Decasan in the treatment of infected wounds after urological surgeries

S.P. Pasechnikov, the Chief Urologist of the Ministry of Health of Ukraine, the Scientific Supervisor of GUC, Dr. Med. Sci, Professor;
O.D. Nikitin (The Institute for Urology of the Academy of Medical Sciences of Ukraine, Kyiv)

The problem of prevention and treatment of postoperative purulent complications in Urology is still a current issue as of today. To a substantial degree this is related to the increasing number of complex surgeries using modern technologies, the increasing volume and duration of surgical interventions, accompanied by increased tissue trauma and blood loss, which contributes to the development of postoperative wound infections [8].

The number of postoperative purulent complications in elective abdominal surgery is 6-8 % on the average (0.8-2% in "clean" surgeries and up to 20 % in contaminated surgeries) [2, 6, 14]. The most frequent wound-related purulent inflammatory complications in Urology occur after surgeries for purulent pyelonephritis and pyonephrosis, with incidence from 6.8 to 42 %, according to different authors [3, 6].

According to CDC's National Nosocomial Infections Surveillance (NNIS), USA, surgical site infections (SSI) are the third most common nosocomial infection, contributing to 14 and 16% of all nosocomial infections in hospitalised patients [15].

Between 1986 and 1996 a total of 15 523 cases of SSI were documented in 593 344 surgical procedures in hospitals subject to epidemiological monitoring of SSI within the NNIS system. Of the above in 2/3 patients the process was localized in the area of incision and in 1/3 cases the organs or cavities adjacent to the surgical site. The emergence of SSI extends hospital stay by 10 days and increases the cost of hospitalisation by 2000 USD [5, 14].

Infectious complications, developing in hospitalised patients may be caused by either community-acquired or nosocomial flora [9]. According to NNIS and domestic authors, the distribution of pathogens, isolated in SSI, has not undergone any substantial changes during the recent decade, despite of differences of these indices across various surgical clinics [15]. The following pathogens are the most frequently isolated ones: Staphylococcus aureus, coagulase-negative Staphylococci, Enterococcus spp. and Escherichia coli. Increasingly important role in the development of SSI is being played by antibiotic-resistant strains, such as methicillin-resistant S. aureus (MRSA) and Candida albicans [12].

Microbial contamination of postoperative wound is inevitable even in ideal adherence to aseptic and antiseptic regulations; by the end of surgical procedures 80-90% of wounds are already contaminated by various microflora, most frequently Staphylococci [7]. However, as demonstrated by A. Biver with extensive clinical material, purulent complications develop only in 2-30% of cases. This is likely explained by the fact that microbial content in the surgical wound should be not less than 105 for SSI to develop [13].

For development of wound infection decisive not only the species of the pathogen, but also the condition of host, as well as the functional condition of the damaged tissues are of decisive importance. That is why I.V. Davydovsky has stressed that the guiding principle of surgeons should be "not fighting the bacteria in the wound, but rather struggling for anatomical cleanliness of the wound" [4].

Postoperative infection in Urology may be divided into wound infection (mostly caused by S. aureus) and urinary tract infection (mostly caused by Gram-negative aerobes of the Enterobacteriaceae family) [6, 7]. In patients with indwelling urinary catheters there is a risk for postoperative infection of nosocomial origin. In addition there are a number of factors that contribute to post-operative purulent and inflammatory complications (see Table 1).

It is well known that the widespread use of broad-spectrum antibiotics causes the selection of resistant populations from infective locus or from patient's endogenous microflora. Resistant microbial strains may be transferred from one patient to another via various items in violations of hygienic regimen in the surgical department. Within 48 hours of patient's stay in a surgical hospital setting there is contamination of his/her biological eco-niches (skin, mucous membranes of the respiratory tract and digestive tract) by hospital strains of organisms, resistant to most antibiotics in use [1, 10]. Under this condition antiseptic agents for local therapy acquire great significance.

Against the background of reassessing the role of antibiotics, there is a re-emerging interest in antiseptic prophylaxis of infections and antiseptic therapy. The agents of microbial decontamination are chemical compounds, and, in certain cases, biologicals (bacteriophages, bacterial agents, etc.).

