The Impact Of Surgical Glue Use As A Biliostatic and Hemostatic Agent During Liver Resection In Pediatric Patients

Original Article

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ABSTRACT

Background: Paediatric liver resection presents unique challenges, particularly in achieving effective haemostasis and biliostasis. surgical glue is a synthetic surgical adhesive material composed primarily of modified n-butyl-2-cyanoacrylate, has shown a promise in various surgical applications. This study aimed to evaluate the impact of the surgical glue application on alleviation of postoperative complications in paediatric liver resections.

Patients and Methods: This retrospective study was conducted on 22 paediatric patients underwent liver resection, those receiving intraoperative surgical glue on the transacted liver surface. the current research was planned to investigate the mitigating action of the surgical glue on the hepatic resection related biliary leakage and bleeding.

Results: The mean age was 3.1 years (±3.15). Hepatoblastoma was the most common pathology (50%). Right hepatectomy was performed in 59.09% of cases. Following the application of the surgical glue, postoperative biliary leakage showed no effect when compared with the results in literature, occurring in 18.18% of patients, with varying degrees of severity. however, the incidence of postoperative bleeding was markedly improved, observed in just 5.26% of patients. The mean hospital stay was 11.6 days (±4.94), ranging from 3 to 22 days.

Conclusion: This study highlights the use of a haemostatic and a biliostatic agent like surgical glue that may potentially impact the outcome after liver resection in paediatric patients regarding bleeding.

Key Words: Biliary leakage; Hepatoblastoma; Paediatric liver resection; Surgical glue; Postoperative complications.

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INTRODUCTION

Pediatric liver resection presents unique challenges due to the delicate nature of the patient population and the complexity of the procedures involved. These surgeries require meticulous surgical techniques and comprehensive perioperative management[1,2].

Moreover, cumulative evidence suggested that a primary concern in liver resection is achieving effective hemostasis and biliostasis to prevent postoperative complications[3,4], so surgical adhesives have gained attention as a potential solution to these challenges[5,6].

surgical glue, a synthetic surgical adhesive composed primarily of modified n-butyl-2-cyanoacrylate, has shown a promise in various surgical applications, including liver resections[7,8]. This adhesive polymerizes rapidly upon contact with living tissues, forming a thin, elastic film that provides a firm adherence and high tensile strength[9].

Besides ,The adhesive properties of the surgical glue, it also creates an impermeable barrier to blood and other fluids, potentially reducing the risk of postoperative complications such as bile leakage and hemorrhage. Additionally, its bio-inert state upon polymerization serves as an antiseptic barrier, enhancing its utility in complex pediatric surgeries[7,8].

Likewise, clinical evaluations have demonstrated favorable outcomes with the application of the surgical glue during liver resections in adult patients, including lower rates of biliary leakage and other related complications. These findings are supported by retrospective analyses and prospective randomized trials that highlight the adhesive's safety and efficacy in managing intraoperative and postoperative challenges[8,9].

On the other hand , concerns primarily revolve around the variability in fluid dynamics and anatomical differences

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between pediatric and adult patients, necessitating tailored surgical approaches[10]. Therefore, in line with this assertion the need for prospective multicenter trials remains critical to better understand and optimize the use of the surgical glue in this sensitive patient population[11].

The current research was planned to investigate the mitigating action of the surgical glue on the hepatic resection related biliary leakage and bleeding.

PATIENTS AND METHODS:

The surgical glue (Gluebran 2)

Synthetic biodegradable cyanoacrylate (glubran®2) was obtained from GEM italy (the italian manufacturer ,and distributer of medical devices). The product is applied as a spray over liver raw surface area after achieving complete anatomical liver resection and usual hemostasis using diathermy and harmonic devices.

Study population

This retrospective case note review study was carried out on 22 patients who underwent liver resection for diverse pathological lesions from November 2022 to November 2023, Ethical committee approval code is N146-2024 obtained from research ethical committee (REC) at faculty of medicine. Cairo University.

The current research encompassed children with liver masses regardless their age and sex admitted for surgical anatomical liver resection with Glubran 2 application intra operatively for rumination its pivotal effect as a biliostatic and hemostatic agent .

The study outcomes

After achieving completer liver resection the surgical glue is sprayed directly over the raw surface of the liver (figures 1,2).

