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Surveillance of the incidence and causative pathogens of meningitis and surgical site infection after craniotomies for brain tumors in neurosurgical ICU and ward: a cohort study

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Abstract

Background: Postoperative meningitis and surgical site infections (SSI) is a challenging issue that may result in serious morbidity and mortality. This study aims at decreasing the incidence and identifying the causative pathogens of postoperative meningitis and SSI in patients undergoing craniotomies.

Results: The study is a cohort study designed in ASA I and II patients undergoing elective craniotomies for brain tumors, to compare the incidence of meningitis and surgical sites infections between an intervention group who received proposed prophylactic antibiotics from April 2014 to April 2015 and a control group from April 2013 to April 2014 when prophylactic antibiotic protocols were lacking. 488 (four hundred and eighty eight) patients were included. The incidence of meningitis was 3.5% in the pre-protocol group and 2.1% in the post-protocol group ($p = 0.331$), while that of surgical site infections was 4% in the pre-protocol group and 3.5% in the post-protocol group ($p = 0.747$). The following pathogens [Pseudomonas, Enterococci, Ecoli and MRSA] decreased, while [Klebsiella, Staphylococcus and Acinetobacter] increased after application of the protocol.

Conclusions: Although the incidence of both meningitis and surgical site infections decreased after application of the prophylactic antibiotic protocol this was not statistically significant. The main pathogens were mostly gram-negative bacteria which could indicate an alteration of the causative organisms and may modify the choice of prophylactic antibiotics.

Keywords: Meningitis, SSI, Elective craniotomies, Gram-negative bacteria, Unasyn, Cefotaxime

Background

Postoperative meningitis is a rare but life threatening complication in patients undergoing craniotomies (Korinek 1997; Blomstedt 1987). The incidence varied between 0.3 and 8.9% (Korinek 1997; McClelland and Hall 2007; Korinek et al. 2006; Sneh-Arbib et al. 2013; Sharma et al. 2009; Kourbeti et al. 2007; Reichert et al. 2002). Risk factors include, GCS (Glasgow coma scale) < 10, total shaving of the

scalp, postoperative CSF (Cerebrospinal fluid) leakage, CSF shunts, emergency surgery, concomitant infection at the incision site, surgical duration > four hours and reoperation (Korinek et al. 2006; van de Beek et al. 2010).

Surgical site infection (SSI) after craniotomies is a serious complication. The incidence is quite variable between 0 and > 9.0% (McClelland 2008; Bellusse et al. 2015). Risk factors include multiple operations, CSF leak, altered sensorium, age, use of corticosteroids and diabetes (Buang and Haspani 2012).

Both meningitis and SSI may result in serious morbidity and mortality, with a prolonged hospital stay,

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multiple surgeries and high costs (Korinek 1997; Blomstedt 1987; Kourbeti et al. 2007; Bellusse et al. 2015; Rebuck et al. 2000).

Therefore, we designed a Cohort study to detect the consequences of a prophylactic antibiotic protocol suggested by our department on reduction of the incidence of meningitis and SSI in our neurosurgical ICU and ward following elective craniotomies, taking in consideration the incidence and pattern of causative organisms.

Methods

After approval of the ethical committee of the anesthesia department, we performed a Cohort study, in otherwise healthy ASA I and ASA II patients undergoing neurosurgical procedures, to compare the incidence of postoperative meningitis and SSI between an intervention group who received prophylactic antibiotics according to a proposed protocol, and a control group who followed the records of patients during the period from April 2013 to April 2014 when prophylactic antibiotic protocols were lacking or were not implemented.

Patients' selection

Our study included all patients scheduled for elective cranial neurosurgical procedure either supratentorial or infratentorial tumors.

Inclusion criteria were as follows; age between 21 and 60 years, ASA physical status I and II with no source of preoperative infection as evidenced by normal preoperative TLC and temperature.

Whereas, exclusion criteria were; patients showing signs of pre-operative infection {fever and high TLC}, patients with CSF infection after hospital discharge {i.e. Community acquired}, emergency patients, trauma patients and patients undergoing multiple operations.