The antiseptics most frequently used in contemporary healthcare are surface-active agents (surfactants). Depending on chemical properties surfactants are divided into ionic and non-ionic agents. Ionic surfactants are the molecules that carry either a positive charge, the cationic surfactants (quaternary ammonium compounds - decamethoxin, degmin, ethonium and cerigel) or the molecules that carry negative charge, the anionic surfactants (alkaline soaps, alkyl and arylsulphones and iodophors — iodonat and iodopiron). Being chemical antiseptics, ionic surfactants exert bactericidal action. Cationic surfactants possess high antimicrobial activity, since under natural conditions microbial cells are characterised by an overall negative charge. Antiseptics are bound to phosphatide groups of the lipids of cytoplasmatic membrane of microbial cells, which leads to impaired permeability. Gram-positive and Gram-negative bacteria, yeast and filamentous fungi are sensitive to cationic surfactants; the activity of these antiseptic agents elevates with increasing pH of the environment [9].

At the same time, the bacterial cell contains the molecules with a positive charge, which is the reason why anionic surfactants possess destructive effect on bacteria due to interaction with reaction-capable groups of membrane proteins; however, this requires higher concentrations of the drugs [2].

Among a large number of antiseptic agents, there is a cationic surfactants of increasing clinical importance, namely decamethoxin (Decametoxinum) [1,10 - Decamethylene - (N,N - dimethylmenthoxycarbonylmethyl) ammonium chloride], a bis-quaternary ammonium derivative compound, a highly active and a fast-acting drug, which consists of a synthetic decamethylene part of the molecule and menthol ether of peppermint oil.

Table 1. Risk factors of postoperative infectious complications in Urology.

Urological	Others	Intraoperational
Recurrent infections of МВП	Age over 50 years	Violation of aseptic techniques
Oncopathology of genitourinary system	Lesions of cardiac valves (bacterial endocarditis)	Excessive use of diathermocoagulation and other methods of thermal influence
Large volume of residual urine	Haematological disease	Inadequate drainage
Hydronephrosis	Immunosuppression	Intraoperational intestinal damage
Urinary catheters	Remote foci of infection	Intraoperational hypoxia
Neurogenic urinary bladder	Oncological disease of other organs and systems	Significant blood loss
Penile prostheses	Obesity	Prolonged surgery
Radiation therapy (including history of) due to pelvic disease	Metabolic disorders	
Prior pelvic surgery	Prolonged postoperative period	
Congenital anomalies of genitourinary organs	Incorrect preparation of the surgical field (early shaving, excessive use of antiseptics)	
Congenital/artificial communications of genitourinary organs with intestinal lumen	Diabetes mellitus	
	Pregnancy	
	Chemotherapy	
	Artificial heart valves	
	Recent joint replacement surgeries, vascular grafting and placement of stents	
	Preoperative steroids	
	Severe disease of other organs and systems	

The most common dosage form of decamethoxin is a 0.02% solution of the drug, manufactured by YURIA-PHARM Company (Ukraine) under the trade name Decasan.

The antimicrobial effect of decamethoxin is manifested by inactivation of exotoxin and degradation of proteins of pili and flagella, which are located on the surface of the microbial cell. There is blockade of the functions of cellular wall and suppression of vital functions of the cellular areas, responsible for protein synthesis and cell division. This ensures a substantial therapeutic effect without damaging the microbial cell.

Decamethoxin exerts pronounced bactericidal action on Staphylococci, Streptococci, Corynebactrium diphtheriae, Pseudomonas aeruginosa and capsulated bacteria; the fungicidal action of the drug has been reported for yeast-like fungi, epidermophytosis, Trichophyton, microsporia, erythrasma and some moldlike fungi (Aspergillus and Penicillium); the drug exerts antiprotozoal action on Trichomonas and Giardia; also, it is known to have virucidal action. The product has excellent activity against microorganisms resistant to penicillin, chloramphenicol, tetracycline, streptomycin, monomycin, kanamycin, neomycin, novobiocin, erythromycin, oleandomycin, cephalosporins and fluoroquinolones, etc. Bacteriostatic (fungistatic) concentrations of the drug are close to its bactericidal (fungicidal) concentrations. Decamethoxin destroys bacterial exotoxins; in concentrations exceeding 10 g/mL the product dramatically reduces the adhesion of Corynebacteria, Salmonella, Staphylococci and Escherichia.