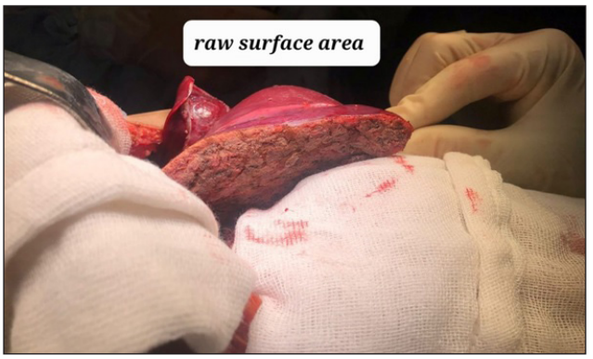

Figure 1: Raw surface area after applying adhesive glue.

Figure 2: Raw surface area after applying adhesive glue.

The Primary outcome measures were defined as the efficacy of intraoperative surgical glue application in preventing postoperative complications such as biliary leakage and bleeding consequently the postoperative hospital stay duration. Secondary outcomes included the reduction of financial burden on the hospital due to shortened hospital stays, decreased need for postoperative interventions e.g., pigtail insertion under general anesthesia for biliary collection drainage, and reduced necessity for postoperative Endoscopic retrograde cholangiopancreatography (ERCP) procedures or reoperation.

Statistical analysis:

Statistical analysis was done by SPSS v26 (IBM Inc., Chicago, IL, USA). Quantitative variables were presented as mean and standard deviation (SD). Qualitative variables were presented as frequency and percentage (%).

RESULTS:

The preoperative data

A total of 22 patients (14 males and 8 females) were included, ages ranged from 2 months to 15 years with a mean value (±SD) of 3.1(±3.15) years and their weight ranged from 6 to 60kg with a mean value (±SD) of 17(±10.73)kg.

There was a notable incidence of hepatoblastoma in 11(50%) patients, followed by hepatic mesenchymal hamartoma in 6(27.27%) patients, clear cell sarcoma (a right renal mass that infiltrates the liver) in 1(4.55%) patient, focal nodular hyperplasia in 1(4.55%) patient, liver haemangioma in 1(4.55%) patient, hepatocellular carcinoma in 1(4.55%) patient, and hydatid Cyst in 1(4.55%) patient as explicit in Table (1).

Type of liver resection

A right hepatectomy was performed in 13(59.09%) patients, left hepatectomy in 5(22.73%) patients, extended left hepatectomy in 4(18.18%) patients, and segmentectomy in 4(18.18%) patients Table 2.

Incidence and Severity of Post-hepatectomy Complications

There was a remarkable amelioration that post hepatectomy bleeding and biliary leakage are the most drastic post operative complications, fortunately, in our study 18 patients (81.82%) did not have post operative biliary leakage which may be attributed to the meticulous dealing with the planned resected biliary system, while Glu bran 2 application on the transected liver surface to seal small bile leaking points seemed to have no additional effect, in our study 4 patients (18.18%) developed biliary leakage after hepatectomy with the surgical glue application on the liver cut surface , and post operative bleeding occurred just in one patient (5.26%), Table 3.

Grades of post hepatectomy biliary leakage and their management options

Along with this data , the grades of biliary leakage after hepatectomy with the surgical glue application were grade A in 1(4.76%) patient , grade B in 2(9.52%) patients, and grade C in 1(4.76%) patient, the source of biliary leak in the the four cases was from the cut surface of the liver, the fourth case had additional cause which was injury on right hepatic biliary duct and so required exploration and Roux en Y hepaticojejunostomy, management strategies were adopted regarding the degree of complication in the form of, Conservative treatment for 1(4.76%) patient, pigtail insertion for 2 patients and exploration was indicated in 1(4.76%) patient Table 4

Hospital stays ranged from 3 to 22 days with a mean value (±SD) of 11.6(±4.94) days.

Table 1: Diagnosis and pathology of the studied patients:

		(*n*= 22)
Diagnosis & pathology	Hepatoblastoma	11(50%)
	Mesenchymal hamartoma	6(27.27%)
	Clear cell sarcoma (right renal mass infiltarate to liver)	1(4.55%)
	Focal nodular hyperplasia	1(4.55%)
	Liver hemangioma	1(4.55%)
	Hepatocellular carcinoma	1(4.55%)
	Hydatid Cyst	1(4.55%)

Data are presented as percentages (%).