Methodology in details

The study was divided into two periods

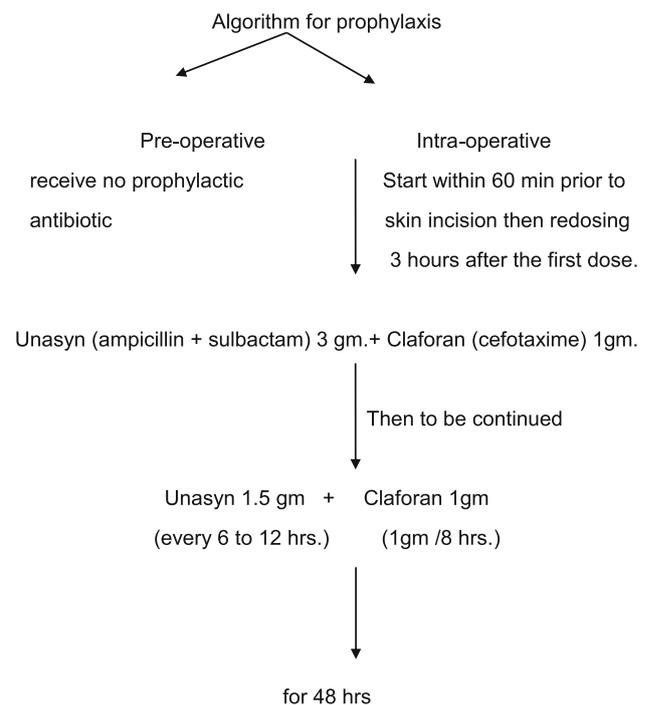
The first period started from April 2013 till April 2014 and served as an observational control period, antibiotic guidelines were lacking or were not implemented.

The second period started April 2014 till April 2015 and served as interventional period, where we implemented a common prophylactic antibiotic protocol. This regimen was chosen on the basis of the bacterial species and resistance pattern usually encountered in the previous CSF and wound swab cultures taken from patients who suffered from meningitis and SSI either in the neurosurgical ICU or in the ward in our institution.

The proposed protocol was:

1. Topical body shower (especially head and neck area) with antiseptic chlorhexidine solution "savlon" pre-operatively.

2. A penicillin sensitivity test prior to unasyn administration.
3. Unasyn 3 g vial + claforan 1 g vial to be given to each patient within 60mins prior to incision and redosing after 3 h.
4. Adding two garamycin ampoules ($80 \times 2 = 160$ mg) to irrigation fluids.
5. Duration of post-operative prophylaxis is 48 h after which we stop all antibiotics, the post-operative prophylaxis included Unasyn 1.5 g every 6 to 12 h and claforan 1 g every 8 h.
6. Patients with inserted extra-ventricular drains, Baker systems, ventriculo-subgial drains, packs or patients having a CSF leak will not stop their antibiotic regimen until a change in condition takes place (e.g stoppage of CSF leak or removal of the foreign body).
7. Application of trivitracin topical spray in daily wound dressing routine.



Duration of post-operative prophylaxis is 48 h after which we stop antibiotic regimen except for patients mentioned previously.

If signs and symptoms of infection appeared (persistent fever > 38.5 + high TLC + high CRP for more than 48 h. postoperatively, nuchal rigidity, severe headache and/or clinical signs of infection as purulent discharge, hotness, swelling, tenderness and/or radiological signs of infection) → culture from suspected site was requested.

But if no obvious clinical signs of infection specific to a certain site, we request pan cultures including CSF and

wound swabs as early as possible. Then start empirical therapy as appropriate.

The primary aim of the study was surveillance of the incidence of both meningitis and SSI before application of the prophylactic antibiotic protocol in comparison to the incidence after its application. SSI infection in our study included patients with superficial and deep wound infections.

Another important aspect of the study was to identify the most common pathogens, their incidence and their pattern of distribution as detected in the CSF and wound swab cultures during the two periods before and after application of the prophylactic antibiotic protocol.

Data collection

Demographic data as age and sex, ASA physical status, Type of operation (supratentorial or infratentorial), patients with elevated TLC during both periods, number of patients having meningitis and/or SSI in either of the study groups as well as types of micro-organisms identified from cultures to be the causative agents of meningitis and/or SSI in either groups.

