancreatic infections: use of prophylactic antibiotics does not reduce extrapancreatic infections; RR 0.71 (95% CI, 0.32-1.58; *P* = .402).

– Need for surgery: is not reduced with antibiotics; RR 0.78 (95% CI, 0.55-1.11; *P* = .167).

– Hospital stay: the use of antibiotics is associated with a lower hospital stay; RR –5.64 (95% CI, -11.01 to 0.27; *P* = .040).

Comments

The limitations of this meta-analysis are that it examines low-quality studies with a small sample size and a great deal of crossover between them, there is no differentiation between causes of mortality, and, lastly, there are large differences in baseline standardized treatment. Nevertheless, the authors consider that the most consistent analysis is the lack of a reduction in the rate of infected necrosis. In methodological terms, the study is excellent and shows that, with current trials, there is no statistically significant benefit with the use of prophylactic antibiotics. However, there are large methodological gaps, with the result that a multicenter clinical trial would be necessary, with a more suitable and predefined sample size, with standardized treatment in line with current knowledge in both groups, and protocol-based administration of antibiotic or placebo that would provide an answer to the question: Should antibiotic prophylaxis be used in severe acute pancreatitis?

Manes G, Uomo I, Menchise A, Rabitti PG, Ferrara EC, Uomo G. Timing of antibiotic prophylaxis in acute pancreatitis: a controlled randomized study with meropenem. Am J Gastroenterol. 2006;101: 1348-53.

The authors compare 2 strategies using antibiotics in severe acute pancreatitis: (i) antibiotic therapy with meropenem from admission, which is readjusted according to the CT scan and maintained only if there is necrosis; (ii) no antibiotic therapy on admission, and the results of the CT are used to guide administration only to the necrotic forms. The study included 215 patients with acute pancreatitis of whom 59 had necrosis. The results are summarized as follows:

– There are no differences in the incidence of sepsis, multiorgan failure and mortality.

– There are fewer extrapancreatic infections in the group that starts early prophylaxis.

– Multi-organ failure: same incidence in both groups (6.6%).

– Mortality: similar in both groups (3 cases in each group, 10 and 10.34%, respectively).

Comments

This trial has a very small sample size, it is poorly organized, and the objectives are not cited a priori. It includes patients with acute pancreatitis–moderate or severe–but it does not select the acute forms. What this clinical trial does show is that the early use of meropenem in necrotic forms, compared with use after CT, reduces extrapancreatic infections but not pancreatic infections.

Eggimann P, Jamdar S, Siriwardena AK. Pro/con debate: antifungal prophylaxis is important to prevent fungal infection in patients with acute necrotizing pancreatitis receiving broad-spectrum antibiotics. Crit Care. 2006;10:229.

In this study, different experts give opposing opinions on the use of antifungal prophylaxis. Philippe Eggimann, an intensivist, defends the generalized use of antifungal prophylaxis with azoles due to their safety and good bioavailability in pancreatic tissue. The justification for this is that *Candida* spp. is isolated in necrotic tissue in 15 to 75% of patients with necrotizing pancreatitis who require surgery, especially in those who previously received antimicrobial prophylaxis. Jamdar and Siriwardena are 2 surgeons who belong to the Hepatobiliary Surgery Unit of a hospital in Manchester. These authors are against the routine use of antifungal prophylaxis and base their arguments on the possibility of selecting resistant species of *Candida*, the lack of data on delaying surgery by using prophylaxis, and, above all, the lack of scientific evidence.

Comments

Prophylaxis with antifungal drugs should be considered in severely ill patients with acute necrotizing pancreatitis and a prolonged stay in the ICU with endovascular catheters, percutaneous drainage, multi-organ dysfunction, and antibiotic therapy.

Transplantation of intra-abdominal organs

Pappas PG, Andes D, Schuster M, et al. Invasive fungal infections in low-risk liver transplant recipients: a multi-center prospective observational study. Am J Transplant. 2006;6:386-91.

These authors carried out a prospective observational study on 200 liver transplant recipients with a low risk of developing invasive fungal infection (IFI) and who did not receive antifungal prophylaxis. Patients were considered as low risk if they had a maximum of 1 of the following conditions: anastomosis with choledochojejunostomy; retransplantation; intraoperative administration of more than 40 units of blood and derivatives; need for reoperation due to intra-abdominal bleeding; reoperation due to dehiscence of sutures or vascular thrombosis; pre-operative serum creatinine ≥ 2 mg/dL; or pre-operative colo-

nization by *Candida* spp. The patients were followed up for 100 days after transplantation to search for evidence of IFI. Of the 193 patients that fulfilled the established criteria, 7 (4%) developed IFI. In 3 (2%), IFI was due to *Candida* spp. and could have been avoided using prophylaxis with fluconazole. Nevertheless, a further 3 patients developed invasive aspergillosis that, in theory, could not have been avoided with prophylactic fluconazole and 1 patient developed late-onset disseminated cryptococcus that could not have been avoided with prophylactic fluconazole during the first months after transplantation.

Comments

According to the authors, these data show that liver recipients at a low risk of developing IFI can be identified using predetermined criteria and that routine antifungal prophylaxis could be omitted in these patients.

Berger N, Wirmsberger R, Kafka R, et al. Infectious complications following 72 consecutive enteric-drained pancreas transplants. Transpl Int. 2006;19: 549-57.

The authors analyzed 72 pancreas recipients with enteric drainage. The severe infectious complications were intra-abdominal infection (n = 12), surgical wound infection (n = 7), sepsis (n = 13), respiratory infection (n = 4), UTI (n = 12), herpes simplex (n = 5), CMV infection/disease (n = 7), post-transplant lymphoproliferative disease (PTLD, n = 3), invasive fungal infection by filamentous fungi (n = 4), clostridial colitis/rotavirus (n = 1), and endocarditis (n = 1). Four patients from the series died of infectious complications: invasive aspergillosis (n = 2), invasive zygomycosis (n = 1), and PTLD (n = 1).

Comments

The main message is the high incidence of infection which still affect this transplant due, among other reasons, to the type of patient (diabetics with advanced disease, patients with uremia undergoing dialysis, etc.), the idiosyncrasy of the surgical technique (opening of the gastrointestinal tract without preparation), and the aggressive nature of immunosuppression protocols.

Castroagudin JF, Ponton C, Bustamante M, et al. Prospective interventional study to evaluate the efficacy and safety of liposomal amphotericin B as prophylaxis of fungal infections in high-risk liver transplant recipients. Transplant Proc. 2005;37: 3965-7.

Over a period of 28 months, these authors collected 100 liver recipients, 21 of whom were considered at high risk of developing a fungal infection by presenting at least 1 of the following criteria: acute liver failure, assisted ventilation > 7 days, retransplantation, relaparotomy, antibiotic therapy > 14 days, need for > 20 units of red cells and/or failure of anastomosis of the bile duct. This group received antifungal prophylaxis with liposomal amphotericin B at 1 mg/kg/day for 7-10 days. One-year survival in the high-risk group, who received antifungal prophylaxis, was 80%. There were no significant differences in the prevalence of IFI in the low-risk group, who did not receive prophylaxis (6.3%), compared with the high-risk group that did receive prophylaxis with liposomal amphotericin B (9.5%), although in the latter group there were 2 infections due to Aspergillus spp., 1 of which was fatal. Two (10%) of the patients who received prophylaxis developed renal insufficiency.

Comments

The authors conclude that liposomal amphotericin B at 1 mg/kg/day is useful for the prevention of IFI in high-risk patients, although they do suggest that higher doses could be necessary to prevent infection by *Aspergillus*.

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