Antibiotic-resistant strains retain sensitivity to the product. In course of decamethoxin therapy there is increased sensitivity of antibiotic-resistant strains to antibiotics. Resistance to decamethoxin itself occurs in a slow fashion. Thus, after 30 passages the resistance of Staphylococcus and Corynebacterium diphtheriae has increased 4-8 times, but was still well below the effective therapeutic doses of the product. No circulation of decamethoxin-resistant strains of organisms was found in nature.

The concentration of decamethoxin in Decasan product does not exert any toxic effects. Prolonged use of the products does not cause allergic reactions.

The presence of such a vast number of advantages has determined the significant interest in Decasan as a local antiseptic used in septic surgery.

The aim of this study was to assess the efficacy and safety of using Decasan (manufactured by YURIA-PHARM, Ukraine) for the treatment of purulent wounds after surgeries for purulent inflammatory renal disease.

Materials and Methods.

A total of 38 subjects aged from 19 to 74 years (mean age 46.5 years) were enrolled in the study; there were 26 females and 12 males. Surgical procedures for calculous pyonephrosis were performed in 23 (60.5 %) patients; surgeries for renal abscess were performed in 7 (18.4 %) patients; surgeries for renal carbuncles were performed in 5 (13.2 %) patients and surgeries for polycystic kidney with suppurated cysts were performed in 3 (7.9 %) patients (see Table 2). Nephrectomy was performed in 27 (71 %) patients; lancing and draining of renal abscess — in 4 (10.5 %) patients; nephrostomy and lancing of carbuncles — in 4 (10.5 %) patients; lancing and draining of suppurated cysts was performed in 3 (7.9 %) patients (see Table 3). The patients were distributed into two groups: main group (21 subjects) and control group (17 subjects). Local therapy in the main group was performed with Decasan; sanitation of wounds in the control group was performed with 0.05 % solution of chlorhexidine bigluconate. Antiseptics were used for irrigation of wound cavities via drainage tubes, for sanitation of wound channels with turundae and for loose wound tamponade. Dressing change was performed several times a day as required. General treatment was identical in both groups and included administration of antibacterial, detoxification, anti-inflammatory, immunomodulating, and desensitizing agents. Along with local application of antiseptics, wound care included adequate drainage and excision of necrotic tissues. Besides, symptomatic treatment of concomitant disease was performed.

Table 2. The characteristics of study subjects by types of purulent inflammatory disease

Diagnosis	Group				Total (n = 38)	
	main (n = 21)		control (n = 17)			
	abs.	%	abs.	%	abs.	%
Pyonephrosis	12	57.1	11	64.7	23	60.5
Renal abscess	5	23.8	2	11.8	7	18.4
Renal carbuncle	2	9.5	3	17.6	5	13.2
Polycystic kidneys with suppurated cysts	2	9.5	1	5.9	3	7.9

Table 3. The characteristics of surgical interventions in study subjects

Diagnosis	Group				Total (n = 38)	
	main (n = 21)		control (n = 17)			
	abs.	%	abs.	%	abs.	%
Nephrectomy	14	66.7	13	76.5	27	7.1
Nephrectomy + excision of the carbuncle	2	9.5	2	11.8	4	10.5
Lancing and drain of renal abscess	3	14.3	1	5.9	4	10.5
Lancing and drain of suppurated cysts	2	9.5	1	5.9	3	7.9

The progress of wound healing was evaluated with clinical, cytological, bacteriological and microscopy methods. The assessments included duration of hospital stay, the presence and the patterns of complications, the rate of wound healing and the subjective reaction to local use of antiseptic agents.

To assess wound healing rate, wound planimetry was performed by drawing its contours on graph paper prior to onset of treatment and then at Day 5, Day 10 and Day 15.

The wound healing rate (WHR) or Popova's index, expressed as a percentage, was calculated using the following formula:

$$WHR = (S - Sn) \times 100 / S \times t,$$

where S is the square of the wound in prior measurement, Sn is the square of the wound at present moment and t is the number of days between the first and the subsequent measurement [10].