Statistical analysis

Numerical data were expressed as mean (SD), while categorical data were presented using number (proportion). Unpaired Student's test was used to compare means, and chi-square test was used to compare proportions. *P*-values less than 0.05 were considered as statistically significant.

Results

Data of 693 patients were collected for this study, 205 patients were excluded from the study according to the exclusion criteria and 488 patients were included, 199 patients underwent cranial surgeries before the application of the antibiotic protocol (pre - protocol group) and 289 patients underwent cranial surgeries after application of the antibiotic protocol (post - protocol group).

There were no significant differences in demographic data between the 2 groups as regards patients' age and sex. However, there was statistical significance (*P* value < 0.0001) as regards ASA classification as most of the patients either in preprotocol or postprotocol groups were ASA physical status I. (Table 1).

There was a statistically significant difference as regards the type of operation (*P* < 0.0001) indicating that most of operations were of supratentorial type whether in the preprotocol or the postprotocol groups. (Table 2).

Although the post-operative total leukocytic count (TLC) was found to be high in 30.7% of patients in the pre-protocol group and in 31.1% of patient in the post-protocol group, this was not statistically significant

and not all patients presenting with high TLC postoperatively developed infections. (Table 2).

Concerning the incidence of meningitis, although the percentage of the infected patients decreased after application of the prophylactic antibiotic protocol from 3.5% (seven patients) to 2.1% (six patients), this was not statistically significant (*P* = 0.331). (Fig. 1).

As regards the incidence of SSI, whereas the percentage of the infected patients decreased after application of the prophylactic antibiotic protocol from 4.0% (eight patients) to 3.5% (ten patients), this was not statistically significant (*P* = 0.747). (Fig. 2).

From the total of 488 patients included in the study, 27 (5.53%) patients developed infections, 12 patients (6.03%) in the preprotocol group and 15 patients (5.19%) in the postprotocol group. The incidence of postoperative meningitis and SSI was analyzed depending on the microbiological profile of the organisms, and their sensitivity pattern. (Table 3).

The most common organisms causing meningitis and SSI in our study were Klebsiella, Enterococci, Staph-aureus, Acinetobacter, E-coli, Pseudomonas and MRSA. The following organisms [Pseudomonas, Enterococci, Ecoli and MRSA] decreased in the period following application of the protocol, while [Staphaureus, Acinetobacter and klebsiella] increased in the period following application of the protocol, though neither the decrease nor the increase were statistically significant. (Table 3).

Discussion

In our study we found that the incidence of postoperative meningitis and SSI infections decreased after application of the proposed prophylactic antibiotic protocol of our department in patients undergoing elective craniotomy for either supra or infratentorial tumors, however, the decrease wasn't statistically significant. The overall incidence of meningitis was 3.5% before the protocol in comparison to 2.1% after its application, while the overall incidence of SSI was 4.0% before the protocol in comparison to 3.5% after its application.

Table 1 Demographic data and ASA classification

		Pre-protocol	Post - protocol	<i>P</i> value
Age (y)		40.63 ± 10.38	41.21 ± 10.87	0.553
sex	male	95 (47.7%)	160 (55.4%)	0.097
	female	104 (52.3%)	129 (44.6%)	
ASA	ASA I	173 (86.9%)†	197 (68.2%)†	* < 0.0001
	ASA II	26 (13.1%)†	92 (31.8%)†	

Data are expressed as Mean ± SD or total number and (%)

*denotes statistically significant difference between ASA I and ASA II in Both groups *P* value was found to be < 0.0001

†denotes statistical significant difference between ASA I and ASA II in the same group, *P* value was found to be < 0.0001 in both groups

Table 2 Type of the operation and Postoperative TLC

		preprotocol	postprotocol	
Type of operation	supratentorial	169 (84.9%)†	214 (74.0%)†	*0.004
	infratentorial	30 (15.1%)†	75 (26.0%)†	
Postoperative TLC		61 (30.7%)	90 (31.1%)	0.909

Data are expressed as total number and (%)

*denotes statistically significant difference in the type of operation between the 2 groups (p -value = 0.004)

† denotes statistical significant difference between Type of operation in the same group, P value was found to be < 0.0001 in both groups

Regarding the causative organisms, before the application of the protocol the common microorganisms were Enterococci, Klebsiella, E-coli, Pseudomonas aeruginosa, Acinetobacter and MRSA, whereas after application of the protocol, the percentage of patients infected with Klebsiella and Acinetobacter increased and four cases were infected with Staphaureus, while the percentage of patients infected with Enterococci and E-coli decreased and none were infected with MRSA nor Pseudomonas.