Table 2: Type of liver resection of the studied patients:

		(*n*= 22)
Type of hepatectomy	Right hepatectomy	13(59.09%)
	Left hepatectomy	1(4.55%)
	Extended left hepatectomy	4(18.18%)
	Segmentectomy	4(18.18%)

Data are presented as percentages (%).

Table 3: Postoperative complications of the studied patients:

		(*n*= 22)
Biliary leakage	Yes	4(18.18%)
	No	18(81.82%)
Bleeding	Yes	1(5.26%)
	No	21(95.45%)

Data are presented as percentages (%).

Table 4: Grades of biliary leakage, management of biliary leakage, and interventions of the studied patients:

		(*n*= 21)
Grades of biliary leakage	Grade A	1(4.76%)
	Grade B	2(9.52%)
	Grade C	1(4.76%)
Type of management for biliary leakage	Pigtail insertion	2 (9.52%)
	Exploration surgery	1 (4.76%)
	Conservative treatment	1 (4.76%)
	ERCP	0 (0%)

Data are presented as percentages (%); ERCP: Endoscopic retrograde cholangiopancreatography.

DISCUSSION

The comprehensive analysis of the present study reveals hepatoblastoma in 50% of pediatric patients undergoing liver resection, consistent with previous reports indicating its prominence among pediatric liver tumors. Ng. *et al.,*[12] reported hepatoblastoma in 37% of cases, and Meyers[13] observed a 43% incidence in Western countries. Hepatic mesenchymal hamartoma was the second most common pathology in our cohort, accounting for 13.64% of cases, which is higher than the 6-7% incidence reported by Ng. *et al*.,[12] and Meyers[13]. Other pathologies, including clear cell sarcoma, focal nodular hyperplasia, liver hemangioma, hepatocellular carcinoma, and hydatid cyst, each had an incidence of 4.55%. While focal nodular hyperplasia aligns with previous reports[12], the incidence of hepatocellular carcinoma in our study was lower than the 21-23% previously reported[12,13].

It's important to note the global trends in pediatric liver cancer incidence. Dasgupta *et al*.,[14] conducted a meta-analysis showing that the incidence of hepatoblastoma is increasing globally, with a pooled annual percentage change of 2.8%.

In our study, right hepatectomy was the most common procedure, performed in 59.09% of patients. This was followed by extended left hepatectomy (18.18%), segmentectomy (18.18%) then left hepatectomy (4.5%), These figures provide insight into the surgical approaches employed in our center for pediatric liver resections.

Our findings differ somewhat from those reported in other studies, which may reflect variations in patient populations, tumor characteristics, or surgical preferences across different centers. For instance, Fleming *et al*.,[15] reported on hepatic metastasectomy in pediatric patients, where they performed 4 hemi hepatectomies and 1 sectionectomy out of 16 patients. The high proportion of right hepatectomies in our study may be related to the predominance of hepatoblastoma in our patient study, as these tumors often involve the right lobe of the liver. The significant number of extended left hepatectomies (18.18%) also suggests that we encountered a substantial number of large or centrally located tumors requiring more extensive resection.

In our study of 22 patients, the use of the surgical glue was showed no reduction in the incidence of biliary leakage, with 4 patients (18.2%) experiencing leakage, while 81.8% of the study did not report any biliary leakage. This incidence is almost near or a bit higher than the results in the literature which depended only in surgical techniques to minimize biliary leakage without applying any sealants like Glu-bran 2. For example, Cauchy *et al.,*[16] documented biliary leakage in 30 out of 223(13.5%) patients within their series, and Martin *et al*.,[17] identified biliary leakage in 528(7.7%) patients within a large, multi-institutional study involving 6,859 patients. However, our findings are consistent with other studies, such as that of Ferrero *et al*.,[18], who reported a bile leakage rate of 21.0% in patients undergoing hepatectomy with biliary reconstruction, though this rate decreased to 4.6% in patients without biliary anastomosis. Similarly, Othman *et al*.,[19] observed a 14% rate of primary biliary complications, including both bile leakage and biliary obstruction, in a pediatric population.

Regarding postoperative bleeding, the application of the surgical glue appeared to be effective, as only 1 out of 22 patients (4.55%) experienced bleeding, while 95.45% of the patients did not report any postoperative bleeding. This is relatively low compared to some reports in the literature. For example, Ferrero *et al*.,[18] reported postoperative bleeding in 28% of patients who underwent hepatectomy with biliary reconstruction, although their rate was 0% in patients without biliary anastomosis.