In bacteriological study of wound discharge in both groups E. coli was detected in 19 (50 %) cases, Staphylococci were detected in 6 (15.8 %) cases, Proteus was found in 7 (18.4 %) cases, Pseudomonas aeruginosa — in 3 (7.9 %) cases, Bacteroides — in 2 (5.2 %) cases and anaerobic Clostridia — in 1 (2.6 %) case. In 29 (76.3 %) patients monoculture was isolated from the wound; whereas in 9 (23.7 %) microbial association was isolated.

Results and Discussion.

The main criterion to assess the efficacy of therapy was hospital stay. Hospital stay in the main group was significantly shorter: 12.4 ± 1.8 days (vs. 21.3 ± 1.4 days in the control group; $p < 0.05$). It is beyond doubt that in most cases the patients do not remain in the hospital until complete healing of the skin edges of the wound. A small skin defect in absence of wound channel and purulent discharge can be managed under out-patient conditions. However, in our view, this does not diminish the value of the above investigational index as a comparative criterion.

WHR was also assessed in patients of both groups at Day 5, Day 10 and Day 15 of treatment. This study was performed in patients with purulent obstructive pyelonephritis after nephrostomy and drainage of purulent foci. As a rule, in such cases the posterior portion of the wound was not sutured in order to provide for maximum drainage of wound discharge. Significant differences of WHR values were noted

at Day 10 and Day 15 of treatment (at Day 10 it was 8.9 ± 0.9 in the main group and 3.1 ± 0.6 in the control group; at Day 15 it was 10.4 ± 1.1 and 4.2 ± 0.8, respectively; $p < 0.05$) (see Table 4).

Of special importance is the possibility of using turundae with Decasan for sanitation of wound channels after removal of tube drainage in patients after nephrectomy for calculous pyonephrosis. It is well known how healing of the so-called wound channel prolongs hospital stay. In wound sanitation by turundae with Decasan significantly shorter hospital stay was achieved in patients of the main group after nephrectomy: 13.4 ± 2.1 days (vs. 20.6 ± 1.9 days in the control group; $p < 0.05$).

In patients of the main group already after the first dressings with Decasan the symptoms of toxaemia disappeared (general weakness, fatigue and headache), the volume of wound discharge and manifestations of infectious and inflammatory processes (hyperaemia, perifocal oedema and tissue infiltration) were also substantially decreased. Microscopic presentation was characterised by positive bacteriological and cytological changes. Thus, already at Day 2-3 from the onset of treatment the specimens contained signs of phagocytic activity, manifested as individual phagocytic cells and histiocytic elements. The numbers of neutrophilic granulocytes and microorganisms have decreased. No positive changes of cytological presentation were detected within the same timeframes in the control group.

In patients of the main group complete clearance of wounds from pus and foci of necrosis occurred by Day 3.8 ± 0.3 from the onset of local treatment (regardless of type of microflora). By Day 4, along with rapid clearance of wound surface, there were such findings, as scarce discharge, individual islets of juicy and pink fine granulations, filling the walls and bed of the wound; also, slight reduction in wound area was noted. Treatment with traditional modalities in patients of the control group allowed achieving wound clearance not until Day 7.5 ± 0.8 (see Table 5).

Table 4. The changes of WHR with time in study subjects by Day 5, 10 and 15 of the postoperative period.

The rate of wound healing	Group	
	main (n = 21)	control (n = 17)
By Day 5	2.1 ± 0.3	1.9 ± 0.2
By Day 10	8.9 ± 0.9	3.1 ± 0.6; $p < 0.05$
By Day 15	10.4 ± 1.1	4.2 ± 0.8; $p < 0.05$

Table 5. Time to wound clearance and complete healing in study subjects

The rate of wound healing	Group	
	main (n = 21)	control (n = 17)
The time from the onset of treatment to wound healing, days	3.8 ± 0.3	7.5 ± 0.8*
The time from the onset of treatment to complete wound healing, days	14.3 ± 2.1	21.4 ± 2.3*