Our results fall within the reported incidence of post-operative CNS infections, including meningitis and SSI, in healthy patients undergoing craniotomy. The overall reported incidence in several studies ranges from 0.15% to 6.1% in patients receiving antimicrobial prophylaxis and 2% to 9.7% in patients with placebo or no antimicrobial prophylaxis (Korinek 1997; Korinek et al. 2006, 2005; Barker II 2007; Whitby et al. 2000; Lietard et al. 2008).

Although Gram-positive organisms such as staphaureus, MRSA, methicillin-resistant coagulase-negative Staphylococcus (MRCNS) were the main target organisms for prophylactic control in meningitis, other organisms are emerging in CSF cultures such as Enterococci as well as gram-negative organisms such as Acinetobacter, E-coli, Klebsiella and Pseudomonas aeruginosa and should be considered in the choice of prophylactic antibiotics (Kourbeti et al. 2007; Wang et al. 2005; O'Neill et al. 2006; Erdem et al. 2008).

Likewise, besides Staphaureus, MRCNS and MRSA, other organisms have been increasingly isolated from SSI in patients after undergoing neurosurgical procedures, e.g. gram-negative bacteria have been isolated as a sole causative pathogen as well as in polymicrobial infections (Korinek 1997; Korinek et al. 2006; Kourbeti et al. 2007; Whitby et al. 2000; Lietard et al. 2008),

Perioperative antibiotic prophylaxis has been recommended for patients undergoing craniotomies to decrease the incidence of postoperative meningitis and SSI (Korinek et al. 2006; 2005; Barker II 2007; Zhu et al. 2001). Several antibiotic protocols have been followed for prophylaxis over the years with no significant advantage of one protocol over the other (Barker II 2007; Whitby et al. 2000; Anonymous 2009). The majority of studies used a single dose of antibiotics given within

sixty minutes prior to surgical incision, to be repeated if the duration of surgery exceeds three to four hours or two half lives of the antibiotics administered preoperatively. Redosing can be done as well if major blood loss occurs (Korinek et al. 2006; 2005; Whitby et al. 2000; Anonymous 2009; Scottish Intercollegiate Guidelines Network 2009).

The incidence of neurosurgical procedures is currently increasing and the wide use of broad spectrum antibiotics may have altered the causative organisms (Erdem et al. 2008; Kim et al. 2012). The choice of appropriate prophylactic antibiotics is challenging specially with the variability of organisms and the increasing incidence of resistant strains (Wang et al. 2005; O'Neill et al. 2006).

In a study by Sharma et al. that included 31,927 patients undergoing routine and emergency neurosurgical procedures over the period from 1994 to 2006, they found a significant decrease in the incidence of meningitis and SSI infection after implementation of a prophylactic antibiotic protocol in 2000. The overall incidence of meningitis was 2.9% and that of SSI was 2.5%. This study supports the results of our study that prophylactic antibiotics may decrease the incidence of meningitis and SSI after craniotomy (Sharma et al. 2009).

In addition, in a meta-analysis comprising six randomized control trials (RCTs) including 1729 patients to detect whether prophylactic antibiotics reduce the incidence of meningitis after craniotomy, they found that although five of the six RCTs didn't individually show a significant benefit from antibiotic prophylaxis, the combined results showed a decrease in the incidence of meningitis from 2.7% to 1.1% ($p = 0.03$) after antimicrobial prophylaxis. This study endorses the results of our study (Barker II 2007).

Congruent with our study, Srinivas D et al. studied the incidence of meningitis in 5449 elective procedures and the prophylactic antibiotic used was cefotaxime 1 g similar to our study except that in our study we used unasin in addition, the incidence of meningitis was 2.2% which is very close to our incidence 2.1% and the causative organisms were mostly gram-negative bacteria (Srinivas et al. 2011).