Our findings underscore the importance application of sealants like surgical glue may play a role in reducing postoperative bleeding.

The relationship between biliary leakage and postoperative outcomes is significant. Yamamoto *et al*.,[20] found that patients with bile leakage had

poor 5-year rates of overall survival and recurrence-free survival. Moreover, Martin *et al*.,[17] reported significantly greater postoperative mortality in patients with bile leaks (6.0% vs 1.7%).

In our study, we observed varying grades of biliary leakage according to the International Study Group of Liver Surgery (ISGLS) classification. Of the 21 patients in our cohort, 1 patient (4.76%) experienced grade A biliary leakage, 2 patients (9.52%) had grade B leakage, and 1 patient (4.76%) suffered from grade C leakage. This distribution provides insight into the severity of biliary complications in our pediatric population undergoing liver resection.

Our findings differ somewhat from those reported in other studies. For instance, Muranushi *et al.,*[21] observed bile leakage in 7.1% of their patients, with 2.3% having grade A leakage and 5.4% having grade B leakage. They did not report any grade C leaks. Similarly, Spetzler *et al.,*[22] reported a total bile leak rate of 14.0%, with 2.8% grade A, 8.0% grade B, and 3.2% grade C leaks.

The management strategies employed in our study reflect the range of approaches available for treating biliary leakage. We used pigtail drainage in 2 patients (9.52%), performed exploration surgery in 1 patient (4.76%), and managed 1 patient (4.76%) conservatively. Notably, we did not use ERCP in any of our patients.

Our management approach aligns with the general principles outlined in the literature. Schertz *et al.,*[23] emphasize the importance of a multidisciplinary approach in managing biliary leaks, involving hepatobiliary surgeons, advanced endoscopists, and interventional radiologists. They note that management can range from conservative approaches to open surgical repair, with minimally invasive procedures playing a crucial role.

The absence of ERCP use in our study is noteworthy. This could be due to the pediatric nature of our population, where ERCP might be technically more challenging or carry higher risks. In contrast, Zheng *et al.,*[24] found that endoscopic drainage was a protective factor for grade B/C bile leakage in their adult population.

Our use of pigtail drainage aligns with the findings of Sakamoto *et al*.,[25], who reported successful treatment of peripheral-type leakage with drainage procedures. Similarly, our conservative management approach for one patient is consistent with the observations of Wu *et al.*,[26], who found that most bile leaks (85%) could be treated conservatively with drainage, antibiotics, and nutritional support.

The need for exploration surgery in one of our patients (4.76%) highlights the potential severity of some biliary leaks. This is consistent with the findings of Kajiwara *et al.,*[27], who reported that 5 out of 81 patients (6.2%) with bile leakage required reoperation.

In our study, the hospital stay for patients undergoing liver resection ranged from 3 to 22 days, with a mean (±SD) of 11.6(±4.94) days. This duration is comparable to some reports in the literature but shorter than others, potentially reflecting differences in patient populations, surgical techniques, or postoperative management protocols.

For instance, Kajiwara *et al*.,[27] reported a median postoperative hospital stay of 14 days (range 8 to 34) for patients with bile leakage, compared to 11 days (range 5 to 62) for those without bile leakage. Our mean stay of 11.6 days falls within this range, suggesting that our postoperative management was relatively efficient, even considering the complications we encountered.

It's worth noting that our study focused on the use of the surgical glue as a hemostatic and biliostatic agent, some studies have reported positive outcomes with its use. For instance, Patrone *et al*.,[8] reported no deaths during hospitalization and 0% 30-day mortality in their group using surgical glue. However, their study population and indications for use may differ from ours.

The relatively wide range of hospital stays in our study (3 to 22 days) reflects the variability in patient recovery and the potential impact of complications. Ye *et al.,*[28] highlighted the importance of assessing the risk of post-hepatectomy liver failure, which can significantly impact hospital stay and mortality.

This study's retrospective design and small sample size limit its generalizability. The single-center nature may introduce institutional bias. Additionally, the heterogeneity of pathologies and surgical procedures may confound the results. The study's short-term focus overlooks potential long-term complications or benefits.

CONCLUSION

Surgical glue application during liver resection shows promising results to be effective hemostatic and not biliostatic agent in pediatric population that requires further investigations and larger studies to prove its effect.

CONFLICT OF INTEREST

There are no conflicts of interest.

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