* - $p < 0.05$

As a result of treatment, during the inflammation phase in both groups there were positive trends concerning cytological presentation (albeit at different times), namely, changing of the necrotic type of cytogram to the inflammatory-regeneration type. The latter was characterised by remission of the inflammatory response, reduction of number of neutrophilic granulocytes to 70%, large numbers of macrophages, active phagocytosis, and increased numbers of polyblasts, reticulocytes and lymphocytes and the advent of individual fibroblasts. Small numbers of microorganisms were observed. The change of cytogram pattern in patients of the main group was complete by Day 3-4; in the control group this had occurred by Day 7-8 from the onset of local treatment.

Thereby, the data of clinical, bacteriological and cytological assessments undoubtedly indicate the superiority of Decasan to chlorhexidine bigluconate.

No Decasan-related adverse events or allergic reactions were documented during the treatment. This is explained by the absence of toxic effect of decamethoxin in the concentration used (0.02 %) and virtually complete absence of absorption of the drug. One patient in the control group had an allergic event of skin rash, which required desensitising therapy.

Conclusions

1. Using Decasan for local treatment of purulent wounds in patients after surgery for purulent inflammatory renal disease has resulted in a positive clinical effect, manifested as acceleration of wound healing and reduced hospital stay.

2. The wide spectrum of antimicrobial, antifungal and antiviral action, along with virtually complete absence of adverse effects and allergic reactions allows recommending Decasan as a local antiseptic agent for the treatment of purulent wounds in the urological practice.

References

1. Beloborodova N.V. The algorithms of antibiotic therapy in severe infections. - 2000.
2. Buyanov V.M., Rodoman G.V. The problems of prevention of suppuration of postoperative wounds// Surgery. - 1996. - No. 9. - p. 132-135.
3. Gostishchev V.K., Buyanov S.N., Galperin E.I. et al. Antibiotic prophylaxis of infectious complications in Surgery: Guidelines. - Glaxo Wellcome, 2000.
4. Davidovsky I.V. Wound infection, wound toxaemia and wound exhaustion. in the book: The Proceedings of the Conference on wound infection. -Moscow, 1946. - p. 21-40.
5. Dellinger E.P. Prophylactic antibiotics in surgery//Clinical microbiology and antimicrobial chemotherapy. - 2001. - Vol. 3, No. 3. - p. 260-265.
6. Eryuhin I.A., Gelfand R.A., Shlyapnikov S.A. Surgical infections: Manual. - St. Petersburg, 2003.
7. Efimenko N.A., Guchev I.A., Sidorenko S.V. Infections in Surgery. Pharmacotherapy and prevention. - Smolensk, 2004.
8. Efimenko N.A., Hrupkin V.I. Hveschuk P.F. et al. Antibiotic prophylaxis and antibiotic therapy of the main forms of surgical infections: Guidelines. — Moscow: The Chief Military Medical administration of the Ministry of Defence of the Russian Federation, 2002.
9. Zubkov M.N. Practical manual on clinical microbiology and antimicrobial therapy for hospital doctors. — Moscow: MGUP, 2002.
10. Rational antimicrobial pharmacotherapy: Manual for practicing physicians/ Ed. by V. P. Yakovleva, S.V. Yakovleva. - Moscow, 2003.
11. Bernard H. R., Cole W. R. The prophylaxis of surgical infection// Surgery. - 1964. - V. 56. - p. 151-157.
12. Ehrenkranz N. J. Antimicrobial Prophylaxis in Surgery: Mechanisms, Misconceptions, and Mischief// Infection Control and Hospital Epidemiology. -1993. - V. 14, No. 2. - p. 99-106.
13. Emori T. G., Gaynes R. P. An overview of nosocomial infections, including the role of the microbiology laboratory// Clin. Microbiol. Rev. - 1993. - V. 6 (4). - p. 428-442.
14. Infection Control and Hospital Epidemiology. - 1999. - V. 20, No. 4. - p. 247-278.
15. SHEA, APIC, CDC, SIS. Consensus paper on the surveillance of surgical wound infections// Infect. Control Hosp. Epidemiol. - 1992. - V. 13 (10). - p. 599-605.