Moreover, in a study by Korneik AM et al. including 6243 patients undergoing elective as well as emergency and multiple operations, antibiotic prophylaxis reduced SSI from 8.8% down to 4.6% (P value 0.0001), but didn't have the same effect on meningitis, it only reduced the incidence from 1.63% to 1.50%. They suggest that the low efficacy of prophylactic antibiotics against meningitis may be due to the use of cloxacillin which doesn't cross the BBB (Blood brain barrier). In our study, cefotaxime crosses the BBB to an extent (Nau et al. 1993), which may have decreased the incidence of meningitis. Another important aspect in the Korneik study is the

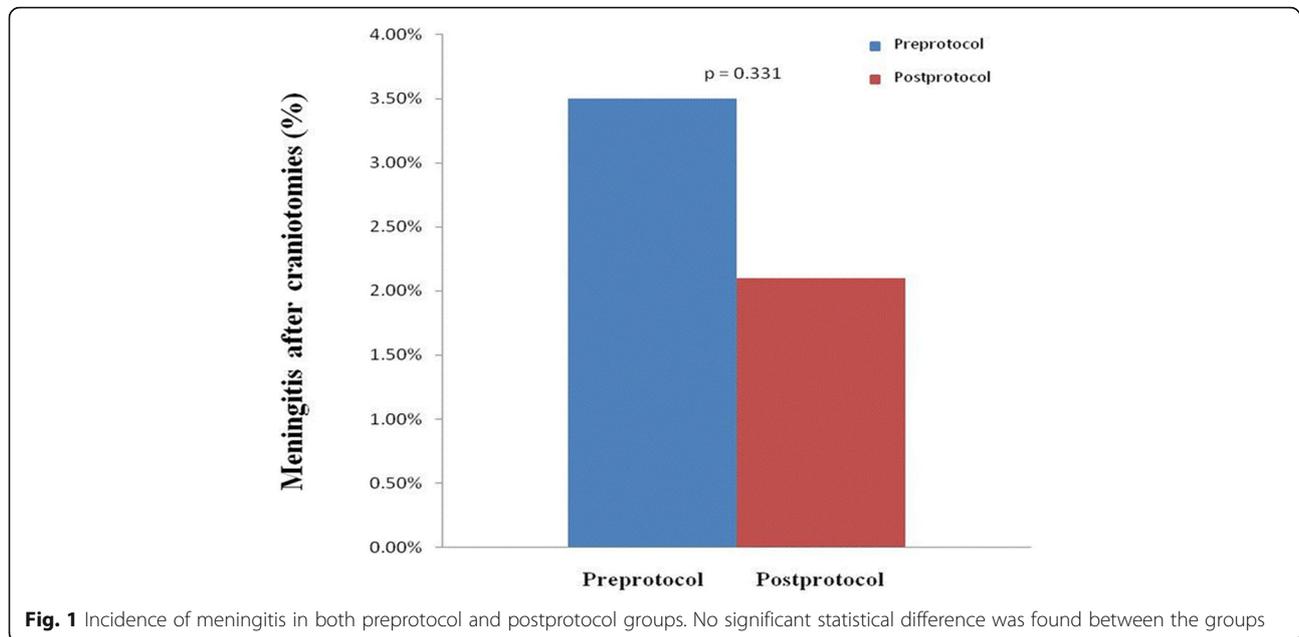


Fig. 1 Incidence of meningitis in both preprotocol and postprotocol groups. No significant statistical difference was found between the groups

pattern of the causative organisms, although staphylococci were the main pathogens causing 38.4% of meningitis, gram-negative bacilli caused 35%, taking in consideration that gram negative bacilli were significantly more frequent in patients with prophylaxis (47.1% versus 12.5%, $p = 0.02$) (Korinek et al. 2006).

While in a study by Kourbeti et al.; including 239 patients and undergoing 334 cranial procedures; the incidence of postoperative meningitis was 4.8% and that of SSI was 9% with application of antibiotic prophylaxis in patients undergoing elective and emergency operations, gram-negative organisms predominated as causative

pathogens of meningitis and SSI, the main organisms were *Acinetobacter* and *Klebsiella* which is in agreement with our study (Kourbeti et al. 2015).

In a study by Reichert MC et al., whereas the incidence of postoperative meningitis was high 8.6% as they included patient with multiple operations and remote site infection, gram-negative organisms were the most common pathogens isolated which is in accordance with our study (Reichert et al. 2002).

Although Erdem et al. found the incidence of postoperative meningitis to be 2.7% in 2265 patients undergoing both elective and emergency craniotomies, the main causative

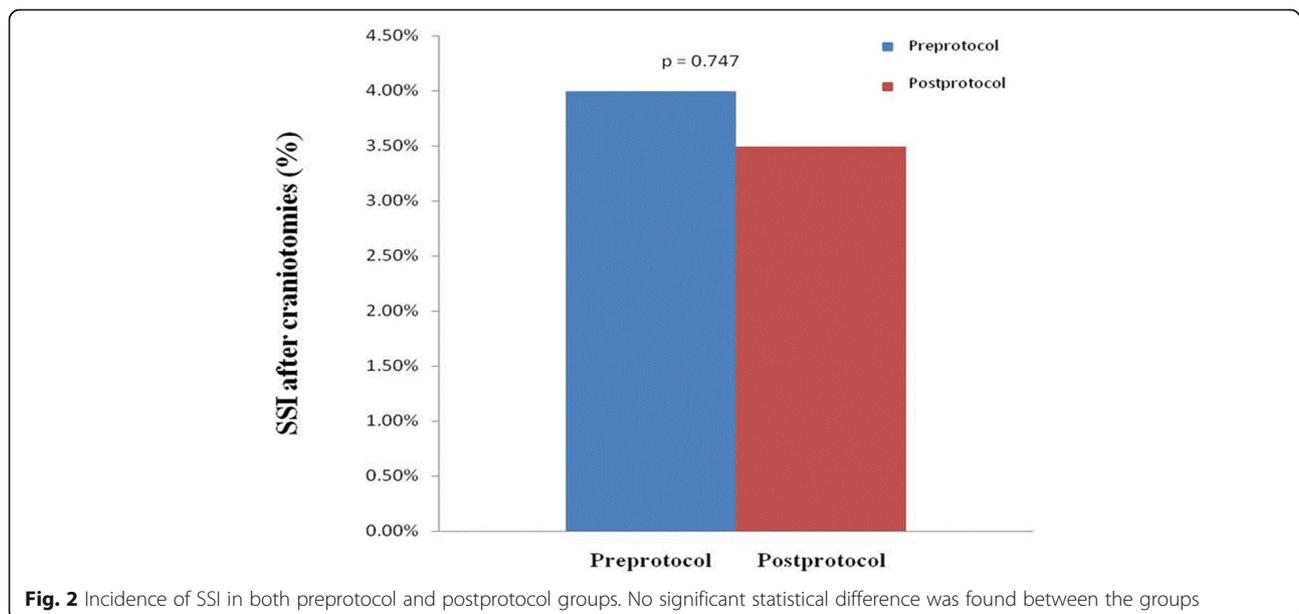


Fig. 2 Incidence of SSI in both preprotocol and postprotocol groups. No significant statistical difference was found between the groups

Table 3 Types of organisms and their distribution in each group

organism	group				P value
	Preprotocol		postprotocol		
klebsiella	2	1.0%	6	2.1%	0.482
acinatobacter	1	.5%	3	1.0%	0.649
pseuodomonas	2	1.0%	0	.0%	0.166
MRSA	1	.5%	0	.0%	0.408
E.coli	2	1.0%	1	.3%	0.570
enterococci	4	2.0%	1	.3%	0.164
staph-aureus	0	.0%	4	1.4%	0.149

Data are expressed as total number and (%)

organisms were staphaureus followed by Acinetobacter. This is in contrast with our study where the main causative organism were Klebsiella, Enterococci, followed by Acinetobacter and staphaureus. Whether they used prophylactic antibiotics weren't specified (Erdem et al. 2008).

In addition, in a study by McClelland S et al., the incidence of meningitis was 0.3% in elective patients undergoing craniotomy, the main causative organisms were *Staphylococcus aureus* followed by *Propionibacterium acne*. The study is in variance with our study, it is also in disagreement with several other studies (McClelland and Hall 2007).

Several studies were concerned mainly with SSI after neurosurgical procedures, whether with or without meningitis.

In a recent surveillance study by Davies BM et al., the incidence of SSI was 3.5% in 2375 cranial neurosurgical patients, whether prophylactic antibiotics were applied or not wasn't the concern of the study. The incidence of SSI is very close to our study however that study included patients who were readmitted to the hospital (Davies et al. 2016).

In accordance with our study, Jiang X et al. estimated the effect of multimodal prevention program on controlling SSI in 3042 patients undergoing emergency and elective cranial procedures over 6 years, strict asepsis and judicious administration of prophylactic antibiotics were the main focus of the prevention program, the mean incidence of SSI was 3.68% taking in consideration that the annual incidence rate decreased from 6.21% in 2008 to 2.28% in 2013 (Jiang et al. 2016).

In addition, in a study by Korniek AM et al. including 4578 patients undergoing craniotomies, prophylactic antibiotics (cloxacillin or amoxicillin-clavulanate) decreased the incidence of SSI from 9.7% to 5.8% ($p < 0.0001$) mainly by decreasing the incidence in clean craniotomies from 10.0% to 4.6% ($p < 0.0001$). The results supports our study though we used different antibiotics and the number of patients was much lower to detect a statistical significance (Korinek et al. 2005).

In disagreement with our results, Lietard C et al. conducted a study in 844 patients undergoing neurosurgical

procedures either craniotomies or spinal surgeries and found the incidence rate of SSI 4.1% and that lack of antibiotic prophylaxis wasn't a risk factor (Lietard et al. 2008).

In incongruity with our study was a surveillance study by Petrica A et al. including 768 patients, they found the incidence of SSI including meningitis 8.16% in patients undergoing elective and emergency craniotomies and most of the patients received antibiotic prophylaxis with no influence on SSI. Moreover, gram positive cocci, particularly staphaureus were the main pathogens followed by Klebsiella (Petrica et al. 2009).

Although, in a study by Sneh-Arbib O et al., the overall rate of SSI in patients undergoing emergent or urgent craniotomy was 5.6% in 502 patients, 3.2% of which were intracerebral infections mostly meningitis and most of the patients received antibiotic prophylaxis, they found no significant association between antibiotic prophylaxis and SSI. However, the pattern of organisms was mostly gram-negative bacteria as found in our study (Sneh-Arbib et al. 2013).

The present study has some limitations as it didn't include trauma or emergency patients or patients solely admitted for shunt insertion, moreover patients readmitted to the hospital for meningitis and SSI infection were excluded from the study which may have altered the overall incidence of infection.

However, this study can be a base for a larger study done over several years ahead to study the incidence of infection, the variability of the causative pathogens, the effect of strict asepsis protocols and the need for modification of antibiotic prophylaxis taking in consideration the emergence of gram-negative organisms and the development of resistance strains.

Conclusion

The results of the present study elucidates that although the incidence of both meningitis and SSI decreased after application of the prophylactic antibiotic protocol this was not statistically significant. An interesting finding is that the main causative pathogens were mostly gram-negative bacteria which could be an indicator of the alteration of the causative organisms and may modify the choice of antibiotic prophylaxis as well as the management of infections in further future studies.

Abbreviations

ASA: American society of anesthesiologists physical status; BBB: Blood brain barrier; CSF: Cerebrospinal fluid; GCS: Glasgow coma scale; ICU: Intensive care unit; MRCNS: Methicillin-resistant coagulase-negative Staphylococcus; MRSA: methicillin resistant staphaureus; SSI: Surgical site infections; TLC: Total leucocytic count

Funding

None.

Availability of data and materials

The data that support the findings of this study are available from the archive of the neurosurgical department but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of the archive of the neurosurgical department.

Authors' contributions

Pr. Dr. Tarek AM Radwan participated in the concept, design, data interpretation and manuscript thorough reviewing. Dr. Rania S Fahmy participated in the concept, design, data analysis, statistical analysis, data interpretation, manuscript writing and reviewing. Dr. Beshoy N Hanna participated in the concept, design, data collection, data analysis, statistical analysis, data interpretation, manuscript writing and reviewing. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The study protocol was approved by the ethical committee of the anesthesia department and registered on 14/2/2015. Written consents was not obtained from the patients, this was waived by the ethical committee as this was an observational study.

Consent for publication

Not applicable.

Competing interests

"The authors declare that they have no competing interests".

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